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Regioselective Functionalization and Diels–Alder Cycloadditions of Exocyclic Dienes in Five-membered Heterocycles

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Abstract. An acid-catalyzed regioselective addition of diverse nucleophiles to *exo*-oxazolidin-2-one dienes was presently carried out, leading to a series of functionalized 4-oxazolin-2-ones. The direct formylation of 4-methyl-4-oxazolin-2-ones provided the corresponding 5-formyl-4-oxazolin-2-ones, which were applied in the construction of the 4,5-dihydrobenzo[*d*]oxazolones through a Staunton-Weinreb annulation process. The reactivity of symmetrical and unsymmetrical *exo*-imidazolidin-2-one dienes was studied in Diels–Alder cycloadditions with dienophiles *N*-phenylmaleimide and benzyne. The aromatization of the [4+2] adducts led to the polycyclic benzo- and naphtho[*d*]imidazol-2-ones, which have potential pharmacological activity.
Keywords: 4,5-dimethylene-2-oxazolidinone dienes; 5-functionalized 4-oxazolin-2-ones; 4,5-dimethylene-2-imidazolidinone dienes; Staunton-Weinreb annulation; Diels–Alder reaction.

Resumen. Se describe la adición regioselectiva catalizada por ácido de diversos nucleófilos a los dienos *exo*-oxazolidinonas que conduce a una serie de 4-oxazolin-2-onas funcionalizadas. La formilación directa de 4-metil-4-oxazolidin-2-onas proporcionó las 5-formil-4-oxazolin-2-onas correspondientes, las cuales se emplearon en la construcción de las 4,5-dihidrobenzo[*d*]oxazolonas mediante un proceso de anillación de Staunton-Weinreb. Se estudió la reactividad de dienos *exo*-imidazolidin-2-onas simétricos y no simétricos en cicloadiciones de Diels-Alder con los dienófilos *N*-fenilmaleimida y bencino. La aromatización de los aductos [4+2] condujo a los benzo- y nafto[*d*]imidazol-2-onas policíclicas como compuestos con actividad farmacológica potencial.
Palabras clave: Dienos 4,5-dimetilen-2-oxazolidinonas; 4-oxazolin-2-onas 5-funcionalizadas; dienos 4,5-dimetilen-2-imidazolidinonas; anillación de Staunton-Weinreb; reacción de Diels–Alder.

Introduction

Conjugated dienes constitute a seminal molecular building block due to their potential use in the construction of six-membered rings through a concerted [4+2] Diels–Alder addition [1]. Moreover, they may have an important role in the regio- and stereoselective synthesis of highly functionalized double bonds [2]. Since the Diels–Alder reaction is relevant from a theoretical [3] and synthetic viewpoint [4], a diversity of dienes has been designed and synthesized, including outer-ring *o*-carbodimethylenes [5]. There has been considerable interest in

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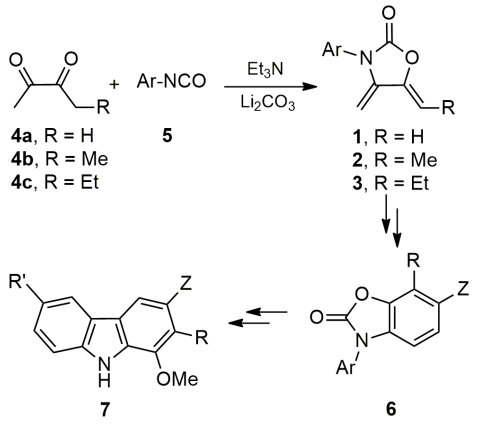
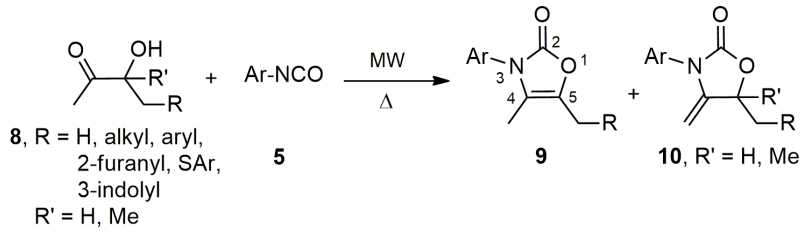
the preparation of *exo*-heterocyclic dienes for the study of their reactivity [5b,5c,6], given that their heteroatoms increase such reactivity and allow for much greater versatility in the functionalization of the cycloadducts.

Over the years, our group has described the regio- and stereoselective one-pot synthesis of novel *N*-substituted *exo*-2-oxazolidinone dienes **1**–**3** [7] via a base-assisted condensation of α-diketones **4** and isocyanates **5** (Scheme 1). This method has been adopted for the synthesis of 1,4-disubstituted exocyclic dienes [8] and heterocycle-fused *endo*-cyclohexenic dienes [9], which undergo regioselective Diels–Alder cycloadditions to monosubstituted dienophiles with electron-withdrawing groups. The corresponding adducts were useful precursors for preparing 2-(3*H*)-benzoxazolones **6** [10], which were involved in a general approach for the formation of the carbazole scaffold **7** [11], being applicable in the total synthesis of natural carbazoles [12]. Furthermore, dienes **1**-**3** have been efficient substrates for the synthesis of $Fe(CO)_3$ complexes and their conversion into conjugated enamido-enol $Fe(CO)_3$ complexes [13], or new polycyclic oxazol-2-one derivatives, in the latter case by reacting them with Fischer (arylalkynyl)(alkoxy)carbenes [14].



Scheme 1. Synthesis of *exo*-2-oxazolidinone dienes **1**–**3** and their conversion into carbazoles **7**.

A single-step and regioselective procedure was developed by our group to prepare 4-oxazolin-2-ones **9** and 4-methylidene-2-oxazolidinones **10** through a solvent-free condensation between isocyanates **5** and α-ketols **8**, carried out under conventional heating or microwave (MW)-assisted thermal conditions (Scheme 2) [15,16]. Both heterocycles served as a building block for the divergent synthesis of propellane compounds [9], α-hydroxyamides [16], aza-polycyclic compounds [17], enantiopure heterocyclic frameworks [18], natural pyridocarbazoles [19], and functionalized indoles [20].



Scheme 2. Preparation of 4-oxazolin-2-ones **9** and 4-methylidene-2-oxazolidinones **10**.

Due to the synthetic potential and versatility of 4-oxazolin-2-ones **9**, a new approach for their formation is presently explored, starting from *N*-substituted *exo*-2-oxazolidinone dienes **1** and **2** and proceeding to a Brønsted acid-promoted addition of a variety of nucleophiles to generate a series of 4-methyl-5-substituted 4-oxazolin-2-ones.

Moreover, novel *exo*-imidazolidin-2-one dienes **15** and **16** were synthesized as part of our ongoing research on the elaboration of new *exo*-heterocyclic dienes and the examination of their reactivity in Diels–Alder reactions (Scheme 3) [21,22]. Symmetrical N,N'-substituted dienes **15** were prepared through two routes.

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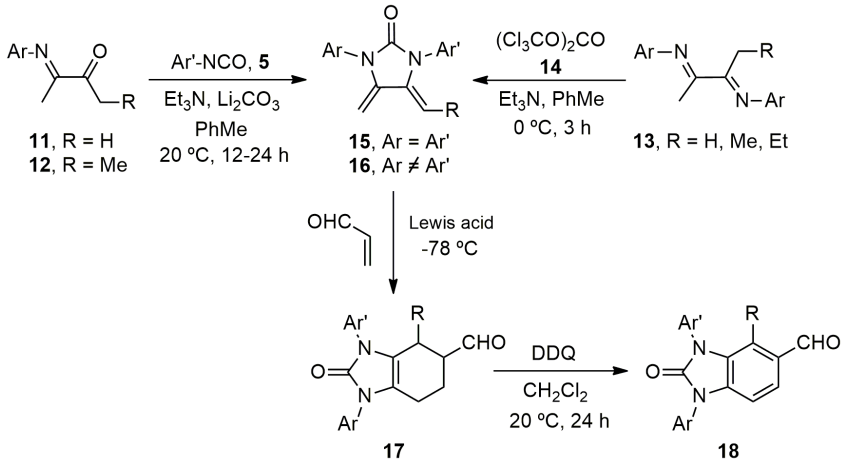
The first one was based on the reaction of α-iminoketones **11**–**12** with isocyanates **5** under basic conditions [21] and the second on a bis-condensation of α-bis-imino compounds **13** with triphosgene (**14**) [22]. The first approach was applied in the case of unsymmetrical dienes **16**, utilizing α-iminoketones **12** and isocyanates **5** substituted by different aryl rings [21]. The Diels–Alder addition of dienes **15** with symmetrical or unsymmetrical dienophiles afforded the respective adducts **17**, which underwent a subsequent aromatization to give to benzimidazol-2-ones **18** (Scheme 3) [21,22]. The processes with unsymmetrical dienes and dienophiles resulted in a mixture of regioisomers, except when catalysis was performed with a Lewis acid [22].



Scheme 3. Synthesis of *exo*-imidazolidin-2-one dienes **15** and **16** as precursors of benzimidazol-2-ones **18**.

Owing to the pharmacological value of benzimidazol-2-ones as potent antagonists of neurokinin NK_1 [23], calcitonin gene-related peptide (CGRP) [24], 5-HT_4 [25], and progesterone [26] receptors, and as anticancer agents [27], a variety of tricyclic benzo[*d*]imidazol-2-ones are herein synthesized through the Diels–Alder cycloadditions of dienes **15** and **16** with symmetrical dienophiles such as *N*-phenylmaleimide (**19**) and benzyne (**20**).

Experimental

General

Melting points were determined with a capillary Krüss KSP 1N melting point apparatus. The IR spectra were recorded on Perkin-Elmer 2000 and Smiths Detection IlluminatIR (ATR) spectrophotometers. ^{1}H (300, 500, or 600 MHz) and ^{13}C (75.4, 125, or 150 MHz) NMR spectra were recorded on Varian Mercury (300 MHz), Varian VNMR System (500 MHz), and Bruker 600AVANCE III (600 MHz) spectrometers, with TMS and $CDCl_3$ as internal standards. Assignment of the NMR signals was made by HMQC, HSQC, and HMBC 2D methods. Mass spectra (MS) were obtained in the electron impact (EI) (70 eV) mode on Thermo Polaris Q-Trace GC Ultra and Hewlett-Packard 5971A spectrometers. High-resolution mass spectra (HRMS) were captured in the ionization mode on Jeol JSM-GcMateII and Bruker MicrOTOF-Q II spectrometers. MW irradiation was generated in a CEM MW reactor. Analytical thin-layer chromatography was carried out on 0.25 plates coated with silica gel 60 F254 (E. Merck), which were visualized by a long- and short-wavelength UV lamp. Flash column chromatography was performed over silica gel (230-400 mesh, Natland International Co.). All air moisture sensitive reactions were carried out under N_2 atmosphere with oven-dried glassware. Triethylamine (TEA) was distilled on NaOH. Toluene and MeOH were freshly distilled over sodium, and DMF, DMSO, and CH_2Cl_2 over 4Å molecular sieves and then over CaH_2. Li_2CO_3 was dried overnight at 200 °C prior to use. All other reagents were employed without further purification. Compounds **1a**–**c**, **2a**–**c**, **15a**, **16a**–**b**, **16d**, and **32a**–**c** were prepared as reported [7,10,15,21,22].

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5-(Methoxymethyl)-4-methyl-3-phenyloxazol-2(3*H*)-one (22a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **1a** (0.121 g, 0.65 mmol), MeOH (1.58 g, 49.4 mmol), and HCl (38 %) (0.061 g, 0.63 mmol) were mixed under N_2 atmosphere at rt. The mixture was stirred for 1 h, dissolved in CH_2Cl_2 (10 mL), and washed in an aqueous saturated solution of $NaHCO_3$ (2 x 5 mL) and water (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 8:2) resulting in **22a** (0.131 g, 92%) as a yellow oil. R*f* 0.32 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 1759, 1598, 1505, 1380, 1191, 1096, 1045, 983, 767, 715, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.95 (s, 3H, C*H*$_3$-C4), 3.42 (s, 3H, C*H*$_3$O), 4.26 (s, 2H, C*H*$_2$OMe), 7.27–7.31 (m, 2H, H-2'), 7.37–7.43 (m, 1H, H-4'), 7.45–7.50 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 58.1 (*C*H$_3$O), 63.1 (*C*H$_2$OMe), 122.9 (C-4), 126.9 (C-2'), 128.5 (C-4'), 129.4 (C-3'), 132.5 (C-5), 133.3 (C-1'), 154.2 (C-2). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{12}H_{13}NO_3$: 219.0895; found: 219.0901.

5-(Methoxymethyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (22b). Following the method for preparing **22a**, a mixture of **1b** (0.050 g, 0.25 mmol), MeOH (1.58 g, 49.4 mmol), and HCl (38 %) (0.053 g, 0.55 mmol) generated **22b** (0.048 g, 83%) as a yellow oil. R*f* 0.21 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 2927, 1755, 1699, 1516, 1452, 1380, 1282, 1244, 1170, 1094, 1045, 985, 820, 756, 723 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.94 (br s, 3H, C*H*$_3$-C4), 2.40 (br s, 3H, C*H*$_3$Ar), 3.42 (s, 3H, C*H*$_3$O), 4.26 (br s, 2H, C*H*$_2$OMe), 7.16–7.19 (m, 2H, H-2'), 7.26–7.29 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 21.1 (*C*H$_3$Ar), 58.1 (*C*H$_3$O), 63.2 (*C*H$_2$OMe), 123.1 (C-4), 126.9 (C-2'), 130.1 (C-3'), 130.7 (C-1'), 132.4 (C-5), 138.7 (C-4'), 154.4 (C-2). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{13}H_{15}NO_3$: 233.1052; found: 233.1054.

5-(Methoxymethyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (22c). Following the method for preparing **22a**, a mixture of **1c** (0.050 g, 0.23 mmol), MeOH (1.58 g, 49.4 mmol), and HCl (38 %) (0.052 g, 0.54 mmol) gave **22c** (0.048 g, 84%) as a yellow oil. R*f* 0.13 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 2933, 1756, 1516, 1444, 1383, 1299, 1250, 1168, 1094, 1044, 984, 835, 757 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.92 (br s, 3H, C*H*$_3$-C4), 3.42 (s, 3H, C*H*$_3$O), 3.83 (s, 3H, C*H*$_3$OAr), 4.25 (br s, 2H, C*H*$_2$OMe), 6.96–6.70 (m, 2H, H-3'), 7.19–7.23 (m, 2H, H-2'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 55.6 (*C*H$_3$O), 58.2 (*C*H$_3$OAr), 63.2 (*C*H$_2$OMe), 114.8 (C-3'), 123.3 (C-4), 126.0 (C-1'), 128.5 (C-2'), 132.3 (C-5), 154.6 (C-2), 159.7 (C-4'). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{13}H_{15}NO_4$: 249.1001; found: 249.1004.

(4-Methyl-2-oxo-3-phenyl-2,3-dihydrooxazol-5-yl)methyl acetate (23a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **1a** (0.029 g, 0.16 mmol) and glacial AcOH (1.05 g, 17.5 mmol) in CH_2Cl_2 (2 mL) were mixed under N_2 atmosphere at rt and stirred for 24 h. The mixture was dissolved in CH_2Cl_2 (5 mL) and washed in an aqueous saturated solution of $NaHCO_3$ (3 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 8:2) to provide **23a** (0.037 g, 95%) as a yellow oil. R*f* 0.25 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 2928, 1765, 1743, 1598, 1505, 1380, 1365, 1220, 1047, 1022, 986, 768, 712, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.98 (br s, 3H, C*H*$_3$-C4), 2.11 (s, 3H, C*H*$_3$CO$_2$), 4.91 (br s, 2H, C*H*$_2$OAc), 7.28–7.31 (m, 2H, H-2"), 7.39–7.44 (m, 1H, H-4"), 7.45–7.50 (m, 2H, H-3"). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.9 (*C*H$_3$-C4), 20.8 (*C*H$_3$CO$_2$), 55.0 (*C*H$_2$OAc), 124.4 (C-4'), 126.9 (C-2"), 128.7 (C-4"), 129.5 (C-3"), 130.5 (C-5'), 133.1 (C-1"), 154.0 (C-2'), 170.7 (CH$_3$*C*O$_2$). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{13}H_{13}NO_4$: 247.0845; found: 247.0845.

(4-Methyl-2-oxo-3-(*p*-tolyl)-2,3-dihydrooxazol-5-yl)methyl acetate (23b). Following the method for preparing **23a**, a mixture of **1b** (0.050 g, 0.25 mmol) and glacial AcOH (1.05 g, 17.5 mmol) in CH_2Cl_2 (4 mL) afforded **23b** (0.053 g, 81 %) as a yellow oil. R*f* 0.28 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 1770, 1744, 1519, 1398, 1364, 1220, 1046, 1022, 988, 820, 756 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.97 (br s, 3H, C*H*$_3$-C4), 2.11 (s, 3H, C*H*$_3$CO$_2$), 2.39 (br s, 3H, C*H*$_3$Ar), 4.91 (br s, 2H, C*H*$_2$OAc), 7.15–7.19 (m, 2H, H-2"), 7.25–7.30 (m, 2H, H-3"). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.9 (*C*H$_3$-C4), 20.8 (*C*H$_3$CO$_2$), 21.1 (*C*H$_3$Ar), 55.1 (*C*H$_2$OAc), 124.6 (C-4'), 126.8 (C-2"), 130.2 (C-3"), 130.4 (C-5'), 130.5 (C-1"), 138.9 (C-4"), 154.2 (C-2'), 170.7 (CH$_3$*C*O$_2$). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{14}H_{15}NO_4$: 261.1001; found: 261.1000.

(3-(4-Methoxyphenyl)-4-methyl-2-oxo-2,3-dihydrooxazol-5-yl)methyl acetate (23c). Following the method for preparing **23a**, a mixture of **1c** (0.050 g, 0.23 mmol) and glacial AcOH (1.05 g, 17.5 mmol) in CH_2Cl_2 (4 mL) furnished **23c** (0.037 g, 59 %) as a yellow oil. R*f* 0.13 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 2937, 1766, 1744, 1516,

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1443, 1398, 1365, 1300, 1249, 1221, 1169, 1046, 1025, 987, 837, 757 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.95 (br s, 3H, C*H*$_3$-C4), 2.11 (s, 3H, C*H*$_3$CO$_2$), 3.84 (s, 3H, C*H*$_3$OAr), 4.91 (br s, 2H, C*H*$_2$OAc), 6.96–7.00 (m, 2H, H-3"), 7.18–7.22 (m, 2H, H-2"). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 20.8 (*C*H$_3$CO$_2$), 55.1 (*C*H$_2$OAc), 55.5 (*C*H$_3$OAr), 114.8 (C-3"), 124.7 (C-4'), 125.8 (C-1"), 128.4 (C-2"), 130.3 (C-5'), 154.4 (C-2'), 159.7 (C-4"), 170.7 (CH$_3$*C*O$_2$). HRMS (EI, [M^+]): *m/z* calcd for $C_{14}H_{15}NO_5$: 277.0950; found: 277.0949.

5-(((4-Chlorophenyl)thio)methyl)-4-methyl-3-phenyloxazol-2(3*H*)-one (24a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **1a** (0.06 g, 0.32 mmol), **21c** (0.089 g, 0.62 mmol), and H_3PO_4 (85 %) (0.036 g, 0.31 mmol) in CH_2Cl_2 (5 mL) were mixed under N_2 atmosphere at rt and stirred for 24 h. The mixture was dissolved in CH_2Cl_2 (10 mL) and washed in an aqueous saturated solution of $NaHCO_3$ (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 85:15) to obtain **24a** (0.063 g, 60%) as a yellow solid. R*f* 0.38 (hexane/EtOAc, 7:3); mp 106–108 °C. IR (film): $\bar{\upsilon}$ = 1756, 1698, 1597, 1504, 1476, 1382, 1272, 1186, 1095, 1040, 1012, 981, 819, 766, 709, 604 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.59 (br s, 3H, C*H*$_3$-C4), 3.85 (br s, 2H, C*H*$_2$S), 7.19–7.22 (m, 2H, H-2'), 7.28–7.32 (m, 2H, H-3"), 7.37–7.42 (m, 3H, H-4', H-2"), 7.44–7.49 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.6 (*C*H$_3$-C4), 30.2 (*C*H$_2$S), 121.3 (C-4), 126.9 (C-2'), 128.6 (C-4'), 129.2 (C-3"), 129.5 (C-3'), 131.2 (C-5), 132.8 (C-1"), 133.3 (C-1'), 134.2 (C-4"), 134.3 (C-2"), 154.0 (C-2). HRMS (ESI, [M + H]$^+$): *m/z* calcd for $C_{17}H_{15}ClNO_2S$: 332.0512; found: 332.0465.

5-(((4-Chlorophenyl)thio)methyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (24b). Following the method for preparing **24a**, a mixture of **1b** (0.040 g, 0.20 mmol), **21c** (0.056 g, 0.39 mmol), and H_3PO_4 (85 %) (0.028 g, 0.24 mmol) in CH_2Cl_2 (5 mL) yielded **24b** (0.052 g, 75%) as a yellow solid. R*f* 0.44 (hexane/EtOAc, 7:3); mp 103–104 °C. IR (KBr): $\bar{\upsilon}$ = 1751, 1694, 1516, 1478, 1387, 1270, 1191, 1092, 1039, 1011, 988, 817, 755 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 1.57 (br s, 3H, C*H*$_3$-C4), 2.38 (br s, 3H, C*H*$_3$Ar), 3.85 (br s, 2H, C*H*$_2$S), 7.07–7.10 (m, 2H, H-2'), 7.24–7.27 (m, 2H, H-3'), 7.28–7.31 (m, 2H, H-3"), 7.38–7.41 (m, 2H, H-2"). ^{13}C NMR (150 MHz, $CDCl_3$): δ 8.5 (*C*H$_3$-C4), 21.1 (*C*H$_3$Ar), 30.2 (*C*H$_2$S), 121.4 (C-4), 126.7 (C-2'), 129.1 (C-3"), 130.1 (C-3'), 130.6 (C-1'), 130.9 (C-5), 132.8 (C-1"), 134.1 (C-4"), 134.3 (C-2"), 138.7 (C-4'), 154.1 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{18}H_{16}ClNO_2S$: 345.0590; found: 345.0589.

5-(((4-Chlorophenyl)thio)methyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (24c). Following the method for preparing **24a**, a mixture of **1c** (0.040 g, 0.18 mmol), **21c** (0.054 g, 0.37 mmol), and H_3PO_4 (85 %) (0.029 g, 0.25 mmol) in CH_2Cl_2 (3 mL) generated **24c** (0.049 g, 74%) as a yellow solid. R*f* 0.38 (hexane/EtOAc, 7:3); mp 84–86 °C. IR (film): $\bar{\upsilon}$ = 2930, 1759, 1698, 1515, 1476, 1387, 1300, 1251, 1169, 1095, 1036, 1012, 983, 832, 755 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.55 (br s, 3H, C*H*$_3$-C4), 3.82 (s, 3H, C*H*$_3$O), 3.84 (br s, 2H, C*H*$_2$S), 6.94–6.98 (m, 2H, H-3'), 7.10–7.14 (m, 2H, H-2'), 7.28–7.31 (m, 2H, H-3"), 7.37–7.41 (m, 2H, H-2"). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.5 (*C*H$_3$-C4), 30.2 (*C*H$_2$S), 55.5 (*C*H$_3$O), 114.8 (C-3'), 121.6 (C-4), 125.9 (C-1'), 128.3 (C-2'), 129.1 (C-3"), 130.8 (C-5), 132.9 (C-1"), 134.1 (C-4"), 134.3 (C-2"), 154.3 (C-2), 159.6 (C-4'). HRMS (EI, [M^+]): *m/z* calcd for $C_{18}H_{16}ClNO_3S$: 361.0539; found: 361.0535.

5-(4-Hydroxybenzyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (25a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **1a** (0.06 g, 0.32 mmol), **21d** (0.06 g, 0.64 mmol), and H_3PO_4 (85 %) (0.062 g, 0.54 mmol) in CH_2Cl_2 (5 mL) were mixed under N_2 atmosphere at rt and stirred for 24 h. The mixture was dissolved in CH_2Cl_2 (10 mL) and washed in an aqueous saturated solution of $NaHCO_3$ (2 x 5 mL) and EtOAc (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 7:3), resulting in **25a** (0.058 g, 64 %) as a yellow oil. R*f* 0.21 (hexane/EtOAc, 7:3). IR (film): $\bar{\upsilon}$ = 3328, 1737, 1699, 1614, 1597, 1515, 1504, 1388, 1265, 1227, 1171, 1044, 986, 833, 766, 695 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 1.86 (br s, 3H, C*H*$_3$-C4), 3.67 (br s, 2H, C*H*$_2$Ar), 6.77–6.79 (m, 2H, H-3"), 7.03–7.07 (m, 2H, H-2"), 7.26–7.28 (m, 2H, H-2'), 7.35–7.38 (m, 1H, H-4'), 7.42–7.46 (m, 2H, H-3'). ^{13}C NMR (150 MHz, $CDCl_3$): δ 8.7 (*C*H$_3$-C4), 30.0 (*C*H$_2$Ar), 115.6 (C-3"), 118.5 (C-4), 126.9 (C-2'), 127.6 (C-1"), 128.5 (C-4'), 129.39 (C-2"), 129.43 (C-3'), 133.3 (C-1'), 135.6 (C-5), 155.0 (C-2), 155.5 (C-4"). HRMS (ESI, [M + H]$^+$): *m/z* calcd for $C_{17}H_{15}NO_3$: 282.1130; found: 282.1072.

5-(4-Hydroxybenzyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (25b). Following the method for preparing **25a**, a mixture of **1b** (0.080 g, 0.40 mmol), **21d** (0.075 g, 0.80 mmol), and H_3PO_4 (85 %) (0.077 g, 0.67 mmol) in CH_2Cl_2

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(5 mL) gave **25b** (0.081 g, 69 %) as a yellow solid. R*f* 0.21 (hexane/EtOAc, 7:3); mp 218–220 °C. IR (KBr): $\bar{\upsilon}$ = 3256, 1733, 1695, 1614, 1515, 1452, 1393, 1276, 1261, 1234, 1173, 994, 825, 758 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.88 (br s, 3H, C*H*$_3$-C4), 2.38 (br s, 3H, C*H*$_3$Ar), 3.69 (s, 2H, C*H*$_2$Ar), 5.81 (br, 1H, OH), 6.80–6.83 (m, 2H, H-3"), 7.11–7.14 (m, 2H, H-2"), 7.16–7.19 (m, 2H, H-2'), 7.24–7.26 (m, 2H, H-3'). ^{13}C NMR (150 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 21.1 (*C*H$_3$Ar), 30.1 (*C*H$_2$Ar), 115.6 (C-3"), 118.6 (C-4), 126.8 (C-2'), 128.4 (C-1"), 129.6 (C-2"), 130.1 (C-3'), 130.9 (C-1'), 135.1 (C-5), 138.6 (C-4'), 154.9 (C-2 or C-4"), 155.0 (C-4" or C-2). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{18}H_{17}NO_3$: 295.1208; found: 295.1218.

5-(4-Hydroxybenzyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (25c). Following the method for preparing **25a**, a mixture of **1c** (0.065 g, 0.3 mmol), **21d** (0.056 g, 0.6 mmol), and H_3PO_4 (85 %) (0.058 g, 0.5 mmol) in CH_2Cl_2 (5 mL) provided **25c** (0.079 g, 85 %) as a yellow solid. R*f* 0.12 (hexane/EtOAc, 7:3); mp 194–195 °C. IR (KBr): $\bar{\upsilon}$ = 3359, 1751, 1702, 1611, 1596, 1515, 1444, 1401, 1300, 1247, 1227, 1168, 1028, 989, 833, 757, 683 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.84 (br s, 3H, C*H*$_3$-C4), 3.69 (br s, 2H, C*H*$_2$Ar), 3.83 (s, 3H, C*H*$_3$O), 6.81–6.84 (m, 2H, H-3"), 6.94–6.98 (m, 2H, H-3'), 7.09–7.13 (m, 2H, H-2"), 7.18–7.22 (m, 2H, H-2'), 7.36 (br, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.5 (*C*H$_3$-C4), 30.0 (*C*H$_2$Ar), 55.4 (*C*H$_3$O), 114.6 (C-3'), 115.5 (C-3"), 118.5 (C-4), 126.2 (C-1'), 127.8 (C-1"), 128.3 (C-2'), 129.4 (C-2"), 134.8 (C-5), 154.8 (C-2), 155.5 (C-4"), 159.3 (C-4'). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{18}H_{17}NO_4$: 311.1158; found: 311.1154.

5-(1-Methoxyethyl)-4-methyl-3-phenyloxazol-2(3*H*)-one (26a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **2a** (0.060 g, 0.30 mmol), **21a** (2.37 g, 74.0 mmol), and HCl (38 %) (0.062 g, 0.65 mmol) were mixed and stirred under N_2 atmosphere at -10 ºC for 24 h. The mixture was dissolved in CH_2Cl_2 (5 mL) and washed in an aqueous saturated solution of $NaHCO_3$ (2 x 5 mL) and EtOAc (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 75:25), leading to **26a** (0.046 g, 67%) as a yellow solid. R*f* 0.31 (hexane/EtOAc, 7:3); mp 100–102 °C. IR (KBr): $\bar{\upsilon}$ = 3054, 2987, 2936, 1746, 1693, 1598, 1504, 1396, 1259, 1116, 1090, 991, 767, 752, 712 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.51 (d, *J* = 6.5 Hz, 3H, H-2"), 1.96 (s, 3H, C*H*$_3$-C4), 3.31 (s, 3H, C*H*$_3$O), 4.25 (q, *J* = 6.5 Hz, 1H, H-1"), 7.30–7.33 (m, 2H, H-2'), 7.39–7.43 (m, 1H, H-4'), 7.46–7.51 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 18.7 (C-2"), 55.9 (*C*H$_3$O), 69.4 (C-1"), 121.1 (C-4), 127.0 (C-2'), 128.5 (C-4'), 129.5 (C-3'), 133.3 (C-1'), 134.5 (C-5), 154.3 (C-2). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{13}H_{15}NO_3$: 233.1052; found: 233.1046.

5-(1-Methoxyethyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (26b). Following the method for preparing **26a**, a mixture of **2b** (0.060 g, 0.28 mmol), **21a** (2.38 g, 74.4 mmol), and HCl (38 %) (0.068 g, 0.71 mmol) produced **26b** (0.047 g, 69 %) as a yellow solid. R*f* 0.26 (hexane/EtOAc, 7:3); mp 84–86 °C. IR (film): $\bar{\upsilon}$ = 2986, 2931, 1760, 1698, 1519, 1450, 1398, 1387, 1351, 1258, 1117, 1088, 994, 981, 821, 757, 723 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.50 (d, *J* = 6.5 Hz, 3H, H-2"), 1.94 (s, 3H, C*H*$_3$-C4), 2.39 (br s, 3H, C*H*$_3$Ar), 3.31 (s, 3H, C*H*$_3$O), 4.24 (q, *J* = 6.5 Hz, 1H, H-1"), 7.17–7.21 (m, 2H, H-2'), 7.25–7.30 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.7 (*C*H$_3$-C4), 18.7 (C-2"), 21.1 (*C*H$_3$Ar), 55.9 (*C*H$_3$O), 69.5 (C-1"), 121.3 (C-4), 126.9 (C-2'), 130.1 (C-3'), 130.7 (C-1'), 134.3 (C-5) 138.6 (C-4'), 154.4 (C-2). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{14}H_{17}NO_3$: 247.1208; found: 247.1215.

5-(1-Methoxyethyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (26c). (*Z*)-5-Ethylidene-4-methoxy-3-(4-methoxyphenyl)-4-methyloxazolidin-2-one (26c'). Following the method for preparing **26a**, a mixture of **2c** (0.060 g, 0.26 mmol), **21a** (2.38 g, 74.4 mmol), and HCl (38 %) (0.063 g, 0.66 mmol) afforded **26c** (0.05 g, 73 %) and **26c'** (0.01 g, 15%) as yellow solids. Data for **26c**: R*f* 0.21 (hexane/EtOAc, 7:3); mp 88–90 °C. IR (film): $\bar{\upsilon}$ = 2985, 2936, 1759, 1698, 1610, 1517, 1444, 1399, 1351, 1301, 1252, 1168, 1117, 1088, 1033, 981, 836, 758 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.50 (d, *J* = 6.5 Hz, 3H, H-2"), 1.93 (s, 3H, C*H*$_3$-C4), 3.31 (s, 3H, C*H*$_3$O), 3.84 (s, 3H, C*H*$_3$OAr), 4.24 (q, *J* = 6.5 Hz, 1H, H-1"), 6.96–7.00 (m, 2H, H-3'), 7.20–7.24 (m, 2H, H-2'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.7 (*C*H$_3$-C4), 18.8 (C-2"), 55.5 (*C*H$_3$OAr), 55.9 (*C*H$_3$O), 69.5 (C-1"), 114.8 (C-3'), 121.4 (C-4), 125.9 (C-1'), 128.5 (C-2'), 134.2 (C-5), 154.6 (C-2), 159.6 (C-4'). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{14}H_{17}NO_4$: 263.1158; found 263.1158. Data for **26c'**: R*f* 0.57 (hexane/EtOAc, 7:3); mp 58–60 °C. IR (film): $\bar{\upsilon}$ = 2938, 1785, 1713, 1515, 1376, 1298, 1250, 1169, 1120, 1065, 1035, 833 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.47 (s, 3H, C*H*$_3$-C4), 1.82 (d, *J* = 6.9 Hz, 3H, C*H*$_3$CH=), 3.29 (s, 3H, C*H*$_3$O), 3.82 (s, 3H, C*H*$_3$OAr), 5.03 (q, *J* = 6.9 Hz, 1H, CH$_3$C*H*=), 6.92–6.96 (m, 2H, H-3'), 7.27–7.31 (m, 2H, H-2'). ^{13}C NMR (150 MHz, $CDCl_3$)**:** δ 10.0 (*C*H$_3$CH=), 24.8 (*C*H$_3$-C4),

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50.1 (*C*H_3O), 55.5 (*C*H_3OAr), 92.2 (C-4), 100.6 (CH_3*C*H=), 114.5 (C-3'), 126.6 (C-1'), 127.1 (C-2'), 146.7 (C-5), 153.2 (C-2), 158.7 (C-4'). HRMS (EI, [M^+]): *m/z* calcd for $C_{14}H_{17}NO_4$: 263.1158; found: 263.1159.

5-(1-((4-Chlorophenyl)thio)ethyl)-4-methyl-3-phenyloxazol-2(3*H*)-one (27a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **2a** (0.050 g, 0.25 mmol), **21c** (0.069 g, 0.48 mmol), and H_3PO_4 (85 %) (0.034 g, 0.30 mmol) in CH_2Cl_2 (5 mL) were mixed under N_2 atmosphere at rt and stirred for 24 h. The mixture was dissolved in CH_2Cl_2 (10 mL) and washed in an aqueous saturated solution of $NaHCO_3$ (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 9:1) to furnish **27a** (0.051 g, 60%) as a yellow solid. R*f* 0.50 (hexane/EtOAc, 7:3); mp 128–129 °C. IR (film): $\bar{\upsilon}$ = 2979, 2930, 1760, 1694, 1598, 1504, 1475, 1395, 1384, 1261, 1167, 1094, 1013, 981, 824, 768, 709, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41 (s, 3H, C*H*$_3$-C4), 1.63 (d, *J* = 7.1 Hz, 3H, H-2"), 4.14 (q, *J* = 7.1 Hz, 1H, H-1"), 7.14–7.17 (m, 2H, H-2'), 7.28–7.31 (m, 2H, H-3'"), 7.37–7.41 (m, 3H, H-4', H-2'"), 7.43–7.48 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.4 (*C*H_3-C4), 18.1 (C-2"), 40.0 (C-1"), 120.2 (C-4), 126.9 (C-2'), 128.6 (C-4'), 129.0 (C-3'"), 129.5 (C-3'), 132.4 (C-1'"), 133.3 (C-1'), 134.3 (C-5), 135.0 (C-4'"), 136.6 (C-2'"), 154.0 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{18}H_{16}ClNO_2S$: 345.0590; found: 345.0580.

5-(1-((4-Chlorophenyl)thio)ethyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (27b). Following the method for preparing **27a**, a mixture of **2b** (0.050 g, 0.23 mmol), **21c** (0.067 g, 0.46 mmol), and H_3PO_4 (85 %) (0.032 g, 0.28 mmol) in CH_2Cl_2 (5 mL) yielded **27b** (0.053 g, 64 %) as a yellow solid. R*f* 0.51 (hexane/EtOAc, 7:3); mp 109–111 °C. IR (film): $\bar{\upsilon}$ = 2979, 2928, 1756, 1694, 1572, 1518, 1475, 1396, 1386, 1262, 1168, 1095, 1013, 984, 820, 754 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.38 (s, 3H, C*H*$_3$-C4), 1.62 (d, *J* = 7.0 Hz, 3H, H-2"), 2.37 (s, 3H, C*H*$_3$Ar), 4.13 (q, *J* = 7.0 Hz, 1H, H-1"), 7.00–7.05 (m, 2H, H-2'), 7.23–7.27 (m, 2H, H-3'), 7.28–7.31 (m, 2H, H-3'"), 7.35–7.40 (m, 2H, H-2'"). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.4 (*C*H_3-C4), 18.1 (C-2"), 21.1 (*C*H_3Ar), 40.0 (C-1"), 120.3 (C-4), 126.8 (C-2'), 129.0 (C-3'"), 130.1 (C-3'), 130.6 (C-1'), 132.4 (C-1'"), 134.1 (C-5), 135.0 (C-4'"), 136.6 (C-2'"), 138.7 (C-4'), 154.2 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{19}H_{18}NO_2SCl$: 359.0747; found: 359.0741.

5-(1-((4-Chlorophenyl)thio)ethyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (27c). Following the method for preparing **27a**, a mixture **2c** (0.060 g, 0.26 mmol), **21c** (0.075 g, 0.52 mmol), and H_3PO_4 (85 %) (0.036 g, 0.31 mmol) in CH_2Cl_2 (5 mL) provided **27c** (0.06 g, 62 %) as a yellow solid. R*f* 0.37 (hexane/EtOAc, 7:3); mp 117–119 °C. IR (film): $\bar{\upsilon}$ = 2931, 1754, 1694, 1516, 1475, 1397, 1388, 1301, 1251, 1165, 1095, 1032, 1013, 983, 832 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.37 (s, 3H, C*H*$_3$-C4), 1.63 (d, *J* = 7.0 Hz, 3H, H-2"), 3.82 (s, 3H, C*H*$_3$O), 4.13 (q, *J* = 7.0 Hz, 1H, H-1"), 6.93–6.98 (m, 2H, H-3'), 7.04–7.08 (m, 2H, H-2'), 7.27–7.32 (m, 2H, H-3'"), 7.36–7.40 (m, 2H, H-2'"). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.3 (*C*H_3-C4), 18.1 (C-2"), 40.0 (C-1"), 55.5 (*C*H_3O), 114.8 (C-3'), 120.5 (C-4), 125.8 (C-1'), 128.3 (C-2'), 129.0 (C-3'"), 132.5 (C-1'"), 134.0 (C-5), 135.0 (C-4'"), 136.6 (C-2'"), 154.3 (C-2), 159.6 (C-4'). HRMS (EI, [M^+]): *m/z* calcd for $C_{19}H_{18}NO_3ClS$: 375.0696; found: 375.0690.

5-(1-(4-Hydroxyphenyl)ethyl)-4-methyl-3-phenyloxazol-2(3*H*)-one (28a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **2a** (0.06 g, 0.30 mmol), **21d** (0.052 g, 0.55 mmol), and H_3PO_4 (85 %) (0.086 g, 0.75 mmol) in CH_2Cl_2 (3 mL) were mixed under N_2 atmosphere at rt and stirred for 24 h. The mixture was dissolved in CH_2Cl_2 (5 mL) and washed in an aqueous saturated solution of $NaHCO_3$ (2 x 5 mL) and EtOAc (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 7:3), resulting in **28a** (0.053 g, 60%) as a yellow solid. R*f* 0.33 (hexane/EtOAc, 7:3); mp 168–170 °C. IR (KBr): $\bar{\upsilon}$ = 3398, 2979, 2930, 1732, 1689, 1610, 1594, 1515, 1504, 1389, 1263, 1224, 1174, 1057, 987, 839, 773, 761, 710, 694 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.58 (d, *J* = 7.5 Hz, 3H, H-2"), 1.83 (br s, 3H, C*H*$_3$-C4), 3.91 (q, *J* = 7.5 Hz, 1H, H-1"), 6.81–6.84 (m, 2H, H-3'"), 7.17–7.22 (m, 2H, H-2'"), 7.26–7.30 (m, 2H, H-2'), 7.36–7.40 (m, 1H, H-4'), 7.42–7.47 (m, 2H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H_3-C4), 19.9 (C-2"), 35.4 (C-1"), 115.6 (C-3'"), 117.1 (C-4), 127.1 (C-2'), 128.3 (C-2'"), 128.4 (C-4'), 129.5 (C-3'), 133.5 (C-1'), 134.2 (C-1'"), 138.9 (C-5), 154.8 (C-2), 155.0 (C-4'"). HRMS (EI, [M^+]): *m/z* calcd for $C_{18}H_{17}NO_3$: 295.1208; found: 295.1199.

5-(1-(4-Hydroxyphenyl)ethyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (28b). Following the method for preparing **28a**, a mixture of **2b** (0.060 g, 0.28 mmol), **21d** (0.047 g, 0.50 mmol), and H_3PO_4 (85 %) (0.081 g, 0.7 mmol) in CH_2Cl_2 (5 mL) gave **28b** (0.058 g, 67 %) as a yellow solid. R*f* 0.31 (hexane/EtOAc, 7:3); mp 197–199 °C.

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IR (KBr): $\tilde{\upsilon}$ = 3282, 2980, 1731, 1692, 1614, 1516, 1448, 1393, 1259, 1231, 1173, 835, 756 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 1.57 (d, *J* = 7.2 Hz, 3H, H-2”), 1.81 (br s, 3H, C*H*$_3$-C4), 2.37 (s, 3H, C*H*$_3$Ar), 3.90 (q, *J* = 7.2 Hz, 1H, H-1”), 6.55 (br, 1H, OH), 6.81–6.84 (m, 2H, H-3’”), 7.13–7.16 (m, 2H, H-2’), 7.17–7.20 (m, 2H, H-2’”), 7.23–7.26 (m, 2H, H-3’). ^{13}C NMR (150 MHz, $CDCl_3$): δ 8.7 (*C*H$_3$-C4), 19.9 (C-2”), 21.1 (*C*H$_3$Ar), 35.3 (C-1”), 115.6 (C-3’”), 117.3 (C-4), 126.9 (C-2’), 128.2 (C-2’”), 130.1 (C-3’), 130.8 (C-1’), 134.0 (C-1’”), 138.6 (C-4’), 138.9 (C-5), 155.1 (C-2), 155.3 (C-4’”). HRMS (EI, [M^+]): *m/z* calcd for $C_{19}H_{19}NO_3$: 309.1365; found: 309.1366.

5-(1-(4-Hydroxyphenyl)ethyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (28c). Following the method for preparing **28a**, a mixture of **2c** (0.07 g, 0.3 mmol), **21d** (0.048 g, 0.51 mmol), and H_3PO_4 (85 %) (0.086 g, 0.75 mmol) in CH_2Cl_2 (3 mL) led to **28c** (0.063 g, 64 %) as a yellow solid. R*f* 0.15 (hexane/EtOAc, 7:3); mp 179–180 °C. IR (KBr): $\tilde{\upsilon}$ = 3318, 2972, 1732, 1690, 1611, 1516, 1442, 1393, 1305, 1255, 1228, 1169, 1035, 992, 834 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.58 (d, *J* = 7.3 Hz, 3H, H-2”), 1.79 (s, 3H, C*H*$_3$-C4), 3.82 (s, 3H, C*H*$_3$O), 3.90 (q, *J* = 7.3 Hz, 1H, H-1”), 6.22 (br, 1H, OH), 6.80–6.84 (m, 2H, H-3’”), 6.93–6.97 (m, 2H, H-3’), 7.16–7.21 (m, 4H, H-2’, H-2’”). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.7 (*C*H$_3$-C4), 19.9 (C-2”), 35.4 (C-1”), 55.5 (C*H*$_3$O), 114.7 (C-3’), 115.6 (C-3’”), 117.4 (C-4), 126.1 (C-1’), 128.2 (C-2’”), 128.5 (C-2’), 134.2 (C-1’”), 138.7 (C-5), 155.1 (C-4’”), 155.2 (C-2), 159.5 (C-4’) HRMS (EI, [M^+]): *m/z* calcd for $C_{19}H_{19}NO_4$: 325.1314; found: 325.1308.

5-(Hydroxymethyl)-4-methyl-3-phenyloxazol-2(3*H*)-one (29a). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **23a** (0.150 g, 0.60 mmol) and NaOH (0.036 g, 0.90 mmol) in MeOH/H_2O (8:2) (12 mL) were mixed at rt and stirred for 30 min. The mixture was neutralized with AcOH (1.0 M) and extracted with EtOAc (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 6:4) to produce **29a** (0.11 g, 90 %) as a yellow solid. R*f* 0.05 (hexane/EtOAc, 7:3); mp 126–128 °C. IR (film): $\tilde{\upsilon}$ = 3404, 1756, 1698, 1597, 1504, 1398, 1385, 1277, 1215, 1185, 1047, 1003, 767, 712, 696 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 1.94 (br s, 3H, C*H*$_3$-C4), 2.77 (br, 1H, OH), 4.45 (br d, *J* = 4.8 Hz, 2H, C*H*$_2$OH), 7.29–7.32 (m, 2H, H-2’), 7.40–7.43 (m, 1H, H-4’), 7.46–7.50 (m, 2H, H-3’). ^{13}C NMR (150 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 54.0 (*C*H$_2$OH), 121.6 (C-4), 127.1 (C-2’), 128.7 (C-4’), 129.6 (C-3’), 133.4 (C-1’), 134.9 (C-5), 154.5 (C-2). HRMS (ESI, [M + H]$^+$): *m/z* calcd for $C_{11}H_{12}NO_3$: 206.0817; found: 206.0769.

5-(Hydroxymethyl)-4-methyl-3-(*p*-tolyl)oxazol-2(3*H*)-one (29b). Following the method for preparing **29a**, a mixture of **23b** (0.25 g, 0.96 mmol) and NaOH (0.057 g, 1.43 mmol) in MeOH/H_2O (8:2) (18 mL) furnished **29b** (0.19 g, 91 %) as a yellow solid. R*f* 0.058 (hexane/EtOAc, 7:3); mp 128–131 °C. IR (film): $\tilde{\upsilon}$ = 3411, 2926, 1760, 1740, 1702, 1518, 1398, 1386, 1277, 1213, 1048, 991, 820, 757 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.92 (br s, 3H, C*H*$_3$-C4), 2.39 (br s, 3H, C*H*$_3$Ar), 2.64 (br, 1H, OH), 4.45 (br s, 2H, C*H*$_2$OH), 7.15–7.19 (m, 2H, H-2’), 7.26–7.29 (m, 2H, H-3’). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 21.1 (*C*H$_3$Ar), 54.0 (*C*H$_2$OH), 121.7 (C-4), 126.9 (C-2’), 130.2 (C-3’), 130.7 (C-1’), 134.6 (C-5), 138.8 (C-4’), 154.6 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{12}H_{13}NO_3$: 219.0895; found: 219.0897.

5-(Hydroxymethyl)-3-(4-methoxyphenyl)-4-methyloxazol-2(3*H*)-one (29c). Following the method for preparing **29a**, a mixture of **23c** (0.04 g, 0.14 mmol) and NaOH (0.009 g, 0.22 mmol) in MeOH/H_2O (8:2) (6 mL) afforded **29c** (0.03 g, 87 %) as a yellow solid. R*f* 0.034 (hexane/EtOAc, 7:3); mp 162–164 °C. IR (film): $\tilde{\upsilon}$ = 3413, 2929, 1738, 1698, 1516, 1398, 1249, 1170, 1030, 990, 841, 757 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.92 (br s, 3H, C*H*$_3$-C4), 2.00 (br, 1H, OH), 3.84 (s, 3H, C*H*$_3$O), 4.47 (br s, 2H, C*H*$_2$OH), 6.97–7.00 (m, 2H, H-3’), 7.19–7.22 (m, 2H, H-2’). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.8 (*C*H$_3$-C4), 54.3 (*C*H$_2$OH), 55.6 (*C*H$_3$O), 114.9 (C-3’), 122.0 (C-4), 126.0 (C-1’), 128.5 (C-2’), 134.2 (C-5), 154.6 (C-2), 159.7 (C-4’). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{13}NO_4$: 235.0845; found: 235.0850.

4-Methyl-2-oxo-3-phenyl-2,3-dihydrooxazole-5-carbaldehyde (30a). Method A: In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, **29a** (0.110 g, 0.54 mmol) and IBX (0.760 g, 2.70 mmol) in DMSO (20 mL) were mixed at rt and stirred for 24 h. The mixture was washed with water (2 x 5 mL) and extracted with EtOAc (2 x 5 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 8:2) to provide **30a** (0.07 g, 64 %) as a brown solid. **Method B:** In a round-bottom flask (50 mL) equipped with a magnetic stirring bar, a mixture of DMF (0.042 g, 0.57 mmol) and $POCl_3$ (0.097 g, 0.63 mmol) under N_2 atmosphere at 0 ºC was

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stirred for 30 min. Subsequently, **32a** (0.100 g, 0.46 mmol) dissolved in CH_2Cl_2 (3 mL) was added dropwise and the mixture was stirred at rt for 24 h. The mixture was neutralized with a 5% aqueous solution of NaOH at 0 ºC and extracted with CH_2Cl_2 (4 x 10 mL). The organic layer was dried with Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (40 g/g crude, hexane/EtOAc, 8:2) to yield **30a** (0.03 g, 51%) as a brown solid. R*f* 0.18 (hexane/EtOAc, 7:3); mp 154–155 °C. IR (film): $\bar{\upsilon}$ = 1776, 1723, 1667, 1499, 1401, 1332, 1270, 1056, 729 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6): δ 2.26 (s, 3H, CH_3-C4), 7.52–7.56 (m, 3H, H-2', H-4'), 7.57–7.60 (m, 2H, H-3'), 9.58 (s, 1H, C*H*O). ^{13}C NMR (150 MHz, DMSO-d_6): δ 8.9 (*C*H_3-C4), 127.6 (C-2'), 129.5 (C-4'), 129.6 (C-3'), 132.0 (C-1'), 134.3 (C-5), 141.4 (C-4), 152.0 (C-2), 175.1 (*C*HO). HRMS (ESI, $[M + H]^+$): *m/z* calcd for $C_{11}H_{10}NO_3$: 204.0661; found: 204.0626.

4-Methyl-2-oxo-3-(*p*-tolyl)-2,3-dihydrooxazole-5-carbaldehyde (30b). Method A: Following method A for preparing **30a**, a mixture of **29b** (0.100 g, 0.46 mmol) and IBX (0.638 g, 2.28 mmol) in DMSO (10 mL) resulted in **30b** (0.074 g, 75 %) as a brown solid. **Method B:** Following method B for preparing **30a**, a mixture of DMF (0.039 g, 0.53 mmol), $POCl_3$ (0.088 g, 0.57 mmol), and **32b** (0.050 g, 0.26 mmol) led to **30b** (0.028 g, 48 %) as a brown solid. R*f* 0.21 (hexane/EtOAc, 7:3); mp 141–142 °C. IR (film): $\bar{\upsilon}$ = 2925, 1773, 1668, 1516, 1408, 1337, 1271, 1062, 990, 741 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 2.24 (s, 3H, CH_3-C4), 2.38 (s, 3H, CH_3Ar), 7.35–7.38 (m, 2H, H-3'), 7.39–7.42 (m, 2H, H-2'), 9.57 (s, 1H, C*H*O). ^{13}C NMR (125 MHz, DMSO-d_6): δ 8.9 (*C*H_3-C4), 20.7 (*C*H_3Ar), 127.4 (C-2'), 129.4 (C-1'), 130.0 (C-3'), 134.2 (C-5), 139.3 (C-4'), 141.6 (C-4), 152.1 (C-2), 175.0 (*C*HO). HRMS (EI, $[M^+]$) *m/z* calcd for $C_{12}H_{11}NO_3$: 217.0739; found: 217.0736.

3-(4-methoxyphenyl)-4-methyl-2-oxo-2,3-dihydrooxazole-5-carbaldehyde (30c). Method A: Following method A for preparing **30a**, a mixture of **29c** (0.30 g, 1.3 mmol) and IBX (1.76 g, 6.3 mmol) in DMSO (20 mL) gave **30c** (0.205 g, 69 %) as a brown solid. **Method B:** Following method B for preparing **30a**, a mixture of DMF (0.035 g, 0.48 mmol), $POCl_3$ (0.082 g, 0.54 mmol), and **32c** (0.050 g, 0.24 mmol) generated **30c** (0.032 g, 56 %) as a brown solid. R*f* 0.16 (hexane/EtOAc, 7:3); mp 162–163 °C. IR (film): $\bar{\upsilon}$ = 2931, 1771, 1667, 1516, 1404, 1337, 1301, 1252, 1143, 1029, 837, 746 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6): δ 2.23 (s, 3H, CH_3-C4), 3.82 (s, 3H, CH_3O), 7.08–7.12 (m, 2H, H-3'), 7.43–7.47 (m, 2H, H-2'), 9.56 (s, 1H, C*H*O). ^{13}C NMR (150 MHz, DMSO-d_6): δ 8.9 (*C*H_3-C4), 55.5 (*C*H_3O), 114.8 (C-3'), 124.4 (C-1'), 129.0 (C-2'), 134.2 (C-5), 141.9 (C-4), 152.3 (C-2), 159.8 (C-4'), 175.0 (*C*HO). HRMS (EI, $[M^+]$): *m/z* calcd for $C_{12}H_{11}NO_4$: 233.0688; found: 233.0691.

6-Acetyl-3-(*p*-tolyl)-4,5-dihydrobenzo[*d*]oxazol-2(3*H*)-one (31b). In a round-bottom flask (50 mL) equipped with a magnetic stirring bar, KO*t*-Bu (0.048 g, 0.43 mmol) was added to a solution of **30b** (0.050 g, 0.23 mmol) in anhydride THF (10 mL) under N_2 atmosphere at -78 ºC and stirred for 40 min. Then, MVK (0.031 g, 0.44 mmol) was added dropwise and the mixture was stirred for 1 h, then at 0 ºC for 30 min before removing the solvent under vacuum. The residue was purified by column chromatography over silica gel (30 g/g crude, hexane/EtOAc, 8:2) to produce **31b** (0.013 g, 21 %) as a yellow solid. R*f* 0.31 (hexane/EtOAc, 7:3); mp 113–116 °C. IR (film): $\bar{\upsilon}$ = 2924, 1770, 1668, 1644, 1570, 1516, 1422, 1371, 1322, 1288, 1218, 1004, 819, 748 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 2.37 (s, 3H, CH_3CO), 2.40 (s, 3H, CH_3Ar), 2.66 (br t, *J* = 9.9 Hz, 2H, H-4), 2.79 (br t, *J* = 9.9 Hz, 2H, H-5), 7.12 (br s, 1H, H-7), 7.22–7.24 (m, 2H, H-2'), 7.27–7.30 (m, 2H, H-3'). ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.9 (C-4), 20.9 (C-5), 21.1 (*C*H_3Ar), 24.9 (*C*H_3CO), 124.2 (C-7), 124.9 (C-2'), 128.6 (C-3a), 130.2 (C-3'), 130.5 (C-1'), 131.4 (C-6), 134.1 (C-7a), 138.6 (C-4'), 154.1 (C-2), 196.2 (CH_3*C*O). HRMS (ESI, $[M + H]^+$): *m/z* calcd for $C_{16}H_{16}NO_3$: 270.1130; found: 270.1080.

6-Acetyl-3-(4-methoxyphenyl)-4,5-dihydrobenzo[*d*]oxazol-2(3*H*)-one (31c). Following the method for preparing **31b**, a mixture of **30c** (0.050 g, 0.21 mmol), KO*t*-Bu (0.043 g, 0.38 mmol), and MVK (0.028 g, 0.40 mmol) afforded **31c** (0.014 g, 22 %) as a yellow solid. R*f* 0.35 (hexane/EtOAc, 7:3); mp 168–170 °C. IR (film): $\bar{\upsilon}$ = 2933, 1770, 1669, 1644, 1570, 1515, 1372, 1288, 1252, 1218, 1029, 1002, 834 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 2.37 (s, 3H, CH_3CO), 2.64 (br t, *J* = 9.9 Hz, 2H, H-4), 2.79 (br t, *J* = 9.9 Hz, 2H, H-5), 3.84 (s, 3H, CH_3O), 6.98–7.01 (m, 2H, H-3'), 7.12 (br s, 1H, H-7), 7.25–7.28 (m, 2H, H-2'). ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.8 (C-4), 20.9 (C-5), 24.9 (*C*H_3CO), 55.6 (*C*H_3O), 114.9 (C-3'), 124.3 (C-7), 125.7 (C-1'), 126.6 (C-2'), 128.9 (C-3a), 131.3 (C-6), 134.0 (C-7a), 154.3 (C-2), 159.5 (C-4'), 196.3 (CH_3*C*O). HRMS (EI, $[M^+]$): *m/z* calcd for $C_{16}H_{15}NO_4$: 285.1001; found: 285.1011.

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(*E*)-3-((3-Methoxyphenyl)imino)butan-2-one (11c). In a round-bottom flask (250 mL) equipped with a magnetic stirring bar, a mixture of **4a** (0.98 g, 11.4 mmol) and *m*-anisidine (1.40 g, 11.4 mmol) in MeOH (150 mL) was stirred under N_2 atmosphere at rt for 24 h. The solvent was removed under vacuum and the residue was purified by column chromatography over silica gel (10 g/g crude, hexane/EtOAc, 98:2) to furnish **11c** (1.63 g, 75 %) as a yellow oil. R*f* 0.75 (hexane/EtOAc, 80:20). IR (film): $\bar{\upsilon}$ = 2938, 1698, 1504, 1243, 1033, 841 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.97 (s, 3H, H-4), 2.51 (s, 3H, H-1), 3.81 (s, 3H, C*H*$_3$O), 6.30–6.37 (m, 2H, H-2', H-4'), 6.66–6.72 (m, 1H, H-6'), 7.23–7.31 (m, 1H, H-5'). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 14.0 (C-4), 24.5 (C-1), 55.2 (*C*H$_3$O), 104.3 (C-2'), 110.0 (C-4'), 110.6 (C-6'), 129.9 (C-5'), 150.8 (C-1'), 160.2 (C-3'), 166.1 (C-3), 200.3 (C-2). MS (70 eV): *m/z* 191 (M^+, 6), 162 (10), 148 (100), 108 (13), 92 (24), 77 (9), 63 (20). HRMS (EI, $[M]^+$): *m/z* calcd for $C_{11}H_{13}NO_2$: 191.0946; found: 191.0956.

1-(3-Methoxyphenyl)-4,5-dimethylene-3-(*p*-tolyl)imidazolidin-2-one (16c). In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, a mixture of **11c** (0.499 g, 2.61 mmol), dried Li_2CO_3 (1.93 g, 26.1 mmol), and dried Et_3N (0.659 g, 6.53 mmol) in anhydrous PhMe (30 mL) was stirred at rt under N_2 atmosphere in the dark for 90 min. Subsequently, a solution of **5b** (1.04 g, 7.83 mmol) in PhMe (10 mL) was added dropwise, and the mixture was stirred at rt for 24 h. The mixture was filtered over Celite and washed with CH_2Cl_2 (3 x 20 mL), and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (10 g/g crude, hexane/EtOAc, 95:5) to provide **16c** (0.610 g, 76%) as a white solid. R*f* 0.65 (hexane/EtOAc, 80:20); mp 112–113 °C. IR (film): $\bar{\upsilon}$ = 1737, 1604, 1517, 1494, 1399, 1267, 1044, 818, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H, C*H*$_3$Ar), 3.82 (s, 3H, C*H*$_3$O), 4.32 (d, *J* = 2.4 Hz, 1H, =C*H*), 4.39 (d, *J* = 2.4 Hz, 1H, =C*H*), 4.79 (d, *J* = 2.4 Hz, 1H, =C*H*), 4.82 (d, *J* = 2.4 Hz, 1H, =C*H*), 6.91 (dm, *J* = 8.1 Hz, 1H, H-4'), 6.95 (dd, *J* = 2.4, 2.1 Hz, 1H, H-2'), 6.99 (dm, *J*= 8.1 Hz, 1H, H-6'), 7.28 (s, 4H, H-2", H-3"), 7.37 (t, *J* = 8.1 Hz, 1H, H-5'). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.2 (*C*H$_3$Ar), 55.4 (*C*H$_3$O), 82.7 (*C*H$_2$=), 82.9 (*C*H$_2$=), 112.9 (C-2'), 114.0 (C-4'), 119.7 (C-6'), 127.3 (C-2"), 130.0 (C-5'), 130.1 (C-3"), 131.5 (C-1"), 135.3 (C-1'), 137.9 (C-4"), 140.0 (C-4 or C-5), 140.2 (C-5 or C-4), 153.5 (C-2), 160.3 (C-3'). HRMS (EI, $[M]^+$): *m/z* calcd for $C_{19}H_{18}N_2O_2$: 306.1368; found: 306.1376.

1,3,6-Triphenyl-4,4a,7a,8-tetrahydroimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (**33a**) [21]. In a round-bottom flask (100 mL) equipped with a magnetic stirring bar, a mixture of **15a** (0.05 g, 0.19 mmol) and **19** (0.036 g, 0.21 mmol) in anhydrous CH_2Cl_2 (20 mL) was stirred at 0 ºC under N_2 atmosphere for 1 h. The solvent was removed under vacuum, and the residue was purified by column chromatography over silica gel (20 g/g crude, hexane/EtOAc, 8:2), leading to **33a** (0.075 g, 90%) as a pale green solid. R*f* 0.20 (hexane/EtOAc, 7:3); mp 128–129 °C [Lit. [21] 128–129 °C].

1-(4-Methoxyphenyl)-3,6-diphenyl-4,4a,7a,8-tetrahydroimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (**33b**). Following the procedure for **33a**, a mixture of **16a** (0.10 g, 0.34 mmol) and **19** (0.065 g, 0.38 mmol) yielded **33b** (0.151 g, 95 %) as a pale green solid. R*f* 0.40 (hexane/EtOAc, 1:1); mp 107–108 °C. IR (KBr): $\bar{\upsilon}$ = 2917, 1710, 1514, 1501, 1383, 1250, 1170, 1028, 838, 735, 693 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.74–2.86 (m, 2H, H-4, H-8), 3.05 (d, *J* = 16.0 Hz, 1H, H-4 or H-8), 3.10 (d, *J* = 15.0 Hz, 1H, H-8 or H-4), 3.42–3.52 (m, 2H, H-4a, H-7a), 3.82 (s, 3H, C*H*$_3$O), 6.97 (d, *J* = 8.5 Hz, 2H, H-3'), 7.23–7.30 (m, 4H, H-2', 2ArH), 7.30–7.50 (m, 8H, PhH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.9 (C-4 or C-8), 20.0 (C-8 or C-4), 38.7 (C-4a or C-7a), 38.8 (C-7a or C-4a), 55.5 (*C*H$_3$O), 114.5 (C-3'), 114.6 (C-3a or C-8a), 115.6 (C-8a or C-3a), 126.1 (2ArH), 126.2 (2ArH), 126.9 (C-1'), 127.4 (ArH), 127.6 (2ArH), 128.7 (ArH), 129.2 (2ArH), 129.3 (2ArH), 131.7 (C-1" or C-1'"), 134.5 (C-1'" or C-1"), 152.4 (C-2), 158.9 (C-4'), 177.8 (C-5, C-7). MS (70 eV): *m/z* 465 (M^+, 58), 444 (77), 415 (43), 339 (26), 321 (36), 291 (59), 217 (54), 122 (91), 53 (100). HRMS (EI, $[M^+]$): *m/z* calcd for $C_{28}H_{23}N_3O_4$: 465.1689; found: 465.1692.

1-(4-Chlorophenyl)-3,6-diphenyl-4,4a,7a,8-tetrahydroimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (**33c**). Following the procedure for **33a**, a mixture of **16b** (0.100 g, 0.34 mmol) and **19** (0.059 g, 0.34 mmol) gave **33c** (0.146 g, 92 %) as a pale green solid. R*f* 0.40 (hexane/EtOAc, 1:1); mp 112–113 °C. IR (film): $\bar{\upsilon}$ = 2970, 2932, 1735, 1708, 1596, 1505, 1388, 1279, 1059 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.74–2.90 (m, 2H, H-4, H-8), 3.06–3.18 (m, 2H, H-4, H-8), 3.43–3.58 (m, 2H, H-4a, H-7a), 7.25–7.53 (m, 14H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 19.9 (C-4 or C-8), 20.0 (C-8 or C-4), 38.6 (C-4a or C-7a), 38.7 (C-7a or C-4a), 114.9 (C-3a or C-8a). 115.6 (C-8a or C-3a), 126.1 (4ArH), 127.2 (2ArH), 127.6 (ArH), 128.8 (C-4"), 129.2 (2ArH),

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129.4 (2ArH), 129.5 (2ArH), 131.5 (Ar), 132.8 (Ar), 133.1 (Ar), 134.0 (Ar), 151.9 (C-2), 177.7 (C-5, C-7). HRMS (EI, [M^+]): *m/z* calcd for $C_{27}H_{20}N_3O_3Cl$: 469.1193; found: 469.1184.

1-(3-Methoxyphenyl)-6-phenyl-3-(*p*-tolyl)-4,4a,7a,8-tetrahydroimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (**33d**). Following the procedure for **33a**, a mixture of **16c** (0.150 g, 0.49 mmol) and **19** (0.093 g, 0.54 mmol) generated **33d** (0.174 g, 74 %) as a white solid. R*f* 0.21 (hexane/EtOAc, 70:30); mp 175–176 °C. IR (film): $\bar{\upsilon}$ = 1717, 1632, 1517, 1411, 1397, 1255, 1131, 853, 820, 785 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.38 (s, 3H, C*H*$_3$), 2.75–2.88 (m, 2H, H-4, H-8), 3.06 (br d, *J* = 15.0 Hz, 1H, H-4 or H-8), 3.13 (br d, *J* =16.0 Hz, H-8 or H-4), 3.41–3.43 (m, 2H, H-4a, H-7a), 3.80 (s, 3H, C*H*$_3$O), 6.87–6.92 (m, 1H, H-4'), 6.89–6.96 (m, 2H, H-2', H-6'), 7.20–7.52 (m, 10H, Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.9 (C-4 or C-8), 20.0 (C-8 or C-4). 21.1 (*C*H$_3$), 38.7 (C-4a or C-7a), 38.8 (C-7a or C-4a), 55.4 (*C*H$_3$O), 111.7 (C-2'), 113.7 (C-4'), 115.0 (C-3a or C-8a), 115.4 (C-8a or C-3a), 118.3 (C-6'), 126.1 (2ArH), 126.2 (2ArH), 128.8 (C-4"), 129.2 (2ArH), 130.0 (2ArH), 130.1 (Ar-H), 131.5 (Ar), 131.6 (Ar), 135.3 (Ar), 137.6 (Ar), 152.2 (C-2), 160.3 (C-3'), 177.7 (C-5 or C-7), 177.8 (C-7 or C-5). HRMS (EI, [M^+]): *m/z* calcd for $C_{28}H_{23}N_3O_4$: 465.1689; found: 465.1652.

1,3-Diphenyl-4,9-dihydro-1*H*-naphtho[2,3-*d*]imidazol-2(3*H*)-one (35a). In a round-bottom flask (50 mL) equipped with a magnetic stirring bar, TBAF in furane (1.0 M) (0.120 g, 0.46 mmol) was added dropwise at 0 ºC under N_2 atmosphere to a mixture of **15a** (0.080 g, 0.31 mmol) and **34** (0.091 g, 0.31 mmol) in anhydrous CH_2Cl_2 (2 mL), stirring it in the dark for 24 h while it rose from 0 ºC to rt. The solvent was removed under vacuum, and the residue was purified by column chromatography over silica gel (10 g/g crude, hexane/EtOAc, 85:15) to obtain **35a** (0.058 g, 56%) as a white solid. R*f* 0.61 (hexane/EtOAc, 80:20); mp 211–212 ºC. IR (film): $\bar{\upsilon}$ = 1727, 1681, 1596, 1497, 1470, 1394, 1242, 1182, 1024, 857, 740, 692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.76 (s, 4H, H-4, H-9), 7.18 (br s, 6H, H-6, H-7, H-2', H-2"), 7.34–7.40 (m, 2H, H-4', H-4"), 7.40–7.54 (m, 8H, H-5, H-8, H-3', H-3", H-1', H-1"). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 26.6 (C-4, C-9), 115.2 (C-3a, C-9a), 126.4 (C-2', C-2", C-6, C-7), 127.3 (C-4', C-4"), 129.2 (C-3', C-3"), 129.3 (C-5, C-8), 131.8 (C-4a, C-8a), 135.1 (C-1', C-1"), 152.4 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{23}H_{18}N_2O$: 338.1419; found: 338.1422.

1-Phenyl-3-(*p*-tolyl)-4,9-dihydro-1*H*-naphtho[2,3-*d*]imidazol-2(3*H*)-one (35b). Following the procedure for **35a**, a mixture of **16d** (0.100 g, 0.36 mmol), **34** (0.108 g, 0.36 mmol), and TBAF in furane (1.0 M) (0.141 g, 0.54 mmol) produced **35b** (0.076 g, 60 %) as a white solid. R*f* 0.50 (hexane/EtOAc, 1:1); 189–190 °C. IR (film): $\bar{\upsilon}$ = 1726, 1680, 1603, 1518, 1501, 1473, 1398, 1246, 1175, 859, 738 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.42 (s, 3H, C*H*$_3$), 3.76 (s, 4H, H-4, H-9), 7.20 (br s, 4H, ArH), 7.26–7.44 (m, 5H, ArH), 7.46–7.54 (m, 4H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.1 (*C*H$_3$), 26.5 (C-4 or C-9), 26.6 (C-9 or C-4), 115.0 (C-9a or C-3a), 115.4 (C-3a or C-9a), 126.4 (4ArH), 126.5 (2ArH), 127.3 (ArH), 129.2 (2ArH), 129.3 (2ArH), 129.9 (2ArH), 131.8 (Ar), 131.9 (Ar), 132.3 (Ar), 135.1 (Ar), 137.3 (C-4"), 152.5 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{24}H_{20}N_2O$: 352.1576; found: 352.1568.

1,3,6-Triphenylimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (36a). A mixture of **33a** (0.070 g, 0.16 mmoles) and DDQ (0.073 g, 0.32 mmol) in anhydrous CH_2Cl_2 (15 mL) was stirred at 20 ºC under N_2 atmosphere for 24 h. The mixture was filtered over a mixture of Celite/silica gel (3:5 g) with CH_2Cl_2. The solvent was removed under vacuum, and the residue was purified by column chromatography over silica gel (20 g/g crude, hexane/EtOAc, 95:5) to provide **36a** (0.058 g, 90%) as a white solid. R*f* 0.52 (hexane/EtOAc, 1:1); mp 190–191 °C. IR (KBr): $\bar{\upsilon}$ = 1727, 1593, 1498, 1383, 1272, 1105, 756, 692 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.37–7.41 (m, 1H, ArH), 7.42–7.45 (m, 2H, ArH), 7.47–7.54 (m, 4H, ArH), 7.58–7.64 (m, 8H, ArH), 7.62 (s, 2H, H-4, H-8). ^{13}C NMR (125 MHz, $CDCl_3$): δ 104.4 (C-4, C-8), 126.3 (C-2', C-2"), 126.4 (C-4a, C-7a), 126.4 (C-2'"), 127.9 (C-4'"), 128.9 (2ArH), 129.1 (2ArH), 130.0 (C-3', C-3"), 131.8 (C-1'"), 133.2 (C-1', C-1"), 134.3 (C-3a, C-8a), 152.3 (C-2), 167.1 (C-5, C-7). HRMS (EI, [M^+]): *m/z* calcd for $C_{27}H_{17}N_3O_3$: 431.1270; found: 431.1261.

1-(4-Methoxyphenyl)-3,6-diphenylimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (36b). Following the procedure for **36a**, a mixture of **33b** (0.100 g, 0.21 mmol) and DDQ (0.098 g, 0.43 mmol) yielded **36b** (0.074 g, 75 %) as a yellow solid. R*f* 0.53 (hexane/EtOAc, 1:1); mp 135–136 °C. IR (film): $\bar{\upsilon}$ = 1738, 1592, 1483, 1395, 1264, 1236, 824, 780 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.90 (s, 3H, C*H*$_3$O), 7.08–7.14 (m, 2H, H-3'), 7.35–7.54 (m, 8H, ArH), 7.56 (s, 1H, H-4 or H-8), 7.58–7.66 (m, 5H, H-4 or H-8, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 55.6 (*C*H$_3$O), 104.2 (C-4 or C-8), 104.3 (C-8 or C-4), 115.2 (C-3'), 125.6 (Ar), 126.2 (2ArH), 126.40

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(Ar), 126.42 (ArH), 127.7 (2ArH), 127.9 (2ArH), 128.9 (2ArH), 129.1 (2ArH), 130.0 (2ArH), 131.7 (Ar), 133.3 (Ar), 134.1 (Ar), 134.8 (Ar), 152.5 (C-2), 159.8 (C-4'), 167. 2 (C-5, C-7). HRMS (EI, [M^+]): *m/z* calcd for $C_{28}H_{19}N_3O_4$: 461.1376; found: 461.1381.

1-(4-Chlorophenyl)-3,6-diphenylimidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (36c). Following the procedure for **36a**, a mixture of **33c** (0.071 g, 0.15 mmol) and DDQ (0.069 g, 0.30 mmol) gave **36c** (0.071 g, 72 %) as a yellow solid. R*f* 0.61 (hexane/EtOAc, 1:1); p.f. 117–118 °C. IR (film): $\bar{\upsilon}$ = 1734, 1708, 1596, 1519, 1505, 1387, 1277, 1059, 874, 751 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.39–7.47 (m, 3H, Ar-H), 7.48–7.67 (m, 13H, Ar-H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 104.2 (C-4 or C-8), 104.5 (C-8 or C-4), 126.2 (2Ar-H), 126.4 (2ArH), 126.5 (Ar), 126.6 (Ar), 127.5 (2ArH), 128.0 (ArH), 129.0 (ArH), 129.1 (2ArH), 130.1 (2ArH), 130.2 (2ArH), 131.6 (Ar), 131.7 (Ar), 133.0 (Ar), 133.8 (Ar), 134.3 (C-3a or C-8a), 134.7 (C-8a or C-3a), 152.1 (C-2), 167.0 (C-5, C-7). HRMS (EI, [M^+]): *m/z* calcd for $C_{27}H_{16}N_3O_3Cl$: 465.0880; found: 465.0875.

1-(3-Methoxyphenyl)-6-phenyl-3-(*p*-tolyl)imidazo[4,5-*f*]isoindole-2,5,7(1*H*,3*H*,6*H*)-trione (36d). Following the procedure for **36a**, a mixture of **33d** (0.100 g, 0.21 mmol) and DDQ (0.098 g, 0.43 mmol) furnished **36d** (0.074 g, 75 %) as a yellow solid. R*f* 0.50 (hexane/EtOAc, 1:1); mp 113–114 °C. IR (film): $\bar{\upsilon}$ = 1730, 1710, 1600, 1499, 1385, 1281, 1111, 762, 688 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.47 (s, 3H, C*H*$_3$), 3.87 (s, 3H, C*H*$_3$O), 7.05 (ddd, *J* = 8.4, 2.7, 0.9 Hz, 1H, H-4'), 7.11–7.18 (m, 2H, H-2', H-6'), 7.37–7.54 (m, 10H, H-5', H-2", H-3", PhH), 7.57 (d, *J* = 0.5 Hz, 1H, H-4 or H-8), 7.64 (d, *J* = 0.5 Hz, 1H, H-8 or H-4). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.2 (*C*H$_3$), 55.5 (*C*H$_3$O), 104.3 (C-4 or C-8), 104.4 (C-8 or C-4), 112.1 (C-6'), 114.7 (C-4'), 118.2 (C-2'), 126.1 (2ArH), 126.2 (Ar), 126.3 (Ar), 126.4 (2ArH), 127.9 (ArH), 129.1 (2ArH), 130.4 (Ar), 130.5 (2ArH), 130.5 (ArH), 131.7 (Ar), 134.1 (Ar), 134.2 (Ar), 134.4 (Ar), 139.1 (Ar), 152.3 (C-2), 160.7 (C-3'), 167.2 (C-5, C-7). HRMS (EI, [M^+]): *m/z* calcd for $C_{29}H_{21}N_3O_4$: 475.1532; found: 475.1537.

1,3-Diphenyl-1*H*-naphtho[2,3-*d*]imidazol-2(3*H*)-one (37a). A mixture of **35a** (0.086 g, 0.25 mmol) and DDQ (0.114 g, 0.50 mmol) in anhydrous CH_2Cl_2 (5 mL) was stirred under N_2 atmosphere at rt for 24 h. The mixture was filtered over Celite and washed with CH_2Cl_2 (15 mL). The filtered solution was concentrated under vacuum, and the residue purified by column chromatography over silica gel (10 g/g of crude, hexane/EtOAc, 8:2) to deliver **37a** (0.084 g, 99 %) as a white solid. R$_f$ 0.52 (hexane/EtOAc, 8:2); mp 211–212 °C. IR (film): $\bar{\upsilon}$ = 1728, 1497, 1471, 1394, 1245, 743, 692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.32–7.39 (m, 2H, H-6, H-7), 7.42–7.49 (m, 4H, H-4, H-9, H-4', H-4"), 7.55–7.63 (m, 4H, H-3', H-3"), 7.64–7.70 (m, 4H, H-2', H-2"), 7.70–7.78 (m, 2H, H-5, H-8). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 104.7 (C-4, C-9), 124.5 (C-6, C-7), 126.3 (C-2', C-2"), 127.2 (C-5, C-8), 127.9 (C-4', C-4"), 129.6 (C-3', C-3"), 130.0 (C-3a, C-9a), 130.3 (C-4a, C-8a), 134.5 (C-1'), 134.7 (C-1"), 153.1 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{23}H_{16}N_2O$: 336.1263; found: 336.1267.

1-Phenyl-3-(*p*-tolyl)-1*H*-naphtho[2,3-*d*]imidazol-2(3*H*)-one (37b). Following the procedure for **37a**, a mixture of **35b** (0.080 g, 0.23 mmol) and DDQ (0.104 g, 0.46 mmol) in CH_2Cl_2 (15 mL) resulted in **37b** (0.077 g, 97 %) as a white solid. R$_f$ 0.55 (hexane/EtOAc, 1:1); mp 178–179 °C. IR (film): $\bar{\upsilon}$ = 1727, 1603, 1518, 1502, 1472, 1397, 1246, 1176, 856, 744 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.46 (s, 3H, ArC*H*$_3$), 7.33–7.38 (m, 2H, H-6, H-7), 7.38–7.42 (m, 3H, H-4 or H-9, H-3"), 7.45 (s, 1H, H-9 or H-4), 7.42–7.49 (m, 1H, H-4'), 7.51–7.56 (m, 2H, H-2"), 7.56–7.63 (m, 2H, H-3'), 7.65–7.70 (m, 2H, H-2'), 7.71–7.78 (m, 2H. H-5, H-8). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.2 (Ar*C*H$_3$), 104.7 (C-4, C-9), 124.4 (C-6 or C-7), 124.5 (C-7 or C-6), 126.2 (C-2"), 126.3 (C-2'), 127.1 (C-5 or C-8), 127.2 (C-8 or C-5), 127.9 (C-4'), 129.6 (C-3'), 129.9 (Ar), 130.0 (Ar), 130.26 (C-3"), 130.29 (Ar), 130.6 (Ar), 131.7 (Ar), 134.5 (Ar), 138.0 (C-4"), 153.2 (C-2). HRMS (EI, [M^+]): *m/z* calcd for $C_{24}H_{18}N_2O$: 350.1419; found: 350.1418.

Results and discussion

Regioselective functionalization of exo-oxazolidin-2-one dienes 1 and 2

The previously reported method [7,10] was applied for the preparation of dienes **1a**–**c**, which were submitted to the Brønsted acid-catalyzed addition of a series of nucleophiles (Table 1). Thus, the addition of MeOH/HCl at room temperature (rt) for 1 h provided the series of 4-oxazolin-2-ones **22a**–**c** in good yields

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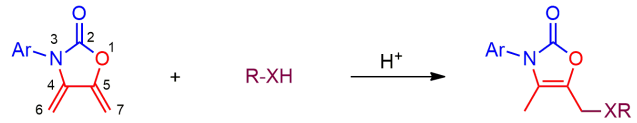
(entries 1–3), while the addition of acetic acid furnished the series **23a**–**c** in moderate to good yields (entries 4–6). Regarding the addition of 4-chlorothiophenol (**21c**) to afford the series of 4-oxazolin-2-ones **24a**–**c**, the optimal catalyst (phosphoric acid) rendered satisfactory yields (entries 7–9).

Table 1. Acid-catalyzed addition of nucleophiles **21a**–**c** to dienes **1a**–**c** to prepare the series of 4-oxazolin-2-ones **22a**–**c**, **23a**–**c**, and **24a**–**c**.[a]



1a, Ar = Ph
1b, Ar = C_6H_4-4-Me
1c, Ar = C_6H_4-4-OMe

21a, X = O, R = Me
21b, X = O, R = Ac
21c, X = S, R = C_6H_4-4-Cl

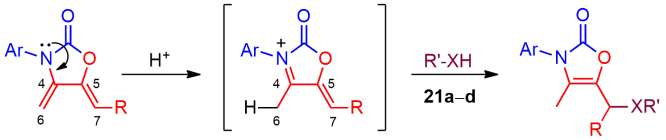
22a–**c**, RX = OMe
23a–**c**, RX = OAc
24a–**c**, RX = SC_6H_4-4-Cl

Entry	**1**	**21**	H^+	Ar	**22**–**24**	Yield (%)[b]
1	**1a**	**21a**	HCl	Ph	**22a**	92
2	**1b**	**21a**	HCl	C_6H_4-4-Me	**22b**	83
3	**1c**	**21a**	HCl	C_6H_4-4-OMe	**22c**	84
4	**1a**	**21b**	AcOH	Ph	**23a**	95
5	**1b**	**21b**	AcOH	C_6H_4-4-Me	**23b**	81
6	**1c**	**21b**	AcOH	C_6H_4-4-OMe	**23c**	59
7	**1a**	**21c**	H_3PO_4	Ph	**24a**	60
8	**1b**	**21c**	H_3PO_4	C_6H_4-4-Me	**24b**	75
9	**1c**	**21c**	H_3PO_4	C_6H_4-4-OMe	**24c**	74

[a] Standard conditions: **1a**–**c** (1.0 mol equiv), **21a**–**c** (2.0–75.0 mol equiv), and H^+ (1.0–11.0 mol equiv), at rt, 1–24 h. For **21b** and **21c**, the reaction was performed in CH_2Cl_2. [b] Isolated yields.

Interestingly, the dienic moiety underwent a regioselective addition of the nucleophiles to the terminal C-7 carbon atom of the double bond, possibly because of the capture of the proton, liberated by the catalyst, from the terminal C-6 carbon atom of the double bond to give species **I** (Scheme 4). The latter C-4/C-6 vinyl bond is more likely to be activated by the heterocyclic nitrogen electron lone pair than is the C-5/C-7 double bond by the oxygen lone pair, which is more electronegative. This difference in reactivity was supported experimentally and by theoretical calculations in relation to the regioselective Diels-Alder additions of dienes **1a**–**c** with unsymmetrical dienophiles [7a], and to the electrophilic addition to the double bond of 4-oxazolin-2-ones **9** [28].

Due to the formation of the conjugated vinylogous iminium ion in **I**, the nucleophiles (**21a**–**c**) attack the terminal C-7 carbon atom of the C-5/C-7 vinylic moiety, which is softer [29] and less hindered than the C-4 iminium carbon atom, leading to the observed products **22**–**24**.



1a–**c**, R = H
2a–**c**, R = Me

I
II

22–**24**, R = H
26–**28**, R = Me

Scheme 4. Mechanism of reaction of dienes **1a**–**c** with nucleophiles **21a**–**d** to furnish 4-oxazolin-2-ones **22**–**28**.

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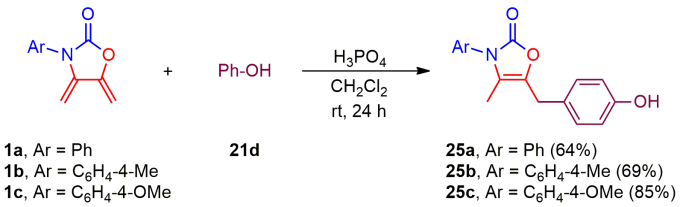
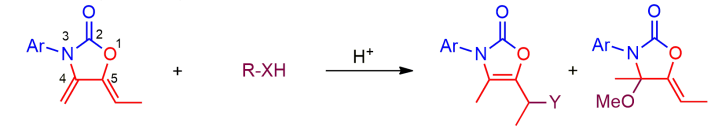
Given that thiophenol **21c** was an efficient nucleophile in the addition to dienes **1a**–**c**, the reaction of phenol (**21d**) with the same dienic substrates was explored, using phosphoric acid as the catalyst and CH_2Cl_2 as the solvent (Scheme 5). In contrast to the series of **22**–**24**, where the oxygen and sulfur atoms were the nucleophilic center, the addition of **21d** took place at the *para* position of the aryl ring to provide the series of 4-oxazolin-2-ones **25a**–**c**. This is probably because of the effect of the greater softness of the aryl ring than the oxygen atom of **21d** when reacting with the soft conjugated iminium species **I**.



Scheme 5. Preparation of 4-oxazolin-2-ones **25a**–**c** by addition of **21d** to **1a**–**c**.

Dienes **2a**–**c** were also synthesized by the reported procedure [7,10], and their reaction with nucleophiles **21a** and **21c**–**d** was catalyzed by a Brønsted acid (Table 2). With these dienes, the addition of MeOH/HCl was carried out at –10 ºC for 24 h to avoid a larger amount of polymerization, resulting in the series of 4-oxazolin-2-ones **26a**–**c** in modest yields (entries 1–3). With diene **2c**, the mixture of adducts **26c**/**26c'** (83:17) found by ^{1}H NMR was separated and characterized. With dienes **2a** and **2b**, the ^{1}H NMR analysis of the crude reaction mixtures detected trace signals attributed to the corresponding regioisomers **26a'** and **26b'**. However, the isolation of these compounds was not viable.

Table 2. Acid-catalyzed addition of nucleophiles **21a**, **21c**, and **21d** to dienes **2a**–**c** for the preparation of the series 4-oxazolin-2-ones **26a**–**c**, **27a**–**c**, and **28a**–**c**.[a]



Entry	**2**	**21**	H^+	Ar	**26**–**28**	Yield (%)[b]
1	**2a**	**21a**	HCl	Ph	**26a**	67
2	**2b**	**21a**	HCl	C_6H_4-4-Me	**26b**	69
3	**2c**	**21a**	HCl	C_6H_4-4-OMe	**26c**/**26c'** (83:17)	73/15
4	**2a**	**21c**	H_3PO_4	Ph	**27a**	60
5	**2b**	**21c**	H_3PO_4	C_6H_4-4-Me	**27b**	64
6	**2c**	**21c**	H_3PO_4	C_6H_4-4-OMe	**27c**	62
7	**2a**	**21d**	H_3PO_4	Ph	**28a**	60
8	**2b**	**21d**	H_3PO_4	C_6H_4-4-Me	**28b**	67
9	**2c**	**21d**	H_3PO_4	C_6H_4-4-OMe	**28c**	64

[a] Standard conditions: **2a**–**c** (1.0 mol equiv), **21a**, **21c**, or **21d** (1.6–240.0 mol equiv), and H^+ (1.2–2.5 mol equiv), at -10–25 ºC, 1–24 h. For **21c** and **21d**, the reactions were carried out in CH_2Cl_2. [b] Isolated yields.

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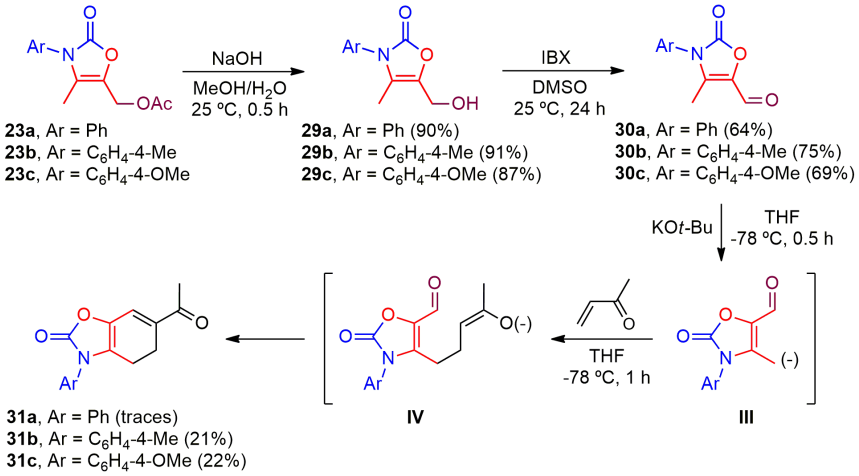
The presence of **26c'** could be explained by the plausible addition of the hard nucleophile (MeOH) to the hard C-4 iminium carbon atom of species **II** (Scheme 4). Another factor is the greater stability of the intermediate species **II** in relation to species **I**, caused by the supplementary methyl group [30].

Of course, the addition of soft nucleophiles **21c** and **21d** did not result in the C-4 addition regioisomers, but rather exclusively to the expected series of 4-oxazolin-2-ones **27a**–**c** and **28a**–**c**, respectively, in modest yields (entries 4–9). On the other hand, the addition of acetic acid (**21b**) promoted the formation of complex mixtures of products.

Conversion of 4-oxazolin-2-ones 23a–c into 4,5-dihydrobenzo[*d*]oxazol-2(3*H*)-ones 31

The satisfactory preparation of 4-oxazolin-2-ones **23a**–**c** allowed for an exploration of a further transformation in route to the construction of a fused six-membered ring, as with 4,5-dihydrobenzo[*d*]oxazol-2(3*H*)-ones **31a**–**c** (Scheme 6). The synthetic route comprised the consecutive saponification and oxidation of 4-oxazolin-2-ones **23a**–**c** to provide alcohols **29a**–**c** and aldehydes **30a**–**c**, respectively. The first step consisted of the common and efficient hydrolysis with NaOH in a mixture of MeOH/H_2O (8:2) to give the desired alcohols **29a**–**c** in high yields. Analogous alcohols prepared with reported procedures have shown great value as synthons in the construction of molecules with potential synthetic and pharmacological activity [31].



Scheme 6. Preparation of 5-formyl-4-oxazolin-2-ones **30a**–**c** and their conversion into compounds **31b**–**c**.

Although diverse reagents were employed, including PCC, PDC, MnO_2, and IBX [32], it was very difficult to establish the optimal oxidation conditions for the conversion of alcohols **29a**–**c** into aldehydes **30a**–**c**. The reaction of IBX in DMSO at rt for 24 h turned out to be the best procedure, furnishing the desired products in good yields (Scheme 6). On the other hand, the starting material was recovered with the use of PCC, and the decomposition of the substrate was observed with PDC or MnO_2.

The Staunton–Weinreb annulation is a valuable strategy for the synthesis of a six-membered ring based on the condensation of an *ortho*-toluate (as the nucleophile) with a conjugated carbonyl compound (as the electrophile), involving a Michael addition followed by a Dieckmann condensation and, if possible, a subsequent aromatization [33]. Hence, the exocyclic crotonaldehyde–like moiety of the 4-oxazolin-2-one scaffold (**30a**–**c**) was examined as a potential synthon in the construction of 4,5-dihydrobenzo[*d*]oxazol-2(3*H*)-ones **31a**–**c** through a Staunton–Weinreb–like reaction (Scheme 6).

The classical procedure of the Staunton–Weinreb cascade annulation involves a strong base, such as LDA or LiHMDS. With either of these two bases, the reaction of **30b**–**c** with MVK as the electrophile led a complex mixture of products. With the base KO*t*-Bu, the reaction provided the desired products **31b**–**c**, but in low yields. It is likely that the presence of the heteroatoms in the 4-oxazolin-2-one ring decreased the acidity of the C-4 methyl protons and consequently diminished the stability of the conjugated anion species **III**. The conjugated addition of the latter species to MVK afforded species **IV**, which underwent the Dieckmann

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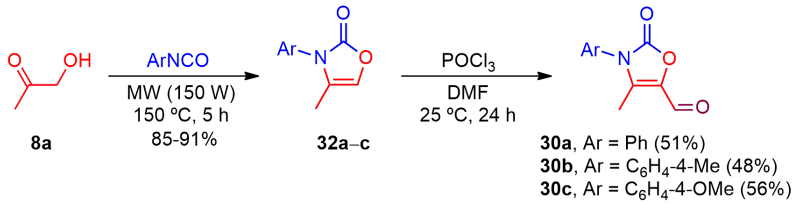
condensation to generate the isolated adducts **31b**–**c**. When the process was carried out with **30a**, the starting material was recovered and only a trace amount of the expected adduct **31a** was obtained.

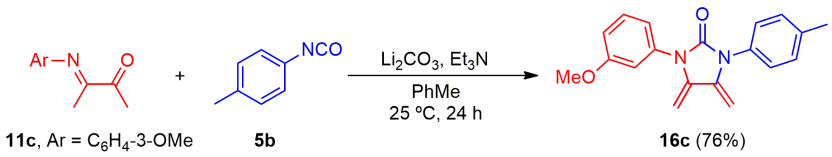
Owing to the interest in insuring a readily supply of aldehydes **30a**–**c**, a shorter synthetic route was designed. Thus, the straightforward construction of the 4-oxazolin-2-ones **32a**–**c** was achieved in accordance with the previously reported methodology [15], involving a solvent-free addition/cyclization/dehydration cascade reaction between ketol **8a** and isocyanates **5a**–**c** under MW irradiation (Scheme 7). With slight modifications in the reaction conditions, such as a reduction in the MW potency (from 200 to 150 W) and an increase in the temperature (from 120 to 150 ºC) and reaction time (from 1.5 to 5.0 h), the yields of 5-formyl-4-oxazolin-2-ones **32a**–**c** were improved. The application of the usual Vilsmeier–Haack reaction conditions to **32a**–**c** gave the desired products **30a**–**c** in modest yields.



Scheme 7. Preparation of 4-oxazolin-2-ones **32a**–**c** and their conversion into aldehydes **30a**–**c**.

Synthesis of tricyclic benzimidazol-2-ones via Diels–Alder cycloadditions of exo-imidazolidin-2-one dienes 15a and 16a–f

The symmetrical diene **15a** and unsymmetrical dienes **16a**–**d** (R = H) were elaborated based on previously described methods [21,22]. The reaction of α-iminoketones **11a-c** with the corresponding isocyanates **5a-d** furnished the desired dienes **15a** and **16a**–**d** in good yields. The new diene **16c** was obtained starting from α-iminoketone **11c** with isocyanate **5b** (Scheme 8).



Scheme 8. Synthesis of diene **16c**.

Preliminary results shown that diene **15a** undergoes Diels–Alder cycloaddition with *N*-phenylmaleimide (**19**) under mild conditions (CH_2Cl_2, 0 ºC, 1 h) to furnish adduct **33a** in high yield [21]. In order to gain more insight into the reactivity of unsymmetrical dienes, analogues **16a**–**c** were submitted to cycloaddition with **19** under the same reaction conditions, leading to adducts **33b**–**d** in high yields (Table 3, entries 2–4). As can be appreciated, the cycloaddition takes place regardless of the substituents located at the aryl ring of the dienes. Hence, reactivity is not dependent on the perturbation of the electron density of *N,N'*-aryl rings on the conjugated dienic moiety, a phenomenon that can be attributed to the almost orthogonal orientation of the aryl ring with respect to the heterocycle. This conformational preference of the substituted aryl rings, shown by quantic calculations and X-ray crystallography [22], impedes their conjugation with the nitrogen lone pairs of the imidazolidin-2-one ring. Thus, the aryl rings do not have any significant electronic effect, which agrees with previous results [21,22].

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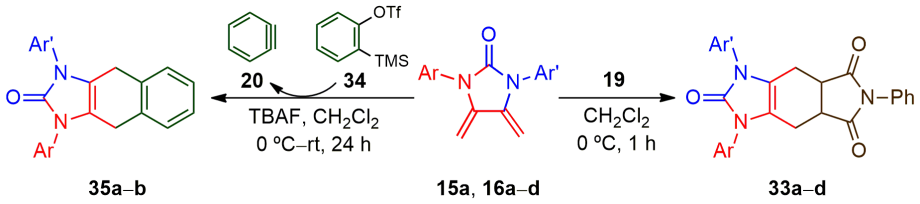
Table 3. Diels–Alder cycloaddition of dienes **15a** and **16a**–**d** to dienophiles **19** and **20** to afford adducts **33a**–**d** and **35a**–**b**.[a]



35a–b **15a, 16a–d** **33a–d**

Entry	Diene	Dienophile	Ar	Ar'	**33** or **35**	Yield (%)[b]
1	**15a**	**19**	Ph	Ph	**33a**	90
2	**16a**	**19**	Ph	C_6H_4-4-OMe	**33b**	95
3	**16b**	**19**	Ph	C_6H_4-4-Cl	**33c**	92
4	**16c**	**19**	C_6H_4-3-OMe	C_6H_4-4-Me	**33d**	74
5	**15a**	**20**	Ph	Ph	**35a**	56
6	**16d**	**20**	C_6H_4-4-Me	Ph	**35b**	60

[a] Standard conditions: Method A: **15a** and **16a**–**c** (1.0 mol equiv) with **19** (1.1 mol equiv), in CH_2Cl_2, 0 °C, 1 h. Method B: **15a** and **16d** (1.0 mol equiv) with **34** (1.0 mol equiv) and TBAF (1.5 mol equiv) in CH_2Cl_2 0 °C–rt, 24 h. [b] Isolated yields.

Benzyne (**20**), an *in situ*-formed highly reactive molecule [34], is one of the most important dienophiles in Diels–Alder cycloadditions, generating linear and non-linear homologation of aromatic multicyclic six-membered rings [4,35], and be involved in natural product synthesis [36]. 2-(Trimethylsilyl)phenyl triflate (**34**) reacts under mild conditions with TBAF to generate **20** (Table 3) [35,36].

Dienes **15a** and **16d** were evaluated in Diels–Alder cycloadditions with benzyne (**20**) (Table 3, entries 5–6). The latter was generated *in situ* by reacting **34** with TBAF in the presence of the corresponding diene at 0 °C. The mixture was stirred until reaching rt (for about 24 h), to obtain adducts **35a**–**b** in moderate yields. Despite the high reactivity of **20**, the conversion rate is not always complete, due to the well-known behavior of **20**. Once formed, this molecule undergoes dimerization, thus decreasing its concentration in the reaction medium [34].

In the Diels–Alder additions with dienophiles **19** and **20**, derivatives **15a** and **16a**–**d** proved to be potent dienes capable of providing a series of tricyclic tetrahydrobenzo[*d*]imidazol-2-ones **33a**–**d** and **35a**–**b**, which in turn can serve as precursors of aromatic analogues with potential synthetic and pharmacological value [23–27].

With the aim of exploring a preliminary synthetic application of adducts **33a**–**d** and **35a**–**b**, they were aromatized with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) under mild conditions, converting them into aromatic tricyclic benzo[*d*]imidazol-2-ones **36a**–**d** (Scheme 9, Eq. 1) and naphtho[2,3-*d*]imidazol-2-ones **37a**–**b** (Eq. 2), respectively, in high to excellent yields. The yields for the second series of aromatic products were higher, because of the greater stability gained by the formation of a naphthalene ring.

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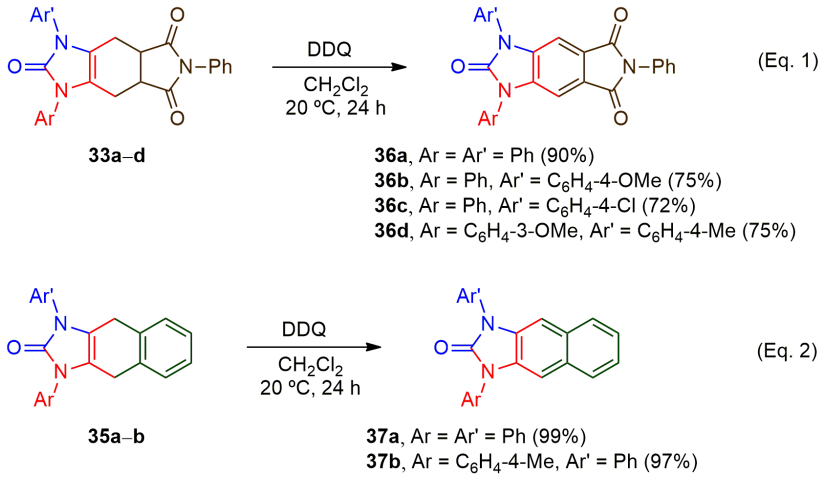

Scheme 9. Synthesis of tricyclic benzo[*d*]imidazol-2-ones **36a**–**d** (Eq. 1) and naphtho[2,3-*d*]imidazol-2-ones **37a**–**b** (Eq. 2).

All the structures of the intermediates and products of these synthetic pathways were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy, assisted by 2D (HMQC, HSQC, and HMBC) experiments and high-resolution mass spectrometry (HRMS).

Conclusions

Dienes **1**–**2** proved to be versatile compounds not only as reactive and regioselective dienes in Diels–Alder additions, as previously demonstrated, but also as substrates for the regioselective synthesis of functionalized 4-oxazolin-2-ones **22**–**28**. The latter compounds were uncommon substrates in a Staunton–Weinreb-like annulation, converting aldehydes **30b**–**c** into 4,5-dihydrobenzo[*d*]oxazol-2(3*H*)-ones **31b**–**c**, although in low yields. A shorter synthetic approach for an alternative preparation of aldehydes **30a**–**c** was carried out through a two-step route starting from ketol **8a**.

Symmetrical *exo*-2-imidazolidinone diene **15a** and unsymmetrical dienes **16a-d** were reactive substrates in the Diels–Alder cycloadditions with dienophiles *N*-phenylmaleimide (**19**) and benzyne (**20**). The corresponding adducts were efficiently aromatized to furnish a series of benzo- and naphtho[*d*]imidazol-2-ones, which potentially have pharmacological activity.

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References

1. (a) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779–807. DOI: https://doi.org/10.1002/anie.198997791; (b) Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, *93*, 741–761. DOI: https://doi.org/10.1021/cr00018a006; (c) Herges, R.; Jiao, H.; von Ragué Schleyer, P. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1376–1378. DOI: https://doi.org/10.1002/anie.199413761; (d) Diedrich, M. K.; Klärner, F.-G. *J. Am. Chem. Soc.* **1998**, *120*, 6212–6218. DOI: https://doi.org/10.1021/ja973936p; (e) Suárez, D.; Sordo, J. A. *Chem. Commun.* **1998**, 385–386. DOI: https://doi.org/10.1039/A707086A; (f) Brocksom, T. J.; Nakamura, J.; Ferreira, M. L.; Brocksom, U. *J. Braz. Chem. Soc.* **2001**, *12*, 597–622. DOI: https://doi.org/10.1590/S0103-50532001000500004; (g) Kumar, A. *Chem. Rev.* **2001**, *101*, 1–19. DOI: https://doi.org/10.1021/cr990410; (h) Tantillo, D. J.; Houk, K. N.; Jung, M. E. *J. Org. Chem.* **2001**, *66*, 1938–1940. DOI: https://doi.org/10.1021/jo001172h; (i) Ayers, P. W.; Morell, C.; De Proft, F.; Geerlings, P. *Chem. Eur. J.* **2007**, *13*, 8240–8247. DOI: https://doi.org/10.1002/chem.200700365; (j) Domingo, L. R.; Sáez, J. A. *Org. Biomol. Chem.* **2009**, *7*, 3576–3583. DOI: https://doi.org/10.1039/B909611F; (k) Wang, Z.; Hirschi, J. S.; Singleton, D. A. *Angew. Chem. Int. Ed.* **2009**, *48*, 9156–9159. DOI: https://doi.org/10.1002/anie.200903293; (l) Ishihara, K.; Sakakura, A. Intermolecular Diels-Alder Reactions, in *Comprehensive Organic Synthesis*; Knochel, P., Molander, G.A., Eds.; Elsevier: Amsterdam, 2014; Vol. 5, Chap. 5.09, 351–408.
2. (a) Patman, R. L.; Bower, J. F.; Kim, I. S.; Krische, M. J. *Aldrichim. Acta* **2008**, *41*, 95–104; (b) Longo, P.; Pragliola, S.; Milano, G.; Guerra, G. *J. Am. Chem. Soc.* **2003**, *125*, 4799–4803. DOI: https://doi.org/10.1021/ja028462; (c) Li, Y.; Chen, J.; Ng, J. J. W.; Chiba, S. *Angew. Chem. Int. Ed.*. **2023**, *62*, e202217735. DOI: https://doi.org/10.1002/anie.202217735.
3. (a) Gleiter, R.; Böhm, M. C. *Pure Appl. Chem.* **1983**, *55*, 237–244. DOI: https://doi.org/10.1351/pac198855020237; (b) Kahn, S. D.; Pau, C. F.; Overman, L. E.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7381–7396. DOI: https://doi.org/10.1021/ja00283a038; (c) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682–708. DOI: https://doi.org/10.1002/anie.199206821; (d) Damoun, S.; Van de Woude, G.; Méndez, F.; Geerlings, P. *J. Phys. Chem. A* **1997**, *101*, 886–893. DOI: https://doi.org/10.1021/jp9611840; (e) Xidos, J. D.; Poirier, R. A.; Pye, C. C.; Burnell, D. J. *J. Org. Chem.* **1998**, *63*, 105–112. DOI: https://doi.org/10.1021/jo9712815; (f) García, J. I.; Martínez-Merino, V.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **1998**, *120*, 2415–2420. DOI: https://doi.org/10.1021/ja97282279; (g) Kong, S.; Evanseck, J. D. *J. Am. Chem. Soc.* **2000**, *122*, 10418–10427. DOI: https://10.1021/ja0010249; (h) Quadrelli, P.; Romano, S.; Toma, L.; Caramella, P. *J. Org. Chem.* **2003**, *68*, 6035–6038. DOI: https://10.1021/jo034401j; (i) Çelebi-Ölçüm, N.; Ess, D. H.; Aviyente, V.; Houk, K. N. *J. Org. Chem.* **2008**, *73*, 7472–7480. DOI: https://10.1021/jo801076t; (j) Domingo, L. R.; Chamorro, E.; Pérez, P. *Org. Biomol. Chem.* **2010**, *8*, 5495–5504. DOI: https://10.1039/c0ob00563k; (k) Ramírez-Gualito, K.; López-Mora, N.; Jiménez-Vázquez, H. A.; Tamariz, J.; Cuevas, G. *J. Mex. Chem. Soc.* **2013**, *57*, 267–275. DOI: https://10.29356/jmcs.v57i4.189; (l) Jasiński, R.; Kubik, M.; Łapczuk-Krygier, A.; Kącka, A.; Dresler, E.; Boguszewska-Czubara, A. *Reac. Kinet. Mech. Cat.* **2014**, *113*, 333–345. DOI: https://10.1007/s11144-014-0753-8; (m) Mlostoń, G.; Urbaniak, K.; Sobiecka, M.; Heimgartner, H.; Würthwein, E.-U.; Zimmer, R.; Lentz, D.; Reissig, H.-U. *Molecules* **2021**, *26*, 2544. DOI: https://10.3390/molecules26092544.
4. (a) Carruthers, W., in: *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1990; (b) Oppolzer, W., in: *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I.; Paquette, L. A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 4.1; (c) Fringuelli, F.; Taticchi, A. *The Diels-Alder Reaction: Selected Practical Methods*; J. Wiley & Sons: Chichester, 2002; (d) Corey, E. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 1650–1667. DOI: https://doi.org/10.1002/1521-3773(20020517)41:10<1650::AID-ANIE1650>3.0.CO;2-B; (e) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem. Int. Ed.* **2002**, *41*, 1668–1698, and references

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cited therein. DOI: https://doi.org/10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z; (f) Reymond, S.; Cossy, J. *Chem Rev.* **2008**, *108*, 5359–5406. DOI: https://doi.org/10.1021/cr078346g; (g) Wang, J.; Ma, D. *Angew. Chem. Int. Ed.* **2019**, *58*, 15731–15735. DOI: https://doi.org/10.1002/anie.201909349; (h) Schwinger, D. P.; Peschel, M. T.; Jaschke, C.; Jandl, C.; de Vivie-Riedle, R.; Bach, T. *J. Org. Chem.* **2022**, *87*, 4838–4851. DOI: https://doi.org/10.1021/acs.joc.2c00186; (i) Ghosh, S.; Erchinger, J. E.; Maji, R.; List, B. *J. Am. Chem. Soc.* **2022**, *144*, 6703–6708. DOI: http://doi.org/10.1021/jacs.2c01971; (j) Li, L.-X.; Min, L.; Yao, T.-B.; Ji, S.-X.; Qiao, C.; Tian, P.-L.; Sun, J.; Li, C.-C. *J. Am. Chem. Soc.* **2022**, *144*, 18823–18828. DOI: https://doi.org/10.1021/jacs.2c09548.

5. (a) Wiersum, U. E. *Aldrichimica Acta* **1981**, *14*, 53–58; (b) Fringuelli, F.; Taticchi, A., in: *Dienes in the Diels-Alder Reaction*; J. Wiley & Sons: New York, 1990; (c) Martin, N.; Seoane, C.; Hanack, M. *Org. Prep. Proc. Int.* **1991**, *23*, 237–272. DOI: https://doi.org/10.1080/00304949109458320; (d) Manoharan, M.; De Proft, F.; Geerlings, P. *J. Org. Chem.* **2000**, *65*, 7971–7976. DOI: https://doi.org/10.1021/jo001156k; (e) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Soc. Rev.* **2014**, *43*, 3106–3135 DOI: https://doi.org/10.1039/c3cs60462d.
6. (a) Haber, M.; Pindur, U. *Tetrahedron* **1991**, *47*, 1925–1936. DOI: https://doi.org/S0040-4020(01)96104-6; (b) Ruiz, N.; Pujol, M. D.; Guillaumet, G.; Coudert, G. *Tetrahedron Lett.* **1992**, *33*, 2965–2968. DOI: https://doi.org/S0040-4039(00)79573-6; (c) Chaloner, L. M.; Crew, A. P. A.; O'Neill, P. M.; Storr, R. C.; Yelland, M. *Tetrahedron* **1992**, *37*, 8101–8116. DOI: https://doi.org/S0040-4020(01)80480-4; (d) Chou, T. S.; Chang, R. C. *J. Org. Chem.* **1993**, *58*, 493–496. DOI: https://doi.org/jo00054a037; (e) Hercouet, A.; Berrée, F.; Lin, C. H.; Toupet, L.; Carboni, B. *Org. Lett.* **2007**, *9*, 1717–1720. DOI: https://doi.org/10.1021/ol070400s; (f) Samanta, S.; Mohapatra, H.; Jana, R.; Ray, J. K. *Tetrahedron Lett.* **2008**, *49*, 7153–7156. DOI: https://doi.org/10.1016/j.tetlet.2008.09.162; (g) Inagaki, F.; Mizutani, M.; Kuroda, N.; Mukai, C. *J. Org. Chem.* **2009**, *74*, 6402–6405. DOI: https://doi.org/10.1021/jo901325d; (h) Zhou, L.; Zhang, M.; Li, W.; Zhang, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 6542–6545. DOI: https://doi.org/10.1002/anie.201403709; (i) Li, G.-N.; Chen, G.-Y.; Niu, Z.-G.; Lei, B.-X.; Feng, H.-J. *J. Heterocycl. Chem.* **2014**, *51*, E367–E371. DOI: https://doi.org/10.1002/jhet.1945; (j) Hirata, G.; Yamada, N.; Sanada, S.; Onodera, G.; Kimura, M. *Org. Lett.* **2015**, *17*, 600–603. DOI: https://doi.org/10.1021/ol503614d.
7. (a) Mandal, A. B.; Gómez, A.; Trujillo, G.; Méndez, F.; Jiménez, H. A.; Rosales, M. J.; Martínez, R.; Delgado, F.; Tamariz, J. *J. Org. Chem.* **1997**, *62*, 4105–4115. DOI: https://doi.org/10.1021/jo962403g; (b) Fuentes, A.; Martínez-Palou, R.; Jiménez-Vázquez, H. A.; Delgado, F.; Reyes, A.; Tamariz, J. *Monatsh. Chem.* **2005**, *136*, 177–192. DOI: https://doi.org/10.1007/s00706-004-0244-0.
8. Martínez, R.; Jiménez-Vázquez, H. A.; Reyes, A.; Tamariz, J. *Helv. Chim. Acta* **2002**, *85*, 464–482. DOI: https://doi.org/10.1002/1522-2675(200202)85:2<464::AID-HLCA464>3.0.CO;2-U.
9. Martínez, R.; Jiménez-Vázquez, H. A.; Delgado, F.; Tamariz, J. *Tetrahedron* **2003**, *59*, 481–492. DOI: https://doi.org/10.1016/S0040-4020(02)01536-3.
10. González-Romero, C.; Bernal, P.; Jiménez, F.; Cruz, M. C.; Fuentes-Benites, A.; Benavides, A.; Bautista, R.; Tamariz, J. *Pure Appl. Chem.* **2007**, *79*, 181–191. DOI: https://doi.org/10.1351/pac200779020181.
11. Mandal, A. B.; Delgado, F.; Tamariz, J. *Synlett* **1998**, 87–89. DOI: https://doi.org/10.1055/s-1998-1571.
12. (a) Bautista, R.; Benavides, A.; Jiménez-Vázquez, H. A.; Tamariz, J. *Nat. Prod. Res.* **2013**, *27*, 1749–1756, and references cited therein. DOI: https://doi.org/10.1080/14786419.2012.751599; (b) Ávila-Melo, J. L.; Benavides, A.; Fuentes-Gutiérrez, A.; Tamariz, J.; Jiménez-Vázquez, H. A. *Synthesis* **2021**, *53*, 2201–2211. DOI: https://doi.org/10.1055/a-1385-9052.
13. Ortega-Jiménez, F.; Benavides, A.; Delgado, F.; Jiménez-Vázquez, H. A.; Tamariz, J. *Organometallics* **2010**, *29*, 149–159. DOI: https://doi.org/10.1021/om900772z.

J. Mex. Chem. Soc. **2025**, *69*(4)
Regular Issue

ISSN-e 2594-0317

14. Reyes, L.; Mendoza, H.; Vázquez, M. A.; Ortega-Jiménez, F.; Fuentes-Benítes, A.; Flores-Conde, M. I.; Jiménez-Vázquez, H.; Miranda, R.; Tamariz, J.; Delgado, F. *Organometallics* **2008**, *27*, 4334–4345. DOI: https://doi.org/10.1021/om8002416.
15. Santoyo, B. M.; González-Romero, C.; Merino, O.; Martínez-Palou, R.; Fuentes-Benites, A.; Jiménez-Vázquez, H. A.; Delgado, F.; Tamariz, J. *Eur. J. Org. Chem.* **2009**, 2505–2518. DOI: https://doi.org/10.1002/ejoc.200900114.
16. Merino, O.; Santoyo, B. M.; Montiel, L. E.; Jiménez-Vázquez, H. A.; Zepeda, L. G.; Tamariz, J. *Tetrahedron Lett.* **2010**, *51*, 3738–3742. DOI: https://doi.org/10.1016/j.tetlet.2010.05.034.
17. Zárate-Zárate, D.; Aguilar, R.; Hernández-Benitez, R. I.; Labarrios, E. M.; Delgado, F.; Tamariz, J. *Tetrahedron.* **2015**, *71*, 6961–6978. DOI: https://doi.org/10.1016/j.tet.2015.07.010.
18. Santoyo, B. M.; González-Romero, C.; Zárate-Zárate, D.; Hernández-Benitez, R. I.; Pelayo, V.; Barrera, E.; Escalante, C. H.; Fuentes-Benites, A.; Martínez-Morales, G.; López, J.; Vázquez, M. A.; Delgado, F.; Jiménez-Vázquez, H. A.; Tamariz, J. *Chirality* **2019**, *31*, 719–749. DOI: https://doi.org/10.1002/chir.23109.
19. Barrera, E.; Hernández-Benitez, R. I.; González-González, C. A.; Escalante, C. H.; Fuentes-Benites, A.; González-Romero, C.; Becerra-Martínez, E.; Delgado, F.; Tamariz, J. *Eur. J. Org. Chem.* **2022**, *2022*, e202200364. DOI: https://doi.org/10.1002/ejoc.202200364.
20. Yescas-Galicia, D.; Restrepo-Osorio, R. A.; García-González, A. N.; Hernández-Benítez, R. I.; Espinoza-Hicks, J. C.; Escalante, C. H.; Barrera, E.; Santoyo, B. M.; Delgado, F.; Tamariz, J. *J. Org. Chem.* **2022**, *87*, 13034–13052. DOI: https://doi.org/10.1021/acs.joc.2c01563.
21. Bautista, R.; Bernal, P.; Herrera, R.; Santoyo, B. M.; Lazcano-Seres, J. M.; Delgado, F.; Tamariz, J. *J. Org. Chem.* **2011**, *79*, 7901–7911. DOI: https://doi.org/10.1021/jo201335y.
22. Espinoza-Hicks, C.; Montoya, P.; Bautista, R.; Jiménez-Vázquez, H. A.; Rodríguez-Valdez, L. M.; Camacho-Dávila, A. A.; Cossío, F. P.; Delgado, F.; Tamariz, J. *J. Org. Chem.* **2018**, *83*, 5347–5364. DOI: https://doi.org/10.1021/acs.joc.7b02344.
23. Rémond, G.; Portevin, B.; Bonnet, J.; Canet, E.; Regoli, D.; De Nanteuil, G. *Eur. J. Med. Chem.* **1997**, *32*, 843–868. DOI: https://doi.org/10.1016/S0223-5234(97)82771-7.
24. Edvinsson, L.; Sams, A.; Jansen-Olesen, I.; Tajti, J.; Kane, S. A.; Rutledge, R. Z.; Koblan, K. S.; Hill, R. G.; Longmore, J. *Eur. J. Pharmacol.* **2001**, *415*, 39–44. DOI: https://doi.org/10.1016/S0014-2999(00)00934-1.
25. Tapia, I.; Alonso-Cires, L.; López-Tudanca, P. L.; Mosquera, R.; Labeaga, L.; Innerárity, A.; Orjales, A. *J. Med. Chem.* **1999**, *42*, 2870–2880. DOI: https://doi.org/10.1021/jm981098j.
26. (a) Zhang, P.; Terefenko, E. A.; Wrobel, J.; Zhang, Z.; Zhu, Y.; Cohen, J.; Marschke, K. B.; Mais, D. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2747–2750. DOI: https://doi.org/10.1016/S0960-894X(01)00554-6; (b) Terefenko, E. A.; Kern, J.; Fensome, A.; Wrobel, J.; Zhu, Y.; Cohen, J.; Winneker, R.; Zhang, Z.; Zhang, P. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3600–3603. DOI: https://doi.org/10.1016/j.bmcl.2005.05.082.
27. Li, Q.; Li, T.; Woods, K. W.; Gu. W.-Z.; Cohen, J.; Stoll, V. S.; Galicia, T.; Hutchins, C.; Frost, D.; Rosenberg, S. H.; Sham, H. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2918–2922. DOI: https://doi.org/10.1016/j.bmcl.2005.03.049.
28. Martínez, R.; Jiménez-Vázquez, H. A.; Tamariz, J. *Tetrahedron.* **2000**, *56*, 3857–3866. DOI: https://doi.org/10.1016/S0040-4020(00)00311-2.
29. Fleming, I., in: *Molecular orbitals and organic chemical reactions. Reference Edition*. John Wiley & Sons: Chichester, UK, 2010.
30. Carrol, F. A., in: *Perspectives on structure and mechanism in organic chemistry*. John Wiley & Sons: New Jersey, 2010.
31. Toda, Y.; Gomyou, S.; Tanaka, S.; Komiyama, Y.; S.; Kikuchi, A.; Suga, H, *Org. Lett.* **2017**, *19*, 5786–5789. DOI: https://doi.org/10.1021/acs.orglett.7b02722; (b) Toda, Y.; Tanaka, S.; Gomyou, S.; Kikuchi, A.; Suga, H. *Chem. Commun*. **2019**, *55*, 5761–5764. DOI: https://doi.org/10.1039/C9CC01983A.

J. Mex. Chem. Soc. **2025**, *69*(4)
Regular Issue

ISSN-e 2594-0317

32. Tojo, G.; Fernández, M. *Oxidation of alcohols to aldehydes and ketones. A guide to current common practice*. Springer Science & Business Media: USA, 2006.
33. Donner, C. D. *Tetrahedron.* **2013**, *69*, 3747–3773. DOI: https:// doi.org/10.1016/j.tet.2013.03.034.
34. (a) Gilchrist, T. L. Supplement C: *The chemistry of triple bonded functional groups, Part 1.* Patai, S; Rappoport, Z. (Eds.). John Wiley and Sons: New York, 1983; (b) Wentrup, C. *Aust. J. Chem.* **2010**, *63*, 979–986. DOI: https:// doi.org/10.1071/CH10179.
35. Holden, C.; Greaney, M. F. *Angew. Chem. Int. Ed.* **2014**, *53*, 5746–5749. DOI: https://10.1002/anie.201402405.
36. (a) Gampe, C. M.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 3766–3778. DOI: https://10.1002/anie.201107485; (b) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550–3577. DOI: https://10.1021/cr200478h.