Five- and Six-Membered Nickelacyclic Carboxylates as Reagents for the Facile Synthesis of δ-Ketocarboxylic Acids, Isocoumarins, and 1,3-Dicarbonyl Derivatives of Benzoic Acid

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Abstract: The nickelacyclic carboxylates **A** and **B** reacted with α-halo ketones to form α,β-unsaturated δ-ketocarboxylic acids which were easily converted into pyranones or isocoumarins. In addition, reaction of the nickelacyclic acyl derivative **C** with α-halo ketones resulted in the formation of substituted 1,3-dicarbonyl compounds with a benzoic acid substituent in the 1-position. In these reactions, many functional groups were tolerated.

Key words: cross coupling, metallacycles, organometallic reagents, nickel, heterocycles

The nickelacyclic carboxylates [Ni(CH_2CH_2COO)$(L)_2$] and [Ni{C(R)=C(R)COO}$(L)_2$] are interesting building blocks for the synthesis of carboxylic acid derivatives in organic chemistry.[1] Reaction of their Ni–C bond with an alkyl halide, for example, gives carboxylic acids,[2] a reaction which was used to construct functionalized side chains in steroids,[3] while insertion of carbon monoxide and reductive elimination allows the formation of cyclic anhydrides,[4] and reaction with carbon dioxide results in the formation of dicarboxylic acids.[5] In addition, the synthesis of methylaspartic acids has been achieved by the reaction of a substituted nickelacycle with isocyanides.[6] Furthermore, alkenes or alkynes have been inserted into the Ni–C bond resulting in saturated or unsaturated carboxylic acids and derivatives,[7] and transmetalation reactions with ZnR_2 to form arylated carboxylic acids or dicarboxylated derivatives has been described.[8] Recently, we have found that organic disulfides reacted to form carboxylic esters with a sulfanyl substituent in the β-position upon workup. Furthermore, we have observed that 2-bromopropiophenone and [Ni{C(Et)=C(Et)COO}(bipy)] reacted to yield a substituted 2*H*-pyran-2-one.[1c]

Continuing our efforts to develop synthetic methods based on nickelacyclic carboxylates, we now report the reaction of α-halo ketones with the unsaturated five-membered nickelacycles [Ni{C(Et)=C(Et)COO}(bipy)] **A** and [Ni(*o*-C_6H_4-COO)(bipy)] **B** resulting in the formation of α,β-unsaturated δ-ketocarboxylic acids **2** and **3** in good yields (Schemes 1 and 2) which could be easily transformed into the corresponding pyranones and isocoumarins **4**. In addition, the six-membered nickelacyclic acyl derivative [Ni{C(O)-*o*-C_6H_4COO}(bipy)] **C**, an intermediate in the formation of **B** that has been little investigated as a reagent for organic synthesis, reacted with α-halo ketones to give substituted 1,3-dicarbonyl compounds of benzoic acid **5** in good yields (Scheme 3).

Reactions of **A**, **B**, and **C** with α-halo ketones were carried out in tetrahydrofuran under argon. In all cases isolation of the products was achieved in a straightforward fashion by evaporation of the solvent, subsequent hydrolysis of the residue with dilute hydrochloric acid and purification by extraction with chloroform. After workup the products were isolated in a pure form. Recrystallization from acetone/heptane resulted, in most cases, in single crystals suitable for X-ray diffraction.

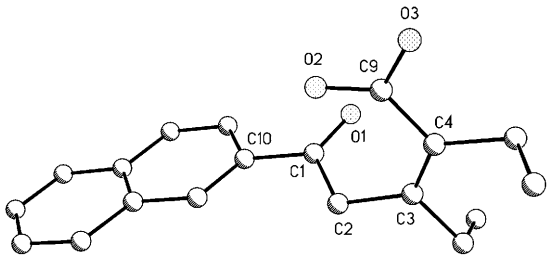

Figure 1 Molecular structure of **2a** (hydrogen atoms are omitted for clarity). Selected bond lengths (Å) and angles (°): C1–C10 1.494(2), C1–O1 1.220(2), C1–C2 1.517(2), C2–C3 1.509(2), C3–C4 1.350(2), C4–C9 1.482(2), C9–O2 1.244(2), C9–O3 1.304(2), C10–C1–C2 116.92(13), C1–C2–C3 116.60(14), C2–C3–C4 124.40(14), C3–C4–C9 121.51(13), C4–C9–O2 123.80(14), C4–C9–O3 115.25(13), O1–C1–C2 122.19(13).

Compound **A** is readily accessible in high yield (90%) by oxidative coupling of hex-3-yne and carbon dioxide using (2,2′-bipyridyl)(η⁴-cycloocta-1,5-diene)nickel [Ni(cod)(bipy)] as precursor.[7c] As shown in Table 1 the reaction of **A** with a variety of α-bromo ketones worked well (Table 1, entries 1–5). Complete conversion of the starting material was normally achieved by stirring the reaction mixture overnight at room temperature. Also α-bromocamphor **1f** (Table 1, entry 6), and even the aliphatic α-chloro ketone **1h** (Table 1, entry 7) reacted in good yields.

Functional groups in the *para* position of the aryl groups of aryl α-bromoalkyl ketones were tolerated. However, the reaction of **1e**, in which the bromide is bonded to a quaternary carbon atom, failed. In the case of the chiral

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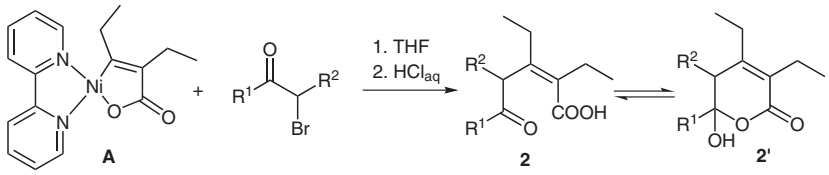
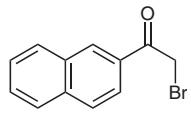
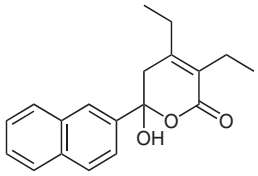
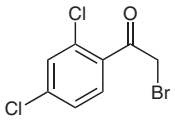
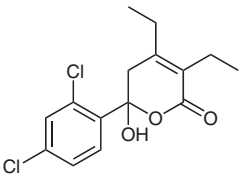
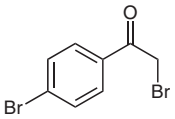
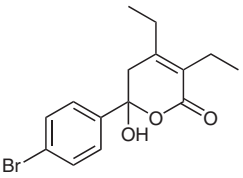
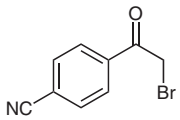
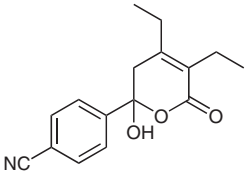
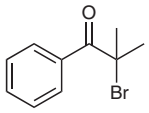
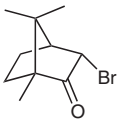
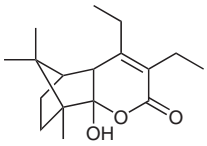
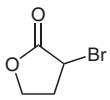
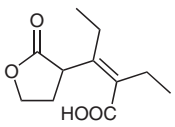
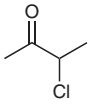
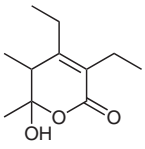


Scheme 1

Table 1 Reaction of **A** with α-Halocarbonyl Compounds

Entry	Substrate	Product	Yield (%)	Ratio **2/2′**
1	**1a** 	**2a′** 	76	1:1
2	**1b** 	**2b′** 	74	1:3.7
3	**1c** 	**2c′** 	72	1:1.8
4	**1d** 	**2d′** 	67	1:6.8
5	**1e** 	–	0	–
6	**1f** 	**2f′** 	86	1:4
7	**1g** 	**2g** 	87	>10:1
8	**1h** 	**2h′** 	81	<1:10

substrate **1f**, retention at the chiral center was observed and only one enantiomer was isolated as judged from NMR spectral data.

The equilibrium between the δ-ketocarboxylic acids **2** and their lactol forms **2′** (Scheme 1) strongly depends on the nature of the substituents (Table 1). Electron-withdrawing

groups at the 5-position of the thus-formed carboxylic acid **2** favor the lactol form **2′** in deuterochloroform at room temperature, according to the results of ^{1}H NMR measurements (Table 1, entries 1–4). The same effect was achieved by a higher degree of substitution at 4-position of the product (Table 1, entries 6, 8). In the case of **2a**/**2a′**, where the δ-ketocarboxylic acid **2a** is more favored in solution than in other cases, the solid product crystallized in this form. Figure 1 shows the X-ray structure of **2a**. In contrast, the other compounds crystallized in the lactol form **2′**. The X-ray structure of one example, **2f′**, is given in Figure 2.

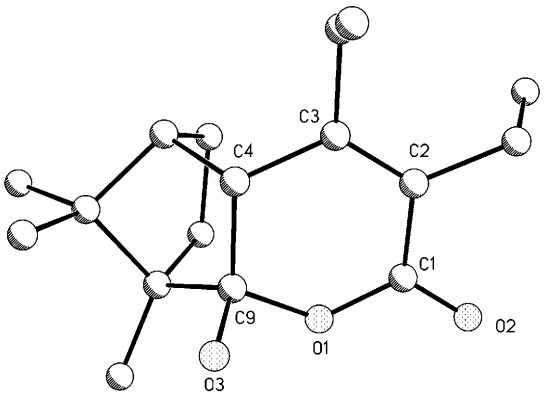


Figure 2 Molecular structure of **2f′** (hydrogen atoms are omitted for clarity, only one of two independent molecules shown). Selected bond lengths (Å) and angles (°): O1–C1 1.332(2), C1–C2 1.477(2), C2–C3 1.335(3), C3–C4 1.494(3), C4–C9 1.546(2), C9–O1 1.459(2), C1–O2 1.222(2), C9–O3 1.384(2), O1–C1–C2 120.49(16), C1–C2–C3 120.57(16), C2–C3–C4 122.19(16), C3–C4–C9 116.09(15), C9–O1–C1 123.57(13), C4–C9–O3 109.35(15), O1–C9–O3 105.86(14).

The nickelalactone **B**, the molecular structure of which is shown in Figure 3, was prepared by an oxidative addition/decarbonylation sequence of phthalic anhydride on (2,2′-bipyridyl)(η^4-cycloocta-1,5-diene)nickel [Ni(cod)(bipy)].[1c] The reaction of **B** was very similar to that of **A** and it reacted with α-bromo ketones to give benzoic acids **3** (Scheme 2, Table 2). Compared to **A**, the reactions of **B** with α-bromo ketones proceeded slowly; therefore longer reaction times were necessary. α-Chloro ketones did not react under usual reaction conditions, but if 2,9-dimethylphenanthroline is used as the supporting ligand for **B** instead of 2,2′-bipyridyl, conversion was observed (Table 2, entry 9). The isolated products crystallized in most cases as the keto acid, only **3h′** was isolated as the lactol.

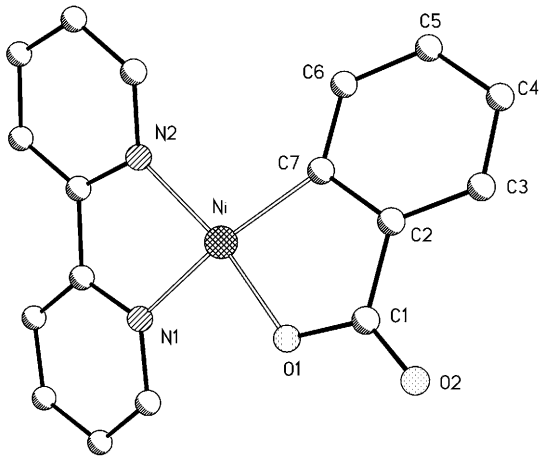
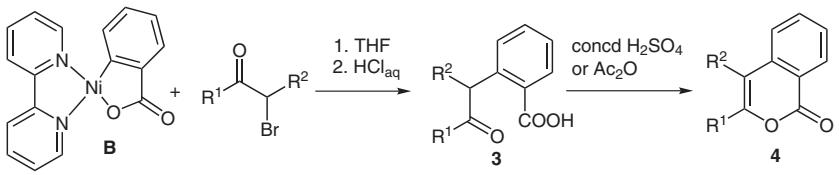


Figure 3 Molecular structure of **B** (hydrogen atoms are omitted for clarity, only one of two independent molecules shown). Selected bond lengths (Å) and angles (°): Ni–O1 1.857(2), Ni–N1 1.939(3), Ni–N2 1.904(3), Ni–C7 1.897(4), C7–C2 1.404(5), C2–C1 1.497(5), C1–O1 1.311(4), C1–O2 1.223(4), O1–Ni–C7 86.15(13), C7–Ni–N2 101.36(14), O1–Ni–N1 91.19(11), N1–Ni–N2 83.40(12), Ni–C7–C2 110.5(3), C7–C2–C1 113.9(3).

In the reaction of **1c** with the nickelalactone **B** a crystalline nickel containing intermediate **D** could be isolated as single crystals. Its X-ray structure (Figure 4) gave evidence for the pathway of the reaction: As expected, the attack of the α-halo ketone on the Ni–C bond resulted in the splitting of this bond with the formation of a new nickel–carboxylate complex with a bidentate coordinated carboxylate group, a Ni–Br bond, the chelating 2,2′-bipyridyl ligand, and an additional tetrahydrofuran ligand that form an octahedral environment around the nickel center.

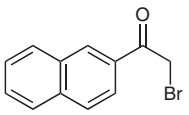
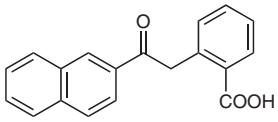
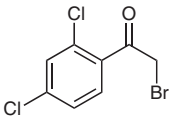
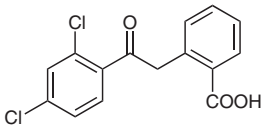
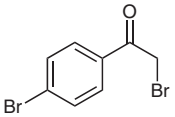
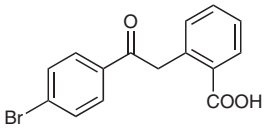
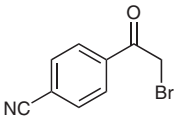
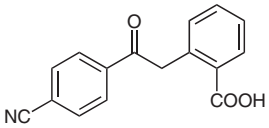
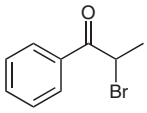
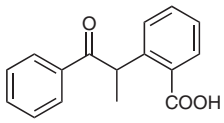
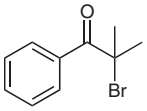
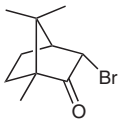
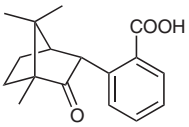
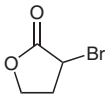
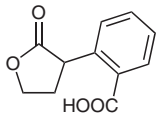
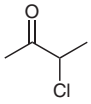
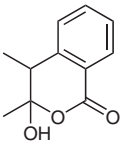
Compounds of the type **3** were readily transformed into the related isocoumarins **4** (Scheme 2) by cyclization with acetic anhydride or sulfuric acid[9] (see experimental section). In the case of **3a**, two different products were obtained depending on the reaction conditions. If acetic anhydride was used, the expected product, 3-(2-naphthyl)isocoumarin (**4a**), was obtained, while the use of sulfuric acid resulted in additional sulfonation of the naphthyl group giving the isocoumarin, 7-(1-oxo-1*H*-2-benzopyran-3-yl)naphthalene-1-sulfonic acid (**4aa**).

Compound **C** was prepared similar to **B**, by oxidative addition of phthalic anhydride to (2,2′-bipyridyl)(η^4-cycloocta-1,5-diene)nickel [Ni(cod)(bipy)].[1c] Decarbonylation was prevented by working at lower reaction temperatures. As shown in Scheme 3, the nickelalactone **C** with its six-membered ring contains a Ni–C(O) bond. Re-



Scheme 2

Table 2 Reaction of **B** with α-Halocarbonyl Compounds

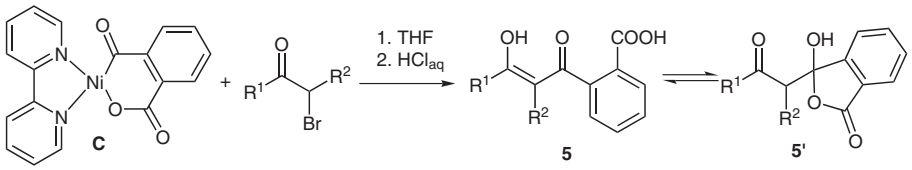
Entry	Substrate	Product	Conditions	Yield (%)
1	**1a** 	**3a** 	r.t., 48 h	79
2	**1b** 	**3b** 	r.t., 24 h	65
3	**1c** 	**3c** 	r.t., 24 h	72
4	**1d** 	**3d** 	r.t., 96 h	59
5	**1i** 	**3i** 	r.t., 72 h	82
6	**1e** 	–		
7	**1f** 	**3f** 	50 °C, 24 h	80
8	**1g** 	**3g** 	r.t., 240 h r.t., 24 h	63 43[a]
9	**1h** 	**3h′** 	r.t., 240 h r.t., 24 h	0 69[a]

[a] 2,9-Dimethylphenanthroline instead of 2,2′-bipyridyl was used as a ligand in complex **B**.

action of this bond with α-halo ketones resulted in the formation of the enol forms of 1,3-dicarbonyl compounds (**5a**, **5c**) if aryl-substituted α-bromo ketones are used. In deuterochloroform solution, an equilibrium was observed between **5c** and the corresponding benzofuranone derivative **5c′**. The use of α-bromo esters instead of α-bromo ketones results in exclusive formation of the cyclic form **5′** (Table 3, entries 3 and 4).

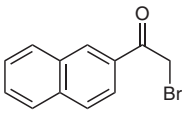
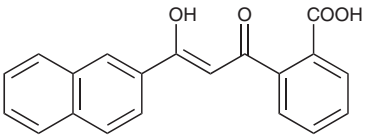
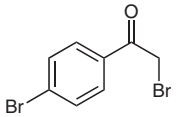
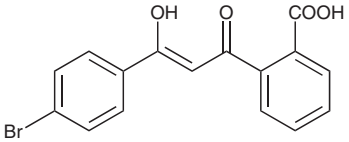
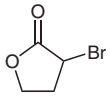
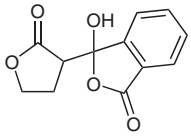
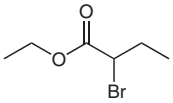
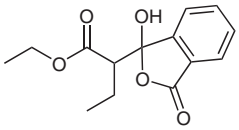
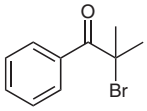
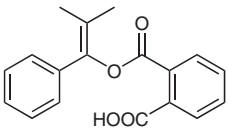
It is noteworthy that 2-bromo-2-methyl-1-phenylpropan-1-one (**1e**) reacted very different to form the monoester of phthalic acid with 2-methyl-1-phenylprop-1-enol (**6**). This may be the result of a radical reaction which starts with the homolytic splitting of the C–Br bond in **1e**, followed by reaction of the Ph–C(O˙)=Me_2 radical with the Ni–acyl bond of **C**.

In conclusion, the reaction between the nickelacyclic carboxylates **A**–**C** and α-halo ketones occurred under mild conditions and could be used for the synthesis of α,β-unsaturated δ-ketocarboxylic acids (**A** and **B** as building blocks) and for the preparation of 1,3-dicarbonyl compounds of benzoic acids (**C** as building blocks). Many substituents such as chloride or cyanide or ester groups were tolerated in these reactions.



Scheme 3

Table 3 Reaction of **C** with α-Halocarbonyl Compounds

Entry	Substrate	Product	Conditions	Yield (%)
1	**1a** 	**5a** 	r.t., 2 h	67
2	**1c** 	**5c** 	r.t., 30 min	73
3	**1g** 	**5g′** 	r.t., 5 min	67
4	**1k** 	**5k′** 	r.t., 5 min	69
5	**1e** 	**6** 	r.t., 5 min	n.d.[a]

[a] Not determined.

Melting points were measured with a Reichert–Jung apparatus Type 302102 and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at r.t. on a Bruker AC 200 MHz spectrometer. All spectra were referenced to deuterated solvent as an internal standard. FAB-MS were obtained on a Finnigan MAT SSQ 710 system (2,4-dimethoxybenzyl alcohol as matrix), IR measurements were carried out on a Perkin Elmer System 2000 FT-IR.

The coupling reactions with **A**, **B**, and **C** were carried out by using Schlenk techniques under an atmosphere of argon. Prior to use, THF was dried (KOH) and distilled (Na/benzophenone). Ac_2O was distilled prior to use. 2-Bromo-2′-acetonaphthone (**1a**), 2,4′-dibromoacetophenone (**1c**), 2-bromoisobutyrophenone (**1e**), (+)-[(1*R*)-*endo*]-3-bromocamphor (**1f**) and α-bromo-γ-butyrolactone (**1g**) were purchased from Aldrich, 3-chlorobutan-2-one (**1h**) from Lancaster, 2-bromo-4′-cyanoacetophenone (**1d**) from Acros Organics, and 2,4-dichlorophenacyl bromide (**1b**) from Fluorochem. These compounds were used without further purification. **A**, **B**, and **C** were prepared according to known procedures.[1e,7c]

If analytical data of known products are accessible, these substances were identified by comparing their mp and NMR spectra with those reported in the literature. For such substances only melting points are given.

Coupling Reactions with Organic Substrates; General Procedure

A red suspension (15 mL) of **A**, **B**, or **C** (1 mmol) and an α-halo ketone (1 mmol) in THF was stirred under an argon atmosphere. In one case (see Table 2) additional heating was necessary. When the reaction was complete as indicated by the green color of the suspension, the solvent was evaporated under reduced pressure. The residue was stirred for 1 h with dil aq HCl (20 mL) and extracted with $CHCl_3$ (2 × 20 mL). The combined organic phases were extracted with sat. aq Na_2CO_3 (2 × 20 mL). Then the combined aqueous solns were acidified (HCl) and extracted with $CHCl_3$ (3 × 20 mL). These organic layers were dried (anhyd Na_2SO_4) and the solvent was removed under vacuum to give the crude product. Further purification was achieved by recrystallization (in most cases from acetone/heptane).

Isocoumarins 4 by Dehydration; General Procedure

A soln (10 mL) of the substituted keto acid **3** (1 mmol) in Ac_2O was refluxed for 2 h, after which time the solvent was evaporated under reduced pressure to give the crude product as colorless solid. Further purification by recrystallization (acetone–heptane) gave isocoumarins as colorless crystals.

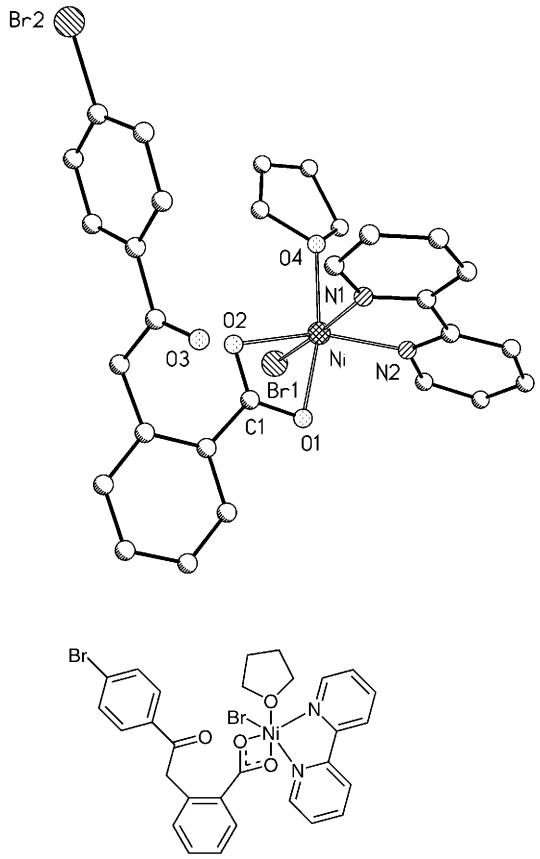


Figure 4 Molecular structure (top) and structural formula (bottom) of [NiBr(**3c**-H)(bipy)(thf)] (**D**) (hydrogen atoms are omitted for clarity). Selected bond lengths (Å) and angles (°): Ni–N1 2.076(4), Ni–N2 2.056(4), Ni–O1 2.069(4), Ni–O2 2.135(3), Ni–O4 2.098(5), Ni–Br1 2.5186, O1–C1 1.267(6), O2–C1 1.260(6), N1–Ni–N2 78.91(16), O1–Ni–O2 62.82(13), Br1–Ni–O4 90.60(13), Br1–Ni–O2 92.22(9), Br1–Ni–O1 92.83(10), N1–Ni–O1 93.41(15), N1–Ni–O2 91.76(14), N1–Ni–O4 83.67(17), O1–C1–O2 120.3(4).

3,4-Diethyl-6-hydroxy-6-(2-naphthyl)-5,6-dihydro-2*H*-pyran-2-one (2a′)

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.6 (CH_3^a), 12.2 (CH_3^b), 13.9 (CH_3^a), 14.0 (CH_3^b), 19.8 (CH_2^a), 22.7 (CH_2^b), 26.5 (CH_2^a), 28.4 (CH_2^b), 40.7 (CH_2^a), 43.6 (CH_2^b), 100.9 (C-OH^a), 122.9 (CH), 123.9 (CH), 124.3 (CH), 126.4 (CH), 126.6(0) (CH), 126.6(3) (CH), 126.9 (>C=^{a}), 127.5 (CH), 127.7 (CH), 128.3 (3 × CH), 128.5 (CH), 129.6 (CH), 129.8 (CH), 132.0 (>C=^{b}), 132.5 (C), 132.8 (C), 133.2 (C), 134.3 (C), 135.5 (C^b), 139.8 (C^a), 148.4 (=C<^{b}), 151.2 (=C<^{a}), 165.4 (COO^a), 173.0 (COO^b), 197.6 (C=O^b); ^{a} hydroxylactone form and ^{b} keto acid form are present in nearly equimolar amounts, so it was not possible to judge to which form a signal belongs in all cases.

MS (DEI): *m*/*z* (%) = 296 (15) [M]$^+$, 278 (4) [M – H_2O]$^+$, 250 (6) [M – H_2O – CO]$^+$, 155 (100), 127 (48) [naphthyl]$^+$, 124 (40).

Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.91; H, 6.80.

6-(2,4-Dichlorophenyl)-3,4-diethyl-6-hydroxy-5,6-dihydro-2*H*-pyran-2-one (2b′)

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): keto acid form: δ = 12.0 (CH_3), 14.0 (CH_3), 22.5(CH_2), 29.0 (CH_2), 48.0 (CH_2), 127.2 (CH phenyl), 130.1 (CH phenyl), 130.2 (CH phenyl), 131.5 (C phenyl), 131.6 (>C=), 136.9 (C phenyl), 137.9 (4-ClC), 148.9 (=C<), 172.6 (COO), 198.5 (C=O); hydroxylactone form: δ = 11.7 (CH_3), 13.9 (CH_3), 19.7 (CH_2), 26.6 (CH_2), 37.3 (CH_2), 99.8 (C-OH), 126.2 (>C=), 126.9 (3-CH phenyl), 128.9 (3-CH phenyl), 131.0 (2-CH phenyl), 132.8 (4-ClC phenyl), 135.2 (2-ClC phenyl), 137.4 (*i*-C phenyl), 152.2 (=C<), 165.3 (COO).

MS (DEI): *m*/*z* (%) = 315 (6) [M]$^+$, 297 (33) [M – H_2O]$^+$, 269 (9) [M – H_2O – CO]$^+$, 175 (52), 173 [2,4-$Cl_2C_6H_3$-C≡O]$^+$ (84), 124 (100).

Anal. Calcd for $C_{15}H_{16}Cl_2O_3$: C, 57.16; H, 5.12. Found: C, 56.96; H, 5.16.

6-(4-Bromophenyl)-3,4-diethyl-6-hydroxy-5,6-dihydro-2*H*-pyran-2-one (2c′)

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): keto acid form: δ = 12.1 (CH_3), 14.0 (CH_3), 22.6 (CH_2), 28.7 (CH_2), 43.5 (CH_2), 128.1 (4-BrC phenyl), 129.6 (2 × 2-CH phenyl), 131.8 (2 × 3-CH phenyl), 131.7 (>C=), 135.8 (*i*-C phenyl), 148.8 (=C<), 172.8 (COO), 196.4 (C=O); hydroxylactone form: δ = 11.6 (CH_3), 13.9 (CH_3), 19.7 (CH_2), 26.5 (CH_2), 40.7 (CH_2), 100.5 (C-OH), 122.9 (4-BrC phenyl), 126.8 (>C=), 127.0 (2 × 2-CH phenyl), 131.5 (2 × 3-CH phenyl), 141.8 (*i*-C phenyl), 151.3 (=C<), 165.4 (COO).

Anal. Calcd for $C_{15}H_{17}BrO_3$: C, 55.40; H ,5.27. Found: C, 55.28; H, 5.23.

6-(4-Cyanophenyl)-3,4-diethyl-6-hydroxy-5,6-dihydro-2*H*-pyran-2-one (2d′)

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): hydroxylactone form: δ = 11.6 (CH_3), 13.7 (CH_3), 19.6 (CH_2), 26.6 (CH_2), 40.5 (CH_2), 100.3 (C-OH), 112.6 (4-NC-C phenyl), 118.4 (CN), 126.2 (2 × 2-CH phenyl), 126.7 (>C=), 132.2 (2 × 3-CH phenyl), 147.5 (*i*-C phenyl), 151.6 (=C<), 165.5 (COO).

MS (DEI): *m*/*z* (%) = 272 (10) [M + 1]$^+$, 254 (32) [M – OH]$^+$, 225 (24) [M – H_2O – CO]$^+$, 130 (100), 130 (100) [NC-C_6H_4-C≡O]$^+$, 124 (88), 102 (55) [NC-C_6H_4]$^+$.

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N 5.16. Found: C, 70.70; H, 6.33; N, 4.92.

(1*R*,2*S*,7*R*,8*R*)-5,6-Diethyl-2-hydroxy-1,11,11-trimethyl-3-oxatricyclo[6.2.1.0^{2,7}]undec-5-en-4-one (2f′)

^{13}C NMR (50 MHz, $CDCl_3$): hydroxylactone form: δ = 9.1 (CH_3), 12.3 (CH_3), 14.2 (CH_3), 19.8 (CH_3), 20.1 (CH_2), 20.4 (CH_2), 20.6 (CH_3), 24.8 (CH_2), 29.8 (CH_2), 45.9 (C), 46.8 (CH), 48.2 (CH), 55.0 (C), 106.7 (C-OH), 127.1 (>C=), 154.1 (=C<), 163.8 (COO).

MS (DEI): *m*/*z* (%) = 279 (62) [M + 1]$^+$, 278 (27) [M]$^+$, 261 (100) [M – OH]$^+$, 260 (26) [M – H_2O]$^+$, 232 (14) [M – H_2O – CO]$^+$, 140 (15).

Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.30; H, 9.43.

(2*Z*)-2-Ethyl-3-(2-oxotetrahydrofuran-3-yl)pent-2-enoic Acid (2g)

^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.08 (m, ^3J = 7.6 Hz, 6 H, 2 × CH_3), 2.1–2.5 (m, 6 H, 3 × CH_2), 4.03 (dd, ^3J = 9.6 Hz, ^3J = 11.3 Hz, 1 H, CH), 4.22 (m, 1 H, C*H*H′), 4.41 (ddd, ^3J = 8.8 Hz, ^3J = 8.8 Hz, ^2J = 2.6 Hz, 1 H, CH*H*′), 10.2–10.6 (br, 1 H, COOH).

^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 13.3 (CH_3), 13.6 (CH_3), 23.0 (CH_2), 26.7 (CH_2), 28.9 (CH_2), 45.2 (CH), 66.6 (OCH_2), 133.1 (>C=), 148.1 (=C<), 173.5 (COO), 176.7 (COO).

MS (DEI): *m*/*z* (%) = 213 (5) [M + 1]$^+$, 194 (100) [M – H_2O]$^+$, 166 (81) [M – H_2O – CO]$^+$, 151 (72), 138 (48), 93 (65).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.33; H, 7.58.

3,4-Diethyl-6-hydroxy-5,6-dimethyl-5,6-dihydro-2*H*-pyran-2-one (2h′)

IR (KBr): 3343 (br, OH), 1673 cm^{-1} (s, C=O).

^1H NMR (200 MHz, $CDCl_3$, 25 °C): hydroxylactone form (major pair of diastereomers): δ = 1.02 (t, ^3J = 7.4 Hz, 3 H, CH_3), 1.09 (d, ^3J = 7.1 Hz, 3 H, CH_3), 1.11 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 2.02 (dq, ^2J = 14.2 Hz, ^3J = 7.6 Hz, 1 H, C*H*H′), 2.25–2.55 (m, 4 H, CH*H*′, CH_2, CH), 3.45 (br, 1 H, OH).

^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): hydroxylactone form (major pair of diastereomers): δ = 12.2 (CH_3), 14.0 (CH_3), 15.8 (CH_3), 19.8 (CH_2), 24.9 (CH_2), 25.7 (CH_3), 41.2 (CH), 102.1 (C-OH), 125.9 (>C=), 157.3 (=C<), 164.9 (COO).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.57; H, 9.25.

2-[2-(2-Naphthyl)-2-oxoethyl]benzoic Acid (3a)

Mp 160–162 °C.

IR (KBr): 3200–2800 (br, OH), 1685 (s, C=O), 1675 cm^{-1} (s, C=O).

^1H NMR (400 MHz, THF-d_8): δ = 4.92 (s, 2 H, CH_2), 7.30 (d, ^3J = 7.6 Hz, 1 H, CH), 7.34 (ddd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.47 (ddd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.51–7.61 (m, 2 H, CH Ph), 7.88–7.94 (m, 2 H, CH Ph), 8.03 (d, ^3J = 8.0 Hz, 1 H, CH), 8.06–8.11 (m, 2 H, CH Ph), 8.69 (s, 1 H, CH), 11.21 (br, 1 H, COOH).

^{13}C NMR (100 MHz, THF-d_8): δ = 45.3 (CH_2), 124.9 (CH), 127.2 (CH), 127.3 (CH), 128.4 (CH), 128.7 (2 × CH), 130.2 (2 × CH), 131.2 (C), 131.8 (CH), 132.4 (CH), 133.3 (CH), 133.7 (C), 136.0 (C), 136.4 (C), 138.8 (C), 168.5 (COO), 196.5 (>C=O).

MS (DEI): *m*/*z* (%) = 290 (8) $[M]^+$, 273 (3) $[M - OH]^+$, 155 (100) $[C_{10}H_7\text{-}CO]^+$, 127 (55) $[C_{10}H_7]^+$, 118 (18) $[\text{-}C_6H_4\text{-}CH_2\text{-}C(O)\text{-}]^+$, 77 (10).

Anal. Calcd for $C_{19}H_{14}O_3$: C, 78.60; H, 4.86. Found: C, 78.47; H, 5.01.

2-[2-(2,4-Dichlorophenyl)-2-oxoethyl]benzoic Acid (3b)

Mp 133–135 °C.

IR (KBr): 3200–2800 (br, OH), 1711 (s, C=O), 1679 (vs, C=O), 1083 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 4.63 (s, 2 H, CH_2), 7.28–7.33 (m, 2 H, CH), 7.43 (ddd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.43 (d, ^4J = 2.0 Hz, 1 H, CH), 7.54 (d, ^3J = 8.4 Hz, 1 H, CH), 7.58 (ddd, ^4J = 1.2, ^3J = 7.4 Hz, ^3J = 7.6 Hz, 1 H, CH), 8.14 (dd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, 1 H, CH), 10.50 (br, 1 H, COOH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.2 (CH_2), 127.3 (CH), 127.7 (CH), 128.0 (C), 130.3 (CH), 130.4 (CH), 131.9 (C), 132.0 (CH), 133.0 (CH), 133.6 (CH), 136.9 (C), 137.1 (C), 137.6 (C), 172.3 (COO), 198.5 (>C=O).

MS (DEI): *m*/*z* (%) = 308 (0.5) $[M(^{35}Cl,^{35}Cl)]^+$, 294 (0.5) $[M(^{37}Cl,^{37}Cl) - H_2O]^+$, 292 (1) $[M(^{37}Cl,^{35}Cl) - H_2O]^+$, 290 (1) $[M(^{35}Cl,^{35}Cl) - H_2O]^+$, 177 (6) $[OC\text{-}C_6H_3{}^{37}Cl_2]^+$, 175 (55) $[OC\text{-}C_6H_3{}^{37}Cl^{35}Cl]^+$, 173 (100) $[OC\text{-}C_6H_3{}^{35}Cl_2]^+$, 149 (3) $[C_6H_3{}^{37}Cl_2]^+$, 147 (9) $[C_6H_3{}^{37}Cl^{35}Cl]^+$, 145 (19) $[C_6H_3{}^{35}Cl_2]^+$, 118 (82) $[C_4H_6\text{-}CH_2\text{-}CO]^+$.

Anal. Calcd for $C_{15}H_{10}Cl_2O_3$: C, 58.28; H, 3.26. Found: C, 58.11; H, 3.28.

2-[2-(4-Bromophenyl)-2-oxoethyl)benzoic Acid (3c)

Mp 163–165 °C (Lit.[10] 162 °C).

2-[2-(4-Cyanophenyl)-2-oxoethyl]benzoic Acid (3d)

Mp 165–167 °C.

IR (KBr): 3200–2800 (br, OH), 2231 (s, C≡N), 1699 cm^{-1} (vs, C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 4.66 (s, 2 H, CH_2), 7.26 (d, ^3J = 7.2 Hz, 1 H, CH), 7.42 (ddd, ^4J = 1.0 Hz, ^3J = 7.8 Hz, ^3J = 8.0 Hz, 1 H, CH), 7.57 (ddd, ^4J = 1.4 Hz, ^3J = 7.4 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.78 (AA′BB′, 2 H, CH Ph), 8.09 (AA′BB′, 2 H, CH Ph), 8.10 (dd, ^4J = 1.2 Hz, ^3J = 8.0 Hz, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.2 (CH_2), 116.2 (CN), 118.0 (CCN), 127.8 (CH), 127.9 (C), 128.5 (2 × CH), 132.1 (CH), 132.5 (2 × CH), 132.8 (CH), 133.6 (CH), 137.0 (C), 140.3 (C), 170.9 (COO), 196.1 (>C=O).

MS (DEI): *m*/*z* (%) = 266 (1) $[M + H]^+$, 248 (5) $[M - OH]^+$, 130 (89) $[OC\text{-}C_6H_4\text{-}CN]^+$, 118 (100) $[C_6H_4\text{-}CH_2\text{-}CO]^+$, 102 (39) $[C_6H_4\text{-}CN]^+$.

Anal. Calcd for $C_{16}H_{11}NO_3$: C, 72.45; N, 5.28; H, 4.18. Found: C, 72.27; N, 5.26; H, 4.30.

2-[(1*R*,2*R*,4*R*)-4,7,7-Trimethyl-3-oxobicyclo[2.2.1]hept-2-yl]benzoic Acid (3f)

Mp 125 °C (dec.).

IR (KBr): 3200–2800 (br, OH), 2966 (s), 1724 (vs, C=O), 1687 (s, C=O), 1447 (m), 1373 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.00 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 1.15 (ddd, ^3J = 4.2 Hz, ^3J = 9.2 Hz, ^2J = 11.0 Hz, 1 H, CHH′), 1.46 (ddd, ^3J = 4.6 Hz, ^3J = 9.2 Hz, ^2J = 11.2 Hz, 1 H, CH*H*), 1.58–1.66 (m, 1 H, CHH′), 1.78 (ddd, ^3J = 4.0 Hz, ^2J = 12.0 Hz, 1 H, CH*H*), 2.45 (t, ^3J = 4.4 Hz, 1 H, CH), 4.88 (d, ^3J = 3.6 Hz, 1 H, CH), 7.10 (d, ^3J = 7.4 Hz, 1 H, CH), 7.33 (ddd, ^4J = 0.8 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.51 (ddd, ^4J = 1.6 Hz, ^3J = 7.2 Hz, ^3J = 7.6 Hz, 1 H, CH), 8.12 (dd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, 1 H, CH), 11.20 (br, 1 H, COOH)

^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.7 (CH_3), 19.3 (CH_3), 19.4 (CH_3), 21.0 (CH_2), 30.2 (CH_2), 46.1 (C), 49.7 (CH), 54.3 (CH), 59.6 (C), 126.8 (CH), 128.7 (C), 129.9 (CH), 132.3 (CH), 133.1 (CH), 140.4 (C), 172.6 (COO), 219.2 (CO).

MS (DEI): *m*/*z* (%) = 272 (55) $[M]^+$, 254 (39) $[M - H_2O]^+$, 244 (23) $[M - CO]^+$, 229 (31) $[M + 1 - CO_2]^+$, 226 (69) $[M - H_2O - CO]^+$, 211 (100) $[M + 1 - H_2O - CO_2]^+$.

Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.87; H, 7.38.

2-(2-Oxotetrahydrofuran-3-yl)benzoic Acid (3g)

Mp 153–155 °C.

IR (KBr): 3200–2800 (br, OH), 2925 (m), 1764 (s, C=O), 1709 cm^{-1} (vs, C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 2.30–2.55 (m, 1 H, CHH′), 2.69–2.87 (m, 1 H, CHH′), 4.31–4.57 (m, 2 H, CHH′-O), 4.70 (dd, ^3J = 9.2 Hz, ^3J = 11.0 Hz, 1 H, CH), 7.33 (dd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.41 (ddd, ^4J = 1.2 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.58 (ddd, ^4J = 1.6 Hz, ^3J = 7.5 Hz, ^3J = 7.6 Hz, 1 H, CH), 8.14 (dd, ^4J = 1.4 Hz, ^3J = 7.8 Hz, 1 H, CH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.8 (CH_2), 44.6 (CH), 66.7 (CH_2O), 127.9 (CH), 127.9 (C), 130.5 (CH), 132.3 (CH), 133.8 (CH), 139.4 (C), 171.5 (COO), 177.5 (COO).

MS (DEI): *m*/*z* (%) = 206 (3) $[M]^+$, 188 (100) $[M - H_2O]^+$, 147 (35) $[M - (CH_2\text{-}COO) - H]^+$, 77 (20) $[C_6H_5]^+$.

Anal. Calcd for $C_{11}H_{10}O_4$: C, 64.08; H, 4.89. Found: C, 64.19; H, 4.76.

3-Hydroxy-3,4-dimethyl-3,4-dihydroisocoumarin (3h′)

Mp 121–122 °C (Lit.[11] 119 °C).

IR (KBr): 3361 (vs, OH), 1708 (vs, C=O), 1691 cm^{-1} (vs, C=O).

^{1}H NMR (400 MHz, $CDCl_3$): major pair of diastereomers, hydroxylactone form: δ = 1.32 (d, ^3J = 7.2 Hz, 3 H, CH_3), 1.68 (s, 3 H, CH_3), 3.15 (q, ^3J = 7.2 Hz, 1 H, CH), 3.97 (br, 1 H, OH), 7.28 (d, ^3J = 8.0 Hz, 1 H, CH), 7.37 (ddd, ^4J = 0.8 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.56 (ddd, ^4J = 1.6 Hz, ^3J = 7.4 Hz, ^3J = 7.6 Hz, 1 H, CH), 8.07 (d, ^3J = 8.0 Hz, 1 H, CH); minor pair of diastereomers, hydroxylactone form: δ = 1.46 (d, ^3J = 7.2 Hz, 3 H, CH_3), 1.71 (s, 3 H, CH_3), 3.25 (q, ^3J = 7.2 Hz, 1 H, CH), 3.90 (br, 1 H, OH), 7.34–7.40 (m, 1 H, CH), 7.38 (t, ^3J = 7.6 Hz, 1 H, CH), 7.59 (ddd, ^4J = 1.6 Hz, ^3J = 7.4 Hz, ^3J = 7.6 Hz, 1 H, CH), 8.09 (d, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): major pair of diastereomers, hydroxylactone form: δ = 18.7 (CH_3), 25.5 (CH_3), 41.7 (CH), 104.6 (C-OH), 126.2 (C), 127.4 (CH), 127.5 (CH), 130.0 (CH), 134.3 (CH), 143.8 (C), 165.0 (COO).

MS (DEI): *m*/*z* (%) = 193 (5) $[M + 1]^+$, 175 (17) $[M – OH]^+$, 132 (100), 104 (51), 77 $[C_6H_5]^+$ (27), 43 (42).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.70; H, 6.36.

2-(1-Methyl-2-oxo-2-phenylethyl)benzoic Acid (3i)
Mp 106–108 °C.

IR (KBr): 3200–2800 (br, OH), 1705 (s, C=O), 1686 (vs, C=O), 1374 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): keto acid form: δ = 1.53 (d, ^3J = 6.8 Hz, 3 H, >$CHCH_3$), 5.87 (q, ^3J = 6.8 Hz, 1 H, >$CHCH_3$), 7.26 (d, ^3J = 8.0 Hz, 1 H, CH), 7.30 (ddd, ^4J = 0.8 Hz, ^3J = 7.6 Hz, ^3J = 7.9 Hz, 1 H, CH), 7.32–7.38 (m, 2 H, CH Ph), 7.41–7.45 (m, 1 H, CH Ph), 7.45 (ddd, ^4J = 1.6 Hz, ^3J = 7.4 Hz, ^3J = 7.6 Hz, 1 H, CH), 7.93–7.99 (m, 2 H, CH Ph), 8.10 (dd, ^4J = 1.4 Hz, ^3J = 7.6 Hz, 1 H, CH), 11.0 (br, 1 H, COOH).

^{13}C NMR (100 MHz, $CDCl_3$): keto acid form: δ = 18.9 (>$CHCH_3$), 43.9 (>$CHCH_3$), 126.8 (CH), 127.0 (C), 128.5 (2 × CH), 128.7 (2 × CH), 128.8 (CH), 132.2 (CH), 132.7 (CH), 133.7 (CH), 136.5 (C), 144.0 (C), 172.9 (COO), 201.1 (>C=O).

MS (DEI): *m*/*z* (%) = 255 (4) $[M + 1]^+$, 237 (52) $[M – OH]^+$, 208 (11) $[M – H_2O – CO]^+$, 132 (100) $[C_6H_5\text{-}CO\text{-}C(CH_3)]^+$, 105 $[C_6H_5\text{-}CO]^+$ (100), 77 (100) $[C_6H_5]^+$.

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.35; H, 5.57.

3-(2-Naphthyl)isocoumarin (4a)
Mp 161–163 °C.

IR (KBr): 1724 (vs, C=O), 1693 (m, C=O), 1636 cm^{-1} (C=C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (s, 1 H, HC=), 7.42–7.51 (m, 4 H, CH), 7.67 (ddd, ^4J = 1.2 Hz, ^3J = 7.8 Hz, ^3J = 8.4 Hz, 1 H, CH), 7.76–7.90 (m, 4 H, CH), 8.27 (d, ^3J = 8.0 Hz, 1 H, CH), 8.38 (s, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 102.1 (-HC=), 120.5 (C), 121.9 (CH), 125.2 (CH), 126.0 (CH), 126.8 (CH), 127.1 (CH), 127.6 (CH), 128.1 (CH), 128.5 (CH), 128.8 (CH), 128.9 (C), 129.6 (CH), 133.1 (C), 133.8 (C), 134.8 (CH), 137.5 (C), 153.5 (=C<), 162.3 (COO).

MS (DEI): *m*/*z* (%) = 272 (100) $[M]^+$, 244 (77) $[M – CO]^+$, 127 (23) $[C_{10}H_7]^+$.

Anal. Calcd for $C_{19}H_{12}O_2$: C, 83.80; H, 4.44. Found: C, 83.59; H, 4.22.

7-(1-Oxo-1*H*-2-benzopyran-3-yl)naphthalene-1-sulfonic Acid Dihydrate [4aa·(H_2O)$_2$]
Mp 120 °C (dec.).

IR (KBr): 3424 (vs, OH), 1731 (vs, C=O), 1636 (s, C=C), 1184 cm^{-1} (vs, SO).

^{1}H NMR (400 MHz, THF-d_8): δ = 5.17 (br, H_2O), 7.36 (s, 1 H, HC=), 7.54 (ddd, ^4J = 1.2 Hz, ^3J = 7.8 Hz, ^3J = 7.8 Hz, 1 H, CH), 7.59 (t, ^3J = 8.0 Hz, 1 H, CH), 7.68 (d, ^3J = 7.6 Hz, 1 H, CH), 7.77 (ddd, ^4J = 1.4 Hz, ^3J = 7.8 Hz, ^3J = 7.8 Hz, 1 H, CH), 8.06–8.15 (m, 3 H, CH), 8.25 (d, ^3J = 8.0 Hz, 1 H, CH), 8.28 (dd, ^4J = 1.0 Hz, ^3J = 7.6 Hz, 1 H, H8), 9.31 (s, 1 H, CH).

^{13}C NMR (100 MHz, THF-d_8): δ = 103.7 (-CH=), 121.8 (C), 123.4 (CH), 123.9 (CH), 126.1 (CH), 127.2 (CH), 129.1 (2 × CH), 129.4 (C), 129.9 (CH), 130.0 (CH), 132.1 (C), 133.7 (CH), 135.5 (CH), 135.5 (C), 138.3 (C), 138.4 (C), 154.1 (=C<), 161.7 (COO).

MS (DEI): *m*/*z* (%) = 352 (68) $[M]^+$, 324 (63) $[M – CO]^+$, 272 (61) $[M – SO_3]^+$, 244 (46) $[M – CO – SO_3]^+$, 215 (55).

Anal. Calcd for $C_{19}H_{16}O_7S$: C, 58.76; S, 8.25; H, 4.15. Found: C, 58.51; S, 8.23; H, 4.21.

3-(2,4-Dichlorophenyl)isocoumarin (4b)
Mp 146–148 °C.

IR (KBr): 1740 (s, C=O), 1699 (w, C=O), 1644 (m, C=C), 1051 cm^{-1} (m, C–Cl).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (s, 1 H, HC=), 7.34 (dd, ^4J = 2.0 Hz, ^3J = 8.4 Hz, 1 H, CH), 7.47–7.51 (m, 2 H, CH), 7.54 (t, ^3J = 7.6 Hz, 1 H, CH), 7.67 (d, ^3J = 8.4 Hz, 1 H, CH′), 7.74 (t, ^3J = 7.6 Hz, 1 H, CH), 8.31 (d, ^3J = 8.0 Hz, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 107.9 (-HC=), 120.7 (C), 126.3 (CH), 127.4 (CH), 128.9 (CH), 129.6 (CH), 130.1 (C), 130.5 (CH′), 131.3 (CH), 133.0 (C), 135.0 (CH), 136.0 (C), 136.7 (C), 150.3 (=C<), 162.0 (COO).

MS (DEI): *m*/*z* (%) = 294 (10) $[M(^{37}Cl,^{37}Cl)]^+$, 292 (52) $[M(^{35}Cl,^{37}Cl)]^+$, 290 (100) $[M(^{35}Cl,^{35}Cl)]^+$, 266 (6) $[M(^{37}Cl,^{37}Cl) – CO]^+$, 264 (41) $[M(^{37}Cl,^{35}Cl) – CO]^+$, 262 (74) $[M(^{35}Cl,^{35}Cl) – CO]^+$, 229 (18) $[M(^{37}Cl) – CO – Cl]^+$, 227 (51) $[M(^{35}Cl) – CO – Cl]^+$, 145 (10) $[C_9H_5O_2]^+$, 89 (30) $[C_6H_4\text{-}CH]^+$.

Anal. Calcd for $C_{15}H_8Cl_2O_2$: C, 61.88; H, 2.77. Found: C, 61.68; H, 2.66.

3-(4-Bromophenyl)isocoumarin (4c)
Mp 135–138 °C (Lit.[10] 132 °C).

(1*S*,4*R*)-4,11,11-Trimethyl-1,2,3,4-tetrahydro-1,4-methano-6*H*-dibenzo[*b*,*d*]pyran-6-one (4f)
Mp 150 °C (dec.).

IR (KBr): 2962 (s), 2876 (m), 1728 (vs, C=O), 1639 (vs, C=C), 1474 (w), 1375 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 1.09 (ddd, ^3J = 3.6 Hz, ^3J = 9.2 Hz, ^2J = 11.8 Hz, 1 H, CHH′), 1.21 (s, 3 H, CH_3), 1.32 (ddd, ^3J = 3.6 Hz, ^3J = 9.2 Hz, ^2J = 11.8 Hz, 1 H, CHH′), 1.81 (ddd, ^3J = 3.6 Hz, ^3J = 9.2 Hz, ^2J = 12.6 Hz, 1 H, CHH′), 2.04 (ddt, ^3J = 3.6 Hz, ^3J = 8.8 Hz, ^2J = 12.0 Hz, 1 H, CHH′), 2.98 (d, ^3J = 3.6 Hz, 1 H, CH), 7.32 (d, ^3J = 8.0 Hz, 1 H, CH), 7.35 (ddd, ^4J = 0.8 Hz, ^3J = 8.0 Hz, ^3J = 8.0 Hz, 1 H, CH), 7.66 (ddd, ^4J = 1.2 Hz, ^3J = 8.0 Hz, ^3J = 8.0 Hz, 1 H, CH), 8.27 (dd, ^4J = 0.8 Hz, ^3J = 8.0 Hz, 1 H, CH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.1 (CH_3), 19.3 (CH_3), 19.4 (CH_3), 26.0 (CH_2), 32.8 (CH_2), 48.0 (CH), 54.4 (C), 56.5 (C), 116.3 (>C=), 120.1 (C), 121.4 (CH), 126.1 (CH), 130.9 (CH), 134.7 (CH), 135.8 (C), 161.8 (=C<), 163.8 (COO).

MS (DEI): *m*/*z* (%) = 224 (30) $[M – 2 \times CH_3]^+$, 180 (100) $[M – CO_2 – 2 \times CH_3]^+$, 152 (45), 76 (20).

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.29; H, 7.13. Found: C, 80.02; H, 7.14.

4-Methyl-3-phenylisocoumarin (4i)
Mp 113–114 °C (Lit.[12] 109–113 °C).

2-[(2*Z*)-3-Hydroxy-3-(2-naphthyl)-1-oxoprop-2-enyl]benzoic Acid (5a)
Mp 169–171 °C.

IR (KBr): 3422 (s, OH), 3200–2800 (br, OH), 1696 (vs, C=O), 1625 cm^{-1} (s, C=C).

^{1}H NMR (400 MHz, THF-d_8): δ = 6.84 (s, 1 H,=CH-), 7.52–7.62 (m, 4 H, CH), 7.69 (dd, ^4J = 1.4 Hz, ^3J = 7.4 Hz, 1 H, CH), 7.85–7.93 (m, 3 H, CH), 8.00 (d, ^3J = 7.6 Hz, 1 H, CH), 8.04 (dd, ^4J = 1.6 Hz, ^3J = 8.8 Hz, 1 H, CH), 8.61 (s, 1 H, CH), 11.54 (br, 1 H, OH), 16.47 (br, 1 H, COOH).

^{13}C NMR (100 MHz, THF-d_8): δ = 97.7 (=CH-), 123.8 (CH), 127.4 (CH), 128.4 (CH), 128.7 (CH), 128.8 (CH), 128.9 (CH), 129.0 (CH), 130.0 (CH), 130.4 (CH), 130.9 (CH), 131.6 (CH), 132.7 (C), 132.9 (C), 133.8 (C), 136.3 (C), 139.8 (C), 168.5 (COO), 182.4 (=C-OH), 192.7 (>C=O).

MS (DEI): *m*/*z* (%) = 318 (48) $[M]^+$, 273 (56) $[M - CO_2 - H]^+$, 155 (100) $[C_{10}H_7\text{-}CO]^+$, 127 (72) $[C_{10}H_7]^+$.

Anal. Calcd for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.20; H, 4.61.

2-[(2*Z*)-3-(4-Bromophenyl)-3-hydroxy-1-oxoprop-2-enyl]benzoic Acid (5c)
Mp 141–143 °C.

IR (KBr): 3422 (s, OH), 3200–2800 (br, OH), 1697 (vs, C=O), 1654 (m, C=C), 1072 cm^{-1} (m, C–Br).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.45 (s, 1 H,=CH-), 7.51–7.62 (m, 2 H, CH), 7.58 (AA′BB′, 2 H, CH), 7.68–7,.75 (m, 1 H, CH), 7.74 (AA′BB′, 2 H, CH), 7.91 (d, ^3J = 7.6 Hz, 1 H, CH), 9.48 (br, 1 H, OH), 15.95 (br, 1 H, COOH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 96.6 (=CH-), 127.3 (C), 128.1 (CH), 128.6 (2 × CH), 129.8 (CH), 130.6 (CH), 130.9 (C), 131.9 (2 × CH), 132.2 (CH), 133.2 (C), 139.0 (C), 171.7 (COO), 181.0 (=C-OH), 197.9 (>C=O).

MS (DEI): *m*/*z* (%) = 348 (9) $[M(^{81}Br)]^+$, 346 (9) $[M(^{79}Br)]^+$, 331 (3) $[M(^{81}Br) - OH]^+$, 329 (4) $[M(^{79}Br) - OH]^+$, 303 (56) $[M(^{81}Br) - COOH]^+$, 301 (68) $[M(^{79}Br) - COOH]^+$, 185 (98) $[OC\text{-}C_6H_4\text{-}^{81}Br]^+$, 183 (100) $[OC\text{-}C_6H_4\text{-}^{79}Br]^+$, 149 (89) $[HOOC\text{-}C_6H_4\text{-}CO]^+$.

Anal. Calcd for $C_{16}H_{11}BrO_4$: C, 55.36; H, 3.19. Found: C, 55.55; H, 3.10.

3-Hydroxy-3-(2-oxotetrahydrofuran-3-yl)-2-benzofuran-1(3*H*)-one (5g′)
Mp 136–138 °C.

IR (KBr): 3351 (s, OH), 1766 (vs, C=O), 1750 (vs, C=O), 1467 cm^{-1} (m).

^{1}H NMR (400 MHz, THF-d_8): two pairs of diastereomers (1:1 mixture): δ = 2.34–2.61 (m, 4 H, 2 × CH_2), 3.22 (t, ^3J = 8.8 Hz, 1 H, CH), 3.52 (t, ^3J = 8.6 Hz, 1 H, CH), 4.11–4.40 (m, 4 H, 2 × CH_2O), 7.09 (br, 1 H, OH), 7.20 (br, 1 H, OH), 7.56–8.08 (m, 8 H, CH).

^{13}C NMR (100 MHz, THF-d_8): δ = 25.5 (CH_2), 25.8 (CH_2), 47.8 (CH), 48.0 (CH), 66.7(CH_2-O), 67.4 (CH_2-O), 105.7 (C-OH), 106.1 (C-OH), 123.5 (CH), 125.2 (CH), 125.3 (CH), 125.6 (CH), 128.3 (C), 128.7 (C), 131.0 (CH), 131.3 (CH), 134.8 (2 × CH), 149.0 (C), 149.4 (C), 167.4 (COO), 167.6 (COO), 173.5 (COO), 175.0 (COO).

MS (DEI): *m*/*z* (%) = 235 (25) $[M + 1]^+$, 217 (44) $[M - OH]^+$, 149 (100) $[HOOC\text{-}C_6H_4\text{-}CO]^+$, 105 (100) $[C_6H_5\text{-}CO]^+$, 86 (100) $[C_4H_6O_2]^+$.

Anal. Calcd for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.77; H, 4.18.

Ethyl 2-(1-Hydroxy-3-oxo-1,3-dihydro-2-benzofuran-1-yl)butanoate (5k′)
Mp 112–113 °C.

IR (KBr): 3283 (s, OH), 1742 (vs, C=O), 1733 (vs, C=O), 1466 (m), 1376 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): major pair of diastereomers: δ = 0.92 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.28 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.90 (quint, ^3J = 7.6 Hz, 2 H, CH_2), 2.73 (dd, ^3J = 5.6 Hz, ^3J = 9.6 Hz, 1 H, CH), 4.24 (q, ^3J = 7.2 Hz, 2 H, CH_2O), 6.05 (br, 1 H, OH), 7.54–7.59 (m, 1 H, CH), 7.63–7.70 (m, 2 H, CH), 7.84 (d, ^3J = 7.2 Hz, 1 H, CH); minor pair of diastereomers: δ = 0.85 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.27 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.71 (quint, ^3J = 7.6 Hz, 2 H, CH_2), 2.98 (dd, ^3J = 3.2 Hz, ^3J = 10.4 Hz, 1 H, CH), 4.24 (q, ^3J = 7.2 Hz, 2 H, CH_2O), 5.82 (br, 1 H, OH), 7.50 (d, ^3J = 7.6 Hz, 1 H, CH), 7.63–7.70 (m, 2 H, CH), 7.81–7.84 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): major pair of diastereomers: δ = 11.8 (CH_3), 14.1 (CH_3), 21.4 (CH_2), 54.2 (CH), 61.7 (CH_2O), 106.7 (C-OH), 124.0 (CH), 125.6 (CH), 127.5 (C), 130.9 (CH), 134.1 (CH), 146.5 (C), 167.6 (COO), 174.2 (COO); minor pair of diastereomers: δ = 12.4 (CH_3), 14.1 (CH_3), 20.2 (CH_2), 54.3 (CH), 61.8 (CH_2O), 106.2 (C-OH), 122.4 (CH), 125.5 (CH), 127.1 (C), 130.8 (CH), 134.6 (CH), 147.5 (C), 167.9 (COO), 172.4 (COO).

MS (DEI): *m*/*z* (%) = 265 (100) $[M + 1]^+$, 247 (98) $[M - OH]^+$, 149 (98) $[HOOC\text{-}C_6H_4\text{-}CO]^+$, 116 (81) $[Et\text{-}O\text{-}C(OH)\text{-}CH(Et)]^+$.

Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.69; H, 6.08.

Mono(2-methyl-1-phenylprop-1-enyl) Phthalate (6)
Mp 148–150 °C.

IR (KBr): 3200–2800 (br, OH), 1740 (vs, C=O), 1694 (vs, C=O), 1383 cm^{-1} (m).

^{1}H NMR (200 MHz, THF-d_8): δ = 1.83 (s, 3 H, CH_3), 1.86 (s, 3 H, CH_3), 7.19–7.37 (m, 3 H, CH), 7.41–7.49 (m, 2 H, CH), 7.51–7.58 (m, 2 H, CH), 7.67–7.78 (m, 2 H, CH), 11.50 (br, 1 H, COO).

^{13}C NMR (50 MHz, THF-d_8): δ = 18.5 (CH_3), 20.0 (CH_3), 122.7 (>C=), 128.3 (CH), 128.4 (2 × CH), 129.5 (CH), 129.7 (CH), 129.9 (2 × CH), 131.3 (CH), 131.5 (CH), 133.1 (C), 133.9 (C), 136.7 (C), 142.4 (=C-O), 165.5 (COO), 168.4 (COO).

MS (DEI): *m*/*z* (%) = 297 (6) $[M + 1]^+$, 148 (100) $[C_6H_5\text{-}C(OH)=C(CH_3)_2]^+$, 133 (100) $[C_6H_5\text{-}C(OH)=C(CH_3)]^+$, 105 (70) $[C_6H_5\text{-}CO]^+$.

Anal. Calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44. Found: C, 72.86, H, 5.46.

Crystal Structure Determination
The intensity data for the compounds were collected on a Nonius KappaCCD diffractometer, using graphite-monochromated Mo-Kα radiation. Data were corrected for Lorentz and polarization effects, but not for absorption effects.[13,14] The structures were solved by direct methods (SHELXS[15]) and refined by full-matrix least squares techniques against Fo^2 (SHELXL-97[16]). All hydrogen atoms of compounds **2a** and of the hydroxy groups of **2f′** were located by difference Fourier synthesis and refined isotropically. All other hydrogen atoms were included at calculated positions with fixed thermal parameters. All nonhydrogen atoms were refined anisotropically.[16] XP (Siemens Analytical X-ray Instruments, Inc.) was used for structure representations.

Crystal data for **2a**:[17] $C_{19}H_{20}O_3$, M_r = 296.35 g·mol^{-1}, colorless prism, size 0.10 × 0.09 × 0.09 mm^3, monoclinic, space group $P2_1/n$, a = 4.9198(2), b = 12.1826(4), c = 25.889(1) Å, β = 92.496(2)°, V = 1550.2(1) Å^3, T = –90 °C, Z = 4, $\rho_{calcd.}$ = 1.270 g·cm^{-3}, μ(Mo-Kα) = 0.85 cm^{-1}, F(000) = 632, 8952 reflections in h(–6/4), k(–15/15), l(–33/31), measured in the range 2.30 ≤ θ ≤ 27.51°, complete-

ness θ_{max} = 99.1%, 3540 independent reflections, R_{int} = 0.048, 2284 reflections with $F_o > 4\sigma(F_o)$, 279 parameters, 0 restraints, $R1_{obs}$ = 0.046, wR^2_{obs} = 0.106, $R1_{all}$ = 0.086, wR^2_{all} = 0.125, GOOF = 1.025, largest difference peak and hole: 0.152/–0.187 e·Å^{-3}.

Crystal data for **2f′**:[17] $C_{17}H_{26}O_3$, M_r = 278.38 g·mol^{-1}, colorless prism, size 0.32 × 0.32 × 0.22 mm^3, orthorhombic, space group $P2_12_12_1$, a = 13.1784(4), b = 14.4968(4), c = 16.7858(4) Å, V = 3206.8(1) Å^3, T = –90 °C, Z = 8, $\rho_{calcd.}$ = 1.153 g·cm^{-3}, μ(Mo-Kα) = 0.77 cm^{-1}, F(000) = 1216, 21743 reflections in h(–16/17), k(–18/18), l(–21/21), measured in the range 2.09° ≤ θ ≤ 27.48°, completeness θ_{max} = 99.6%, 7334 independent reflections, R_{int} = 0.039, 5391 reflections with $F_o > 4\sigma(F_o)$, 369 parameters, 0 restraints, $R1_{obs}$ = 0.047, wR^2_{obs} = 0.109, $R1_{all}$ = 0.075, wR^2_{all} = 0.124, GOOF = 1.008, Flack parameter 0.4(9), largest difference peak and hole: 0.432/–0.174 e·Å^{-3}.

Crystal data for **B**:[17] $C_{17}H_{12}N_2NiO_2$, M_r = 335.00 g·mol^{-1}, green or orange prism, size 0.03 × 0.03 × 0.02 mm^3, triclinic, space group P-1, a = 12.9307(6), b = 12.9653(5), c = 16.2353(4) Å, α = 85.546(2), β = 86.152(2), γ = 88.252(2)°, V = 2706.6(2) Å^3, T = –90 °C, Z = 8, $\rho_{calcd.}$ = 1.644 g·cm^{-3}, μ(Mo-Kα) = 14.42 cm^{-1}, F(000) = 1376, 19330 reflections in h(–13/16), k(–16/16), l(–20/21), measured in the range 1.58° ≤ θ ≤ 27.46°, completeness θ_{max} = 99.2%, 12278 independent reflections, R_{int} = 0.038, 8362 reflections with $F_o > 4\sigma(F_o)$, 793 parameters, 0 restraints, $R1_{obs}$ = 0.049, wR^2_{obs} = 0.110, $R1_{all}$ = 0.087, wR^2_{all} = 0.129, GOOF = 1.019, largest difference peak and hole: 1.405/–0.733 e·Å^{-3}.

Crystal data for **D**:[17] $C_{29}H_{26}Br_2N_2NiO_4$, M_r = 685.05 g·mol^{-1}, green prism, size 0.04 × 0.04 × 0.03 mm^3, triclinic, space group P-1, a = 10.2075(5), b = 12.0923(6), c = 14.1353(5) Å, α = 76.553(3), β = 70.056(3), γ = 79.315(3)°, V = 1584.3(1) Å^3, T = –90 °C, Z = 2, $\rho_{calcd.}$ = 1.436 g·cm^{-3}, μ(Mo-Kα) = 31.67 cm^{-1}, F(000) = 688, 11146 reflections in h(–13/11), k(–15/14), l(–15/18), measured in the range 3.12° ≤ θ ≤ 27.44°, completeness θ_{max} = 98.4%, 7127 independent reflections, R_{int} = 0.031, 5517 reflections with $F_o > 4\sigma(F_o)$, 323 parameters, 0 restraints, $R1_{obs}$ = 0.067, wR^2_{obs} = 0.198, $R1_{all}$ = 0.087, wR^2_{all} = 0.218, GOOF = 1.052, largest difference peak and hole: 1.651/–0.967 e·Å^{-3}.

Additionally, crystallographic data for compounds **A**, **2b′**, **2c′**, **2g**, **2h′**, **3a**, **3b**, **3d**, **3f**, **3g**, **3h′**, **4f**, **4i**, **5a**, **5c**, **5g′**, **6** (crystal structures not shown) are also available[17] and have been deposited with the Cambridge Crystallographic Data Centre, CCDC.

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References

(1) (a) Walther, D. *Coord. Chem. Rev.* **1987**, *79*, 135. (b) Echavarren, A. M.; Castaño, A. M. *Adv. Metal-Org. Chem.* **1998**, *6*, 1. (c) Langer, J.; Fischer, R.; Görls, H.; Walther, D. *J. Organomet. Chem.* **2004**, *689*, 2952. (d) Castaño, A. M.; Echavarren, A. M. *Organometallics* **1994**, *13*, 2262. (e) Uhlig, E.; Fehske, G.; Nestler, B. *Z. Anorg. Allg. Chem* **1980**, *465*, 141.

(2) (a) Fischer, R.; Nestler, B.; Schütz, H. *Z. Anorg. Allg. Chem.* **1989**, *577*, 11. (b) Fischer, R.; Walther, D.; Bräunlich, G.; Undeutsch, B.; Ludwig, W.; Bandmann, H. *J. Organomet. Chem.* **1992**, *427*, 395. (c) Hoberg, H.; Schaefer, D.; Burkhart, G. *J. Organomet. Chem.* **1982**, *228*, C21. (d) Bräunlich, G.; Fischer, R.; Nestler, B.; Walther, D. *Z. Chem.* **1989**, *29*, 417. (e) Hoberg, H.; Ballesteros, A.; Sigan, A.; Jégat, C.; Milchereit, A. *Synthesis* **1991**, 395.

(3) (a) Schönecker, B.; Walther, D.; Fischer, R.; Nestler, B.; Bräunlich, G.; Eibisch, H.; Droeschler, P. *Tetrahedron Lett.* **1990**, *31*, 1257. (b) Bräunlich, G.; Walther, D.; Eibisch, H.; Schönecker, B. *J. Organomet. Chem.* **1993**, *453*, 295. (c) Fischer, R.; Schönecker, B.; Walther, D. *Synthesis* **1993**, 1267.

(4) (a) Hoberg, H.; Schaefer, D.; Burkhart, G.; Krüger, C.; Romão, M. S. *J. Organomet. Chem.* **1984**, *266*, 203. (b) Yamamoto, T.; Igarashi, K.; Komiya, S.; Yamamoto, A. *J. Am. Chem. Soc.* **1980**, *102*, 7448. (c) Hoberg, H.; Ballesteros, A.; Sigan, A.; Jégat, C.; Bärhausen, D.; Milchereit, A. *J. Organomet. Chem.* **1991**, *407*, C23.

(5) (a) Hoberg, H.; Apotecher, B. *J. Organomet. Chem.* **1984**, *270*, C15. (b) Behr, A.; Kanne, U. *J. Organomet. Chem.* **1986**, *317*, C41.

(6) (a) Castaño, A. M.; Echavarren, A. M. *Tetrahedron Lett.* **1993**, *34*, 4361. (b) Echavarren, A. M.; Castaño, A. M. *Tetrahedron* **1995**, *51*, 2369.

(7) (a) Hoberg, H.; Peres, Y.; Krüger, C.; Tsay, Y. T. *Angew. Chem.* **1987**, *99*, 799. (b) Hoberg, H.; Schaefer, D. *J. Organomet. Chem.* **1982**, *238*, 383. (c) Walther, D.; Schönberg, H.; Dinjus, E.; Sieler, J. *J. Organomet. Chem.* **1987**, *334*, 377. (d) Tsuda, T.; Morikawa, S.; Sumiya, R.; Saegusa, T. *J. Org. Chem.* **1988**, *53*, 3140. (e) Tsuda, T.; Morikawa, S.; Hasegawa, N.; Saegusa, T. *J. Org. Chem.* **1990**, *55*, 2978. (f) Walther, D.; Bräunlich, G.; Kempe, R.; Sieler, J. *J. Organomet. Chem.* **1992**, *436*, 109.

(8) (a) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895. (b) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008. (c) O'Brien, E. M.; Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2003**, *125*, 10498.

(9) (a) For a review, see: Napolitano, E. *Org. Prep. Proced. Int.* **1997**, *29*, 631. (b) Tirodkar, R. B.; Usgaonkar, R. N. *Indian J. Chem.* **1970**, *8*, 123. (c) Hussain, A.; Nasim, H.; Muhammad, T.; Malik, A. *Indian J. Heterocycl. Chem.* **1999**, *8*, 189.

(10) Hussain, M. T.; Rama, N. H.; Malik, A. *Indian J. Chem., Sect. B* **2001**, *40*, 372.

(11) Heller, G. *Chem. Ber.* **1935**, *68*, 1085.

(12) Rossi, R.; Carpita, A.; Bellina, F.; Stabile, P.; Mannina, L. *Tetrahedron* **2003**, *59*, 2067.

(13) *COLLECT, Data Collection Software*, Nonius B.V., Netherlands, 1998.

(14) Otwinowski, Z.; Minor, W. *Processing of X-Ray Diffraction Data Collected in Oscillation Mode,* In *Methods in Enzymology*, Vol. 276; Carter, C. W.; Sweet, R. M., Eds.; Academic Press: San Diego, **1997**, 307–326.

(15) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467.

(16) Sheldrick, G. M. SHELXL-97 (Release 97-2), University of Göttingen, Germany, 1997.

(17) CCDC-602921 (**A**), CCDC-602922 (**B**), CCDC-602923 (**D**), CCDC-602924 (**2a**), CCDC-602925 (**2b′**), CCDC-602926 (**2c′**), CCDC-602927 (**2f′**), CCDC-602928 (**2g**), CCDC-602929 (**2h′**), CCDC-602930 (**3a**), CCDC-602931 (**3b**), CCDC-602932 (**3d**), CCDC-602933 (**3f**), CCDC-602934 (**3g**), CCDC-602935 (**3h′**), CCDC-602936 (**4f**), CCDC-602937 (**4i**), CCDC-602938 (**5a**), CCDC-602939 (**5c**), CCDC-602940 (**5g′**) and CCDC-602941 (**6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK, fax: +44(1223)336033; or deposit@ccdc.cam.ac.uk].