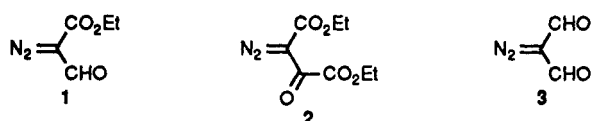


Simple Syntheses of  $\beta$ -Furoic Esters and  $\gamma$ -PyroneErnest Wenkert,\* T. P. Ananthanarayan, Vitor F. Ferreira,<sup>1</sup> Michael G. Hoffmann,<sup>2</sup> and HongSeok Kim

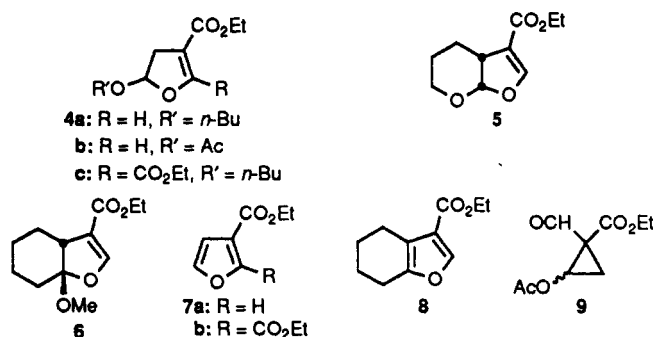
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As part of a broad study of the use of  $\beta$ -oxycyclopropylcarbonyl compounds, prepared by the transition-metal-catalyzed decomposition of  $\alpha$ -diazocarbonyl compounds in the presence of enol derivatives, in organochemical synthesis<sup>3</sup> it was shown some time ago that, contrastingly, the decomposition of  $\alpha$ -diazo- $\beta$ -dicarbonyl compounds under similar conditions led to dihydrofurans, which were convertible readily into  $\beta$ -acylfurans.<sup>4</sup> In order to explore the generality of this experience, it was decided to study this two-step furan synthesis with the use of the least substituted  $\alpha$ -diazo- $\beta$ -dicarbonyl compounds, i.e., ethyl formyldiazoacetate (1),<sup>5</sup> diethyl oxalyldiazoacetate (2),<sup>6</sup> and diazomalonaldehyde (3).<sup>7</sup>



**$\beta$ -Furoic Esters.** The reactions of ethyl formyldiazoacetate (1) with *n*-butyl vinyl ether and with dihydropyran at 55 °C, catalyzed by dirhodium tetraacetate, gave dihydrofuroates 4a and 5 in 78 and 75% yields, respectively.

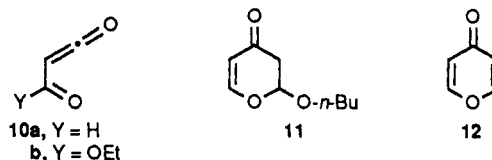


The same type of reaction between the diazo compound and 1-methoxycyclohexene did not succeed, but uncatalyzed decomposition of the diazoester in the enol ether at 115 °C afforded dihydrofuroate 6 (19% yield). Alcohol elimination from the dihydrofuroic esters 4a and 6, catalyzed by sulfuric acid in refluxing carbon tetrachloride, produced  $\beta$ -furoates 7a<sup>8</sup> and 8 (41% and 85% yields, respectively). When a rhodium-catalyzed reaction of the diazo compound was performed at 55 °C on vinyl acetate,

it resulted in the formation of dihydrofuroate 4b (13%) and an isomer mixture of cyclopropanes 9 (17%).<sup>9</sup> The latter was converted into the former product in refluxing carbon tetrachloride (80%). Refluxing the 4b-9 mixture or the dihydrofuroate 4b alone in glacial acetic acid yielded ethyl  $\beta$ -furoate (7a)<sup>8</sup> (32 and 44% yields, respectively). Finally, exposure of diethyl oxalyldiazoacetate (2) to refluxing *n*-butyl vinyl ether in the presence of the rhodium catalyst led in 95% yield to dihydrofuroate 4c, whose treatment with acid gave diethyl furan-2,3-dicarboxylate (7b) (42% yield).

**$\gamma$ -Pyrone.** Whereas diazomalonaldehyde (3) has revealed chemical behavior related to that of its  $\alpha$ -diazo- $\beta$ -dicarbonyl equivalents 1 and 2,<sup>10</sup> its full discussion must await a future communication. However, in the meantime it is worth commenting on the uncatalyzed thermochemistry of the dialdehyde, which has proved to be interesting and useful for synthesis and whose investigation emanated from observations at an early stage of the present study, i.e., at a time when copper or its salts were the popular catalysts for the decomposition of  $\alpha$ -diazocarbonyl compounds and elevated temperatures were required for efficient reactions to take place.<sup>3,4</sup> When diazomalonaldehyde was caused to react with enol ethers under these conditions, a side product tended to accompany the expected dihydrofurans. On the assumption of the side product being the result of an uncatalyzed, thermal process, the following study was undertaken.

Decomposition of diazo compound 3 in refluxing *n*-butyl vinyl ether produced dihydro- $\gamma$ -pyrone 11 (70% yield). Presumably, dediazotization of the starting material had been accompanied by a hydrogen 1,2-shift, yielding formylketene (10a),<sup>11,12</sup> whose cycloaddition (a hetero Diels-Alder reaction of inverse electron demand) with the enol ether had liberated the six-membered heterocycle 11. Treatment of the latter with acid furnished  $\gamma$ -pyrone (12)<sup>13</sup> (96% yield).

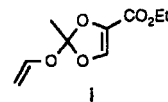


## Experimental Section

UV and IR spectra were recorded as methanol solutions and liquid films, respectively. <sup>1</sup>H NMR spectra of CDCl<sub>3</sub> solutions were obtained at 90 or 360 MHz and <sup>13</sup>C NMR spectra of CDCl<sub>3</sub> solutions at 50.31 MHz. All reactions were carried out under a nitrogen atmosphere.

**Ethyl 5-*n*-Butoxy-4,5-dihydro-3-furancarboxylate (4a).** A solution of 1.00 g (7.0 mmol) of ethyl formyldiazoacetate (1) in

(9) A fourth product (8% yield) proved to be the carbonyl addition compound i: <sup>1</sup>H NMR  $\delta$  (CCl<sub>4</sub>) 1.30 (t, 3, *J* = 7 Hz, ethoxy Me), 1.75 (s, 3, Me), 4.23 (q, 2, *J* = 7 Hz, OCH<sub>2</sub>), 4.17, 4.34, 4.58, 4.74, 6.14, 6.21, 6.30, 6.37 (8-line, 3, vinyl Hs), 7.01 (s, 1, acrylate  $\beta$ -H); <sup>13</sup>C NMR  $\delta$  (CDCl<sub>3</sub>) 14.1 (ethoxy Me), 23.4 (Me), 61.0 (OCH<sub>2</sub>), 97.0 (vinyl  $\beta$ -C), 126.3 (O<sub>3</sub>C), 132.4 ( $\alpha$ -keto C), 135.1 (acrylate  $\beta$ -C), 142.3 (OCH), 158.6 (C=O).



(10) Wenkert, E.; Ferreira, V. F. Unpublished observations. Ferreira, V. F. Ph.D. Dissertation, University of California—San Diego, La Jolla, CA, 1984.

(11) For a photolytic 3  $\rightarrow$  10a conversion, see: Maier, G.; Reisenauer, H. P.; Sayrac, T. *Chem. Ber.* 1982, 115, 2192.

(12) The formation of ethyl methyl malonate on decomposition of diazo compound 1 in refluxing methanol (for several days) indicates the intermediacy of an acylketene (i.e., 10b) also in this dediazotization.

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(1) Conselho Nacional de Pesquisas (Brazil) predoctoral fellowship holder, 1980-1984.

(2) Deutsche Forschungsgemeinschaft (West Germany) postdoctoral fellowship holder, 1985-1986.

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(8) (a) Kubota, T.; Matsuura, T. *J. Chem. Soc.* 1958, 3667. (b) Sornay, R.; Meunier, J.-M.; Fournari, P. *Bull. Soc. Chim. Fr.* 1971, 990.

5 mL of *n*-butyl vinyl ether was added dropwise over an 8-h period to a stirring mixture of 10 mg of dirhodium tetraacetate and 10 mL of *n*-butyl vinyl ether at 55 °C, and the stirring continued at this temperature for 16 h. The mixture was concentrated under vacuum at 30 °C to a 3-mL volume and filtered through a Florisil pad. The latter was washed with methylene chloride, and the combined filtrate and washings were evaporated under vacuum. Chromatography of the residue on silica gel and elution with 4:1 hexane-ethyl acetate afforded 1.17 g (78%) of colorless, liquid ester **4a**: UV  $\lambda_{\max}$  245 nm ( $\epsilon$  9300); IR C=O 1700 (s), C=C 1625 (s)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  ( $\text{CCl}_4$ ) 0.90 (t, 3,  $J$  = 7 Hz, butyl Me), 1.25 (t, 3,  $J$  = 7 Hz, ester Me), 1.4–1.8 (m, 4, 2  $\text{CH}_2$ ), 2.5–3.1 (m, 2, 2 H-4), 3.4–3.9 (m, 2,  $\text{OCH}_2$ ), 4.15 (q, 2,  $J$  = 7 Hz, ester  $\text{OCH}_2$ ), 5.60 (dd, 1,  $J$  = 7, 4 Hz, H-5), 7.15 (t, 1,  $J$  = 2 Hz, H-2). Anal. Calcd for  $\text{C}_{11}\text{H}_{18}\text{O}_4$ : C, 61.66; H, 8.47. Found: C, 61.53; H, 8.40.

**Ethyl 2,9-Dioxabicyclo[4.3.0]non-7-ene-7-carboxylate (5).** The same reaction and workup on 1.00 g (7.0 mmol) of diazo ester **1** and 10 mL of anhydrous dihydropyran led to 1.04 g (75%) of colorless, liquid ester **5**: UV  $\lambda_{\max}$  250 nm ( $\epsilon$  5500); IR C=O 1700 (s), C=C 1625 (s)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  ( $\text{CCl}_4$ ) 1.25 (t, 3,  $J$  = 7 Hz, Me), 1.5–2.0 (m, 4, 2  $\text{CH}_2$ ), 2.8–3.1 (m, 1, H-6), 3.75 (t, 2,  $J$  = 7 Hz,  $\text{OCH}_2$ ), 4.10 (q, 2,  $J$  = 7 Hz, ester  $\text{OCH}_2$ ), 5.80 (d, 1,  $J$  = 8 Hz, H-1), 7.25 (d, 1,  $J$  = 2 Hz, H-8);  $^{13}\text{C NMR}$   $\delta$  14.0 (Me), 19.0 (C-5), 20.7 (C-4), 35.9 (C-6), 59.3 (C-3), 60.1 (ester  $\text{OCH}_2$ ), 106.5 (C-1), 112.4 (C-7), 155.6 (C-8), 164.3 (C=O). Anal. Calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_4$ : C, 60.59; H, 7.12. Found: C, 60.50; H, 7.04.

**Ethyl 7a-Methoxy-3a,4,5,6,7,7a-hexahydrobenzofuran-3-carboxylate (6).** A solution of 775 mg (5.5 mmol) of diazo ester **1** in 5 mL of 1-methoxycyclohexene was added dropwise over a 10-h period to 15 mL of enol ether under nitrogen at 115 °C, and the heating was continued for 12 h. The solution was evaporated under ca. 5 Torr vacuum at room temperature. Chromatography of the residue on silica gel and elution with 10:1 hexane-ethyl acetate gave 410 mg (19%) of colorless, liquid ester **6**: IR ( $\text{CCl}_4$ ) C=O 1702 (s), C=C 1618 (s)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  ( $\text{CCl}_4$ ) 1.26 (t, 3,  $J$  = 7 Hz, Me), 1.2–2.1 (m, 8, 4  $\text{CH}_2$ ), 2.83 (t, 1,  $J$  = 6 Hz, H-3a), 3.23 (s, 3, OMe), 4.12 (q, 2,  $J$  = 7 Hz,  $\text{OCH}_2$ ), 7.13 (d, 1,  $J$  = 2 Hz, H-2);  $^{13}\text{C NMR}$   $\delta$  14.2 (Me), 18.3 (C-5 or C-6), 18.5 (C-6 or C-5), 26.0 (C-4), 28.4 (C-7), 43.5 (C-3a), 49.1 (OMe), 59.5 ( $\text{OCH}_2$ ), 114.2 (C-3 or C-7a), 114.7 (C-7a or C-3), 154.5 (C-2), 164.6 (C=O); exact mass  $m/e$  226.1200 (calcd for  $\text{C}_{12}\text{H}_{18}\text{O}_4$ ,  $m/e$  226.1205).

**Ethyl 3-Furancarboxylate (7a).** A solution of 1.30 g (6.1 mmol) of ester **4a** in 10 mL of carbon tetrachloride was added dropwise to a stirring mixture of 200 mg of concentrated sulfuric acid in 140 mL of carbon tetrachloride at 75 °C over a 3-h period, and the heating was continued for 2 h. The mixture was washed with water, 5% sodium bicarbonate solution, and water again, dried ( $\text{MgSO}_4$ ), and evaporated. Chromatography of the residue on silica gel and elution with 6:1 hexane-ethyl acetate produced 348 mg (41%) of colorless, liquid ester **7a**: IR C=O 1720 (s), C=C 1573 (m), 1502 (m)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$ , identical with the literature data.<sup>8</sup>

A solution of 1.75 g (12.3 mmol) of diazo ester **1** in 10 mL of freshly distilled vinyl acetate was added dropwise over an 8-h period of a stirring mixture of 10 mg of dirhodium tetraacetate and 40 mL of vinyl acetate at 55 °C and the stirring continued at this temperature for 20 h. The mixture was concentrated to 5-mL volume under vacuum at 30 °C and filtered through a Florisil pad. The latter was washed with methylene chloride, and the filtrate and washings were combined and evaporated. Chromatography of the residue on silica gel and elution with 6:1 hexane-ethyl acetate led in the early fractions to 200 mg (8%) of ester **1**<sup>9</sup> and then to 185 mg (8%) of a colorless, liquid cyclopropane ester **9** [ $^1\text{H NMR}$   $\delta$  ( $\text{CCl}_4$ ) 1.1–1.4 (m, 1, *c*-Pr H), 1.30 (t, 3,  $J$  = 7 Hz, Me), 1.8–2.2 (m, 2, *c*-Pr Hs), 2.00 (s, 3, COMe), 4.30 (q, 2,  $J$  = 7 Hz,  $\text{OCH}_2$ ), 10.30 (s, 1, CHO);  $^{13}\text{C NMR}$   $\delta$  14.1 (ethoxy Me), 20.3 ( $\text{CH}_2$ ), 21.6 (acetyl Me), 39.8 ( $\alpha$ -keto C), 61.7 ( $\text{OCH}$ ), 62.6 ( $\text{OCH}_2$ ), 166.5 (ester C=O), 170.1 (acetyl C=O), 196.4 (CH=O)] and, finally, to 520 mg (22%) of a 1.4:1 liquid mixture of esters **4b** [ $^1\text{H NMR}$   $\delta$  ( $\text{CCl}_4$ ) 1.27 (t, 3,  $J$  = 7 Hz, ethoxy Me), 2.05 (s, 3, acetyl Me), 2.5–3.2 (m, 2,  $\text{CH}_2$ ), 4.10 (q, 2,  $J$  = 7 Hz,  $\text{OCH}_2$ ), 6.65 (dd, 1,  $J$  = 7, 4 Hz,  $\text{OCHO}$ ), 7.10 (t, 1,  $J$  = 2 Hz, olefinic H)] and **9** (other isomer) [ $^1\text{H NMR}$   $\delta$  1.1–2.4 (m, 3, *c*-Pr Hs), 1.34 (t, 3,  $J$  = 7 Hz, ethoxy Me), 1.94 (s, 3, acetyl Me), 4.26 (q, 2,  $J$  = 7 Hz,  $\text{OCH}_2$ ), 10.02 (s, 1, CHO)]. A solution of the three-ester **4b–9** mixture in 30 mL of carbon tetrachloride was

refluxed for 72 h and then evaporated. Chromatography of the residue and fast elution with 9:1 hexane-ethyl acetate gave 564 mg (80%) of liquid ester **4b** [UV  $\lambda_{\max}$  239 nm ( $\epsilon$  9600); IR C=O 1740 (s), 1700 (s), C=C 1625 (s)  $\text{cm}^{-1}$ ].

A solution of 444 mg (2.3 mmol) of a **4b–9** mixture in 7 mL of glacial acetic acid was refluxed for 72 h and then concentrated to dryness under vacuum. Chromatography of the residue on silica gel and elution with 9:1 hexane-ethyl acetate afforded 98 mg (32%) of liquid ester **7a**. The same reaction on 450 mg (2.4 mmol) of ester **4b** in 10 mL of glacial acetic acid for 40 h and the same workup led to 135 mg (44%) of liquid ester **7a**.

**Ethyl 4,5,6,7-Tetrahydrobenzofuran-3-carboxylate (8).** A mixture of 77 mg (3.4 mmol) of ester **6** and one drop of concentrated sulfuric acid in 15 mL of carbon tetrachloride was refluxed for 1 h. Workup as in the above preparation of ester **7a** gave 56 mg (85%) of colorless, liquid ester **8**: IR C=O 1715 (s), C=C 1538 (m)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  ( $\text{CCl}_4$ ) 1.30 (t, 3,  $J$  = 7 Hz, Me), 1.5–1.9 (m, 4, 2  $\text{CH}_2$ ), 2.3–2.7 (m, 4, 2 allyl  $\text{CH}_2$ ), 4.20 (q, 2,  $J$  = 7 Hz,  $\text{OCH}_2$ ), 7.65 (s, 1, H-2); exact mass  $m/e$  194.0946 (calcd for  $\text{C}_{11}\text{H}_{14}\text{O}_3$ :  $m/e$  194.0943).

**Diethyl 5-*n*-Butoxy-4,5-dihydrofuran-2,3-dicarboxylate (4c).** A solution of 1.10 g (5.1 mmol) of diethyl oxalodiazooacetate in 10 mL of *n*-butyl vinyl ether was added over a 10-min period to a stirring, refluxing solution of 16 mg of dirhodium tetraacetate in 40 mL of the same ether, and the mixture then heated for another 45 min. It was concentrated under vacuum to a volume of 4 mL and passed through a column of silica gel. Elution with 4:1 hexane-ethyl acetate yielded 1.40 g (95%) of liquid, pale yellow ester **4c**: IR ( $\text{CCl}_4$ ) C=O 1735 (s), 1700 (s), C=C 1640 (m)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  0.90 (t, 3,  $J$  = 6 Hz, Me), 1.25, 1.36 (t, 3 each,  $J$  = 6 Hz, 2 ethoxy Me), 1.3–1.9 (m, 4, methylenes), 2.6–3.3 (m, 2, furan  $\text{CH}_2$ ), 3.65 (m, 2, butoxy  $\text{OCH}_2$ ), 4.10, 4.25 (q, 2 each,  $J$  = 6 Hz, 2  $\text{OCH}_2$ ), 5.61 (dd, 1,  $J$  = 7, 4 Hz,  $\text{O}_2\text{CH}$ ). Anal. Calcd for  $\text{C}_{14}\text{H}_{22}\text{O}_6$ : C, 58.74; H, 7.75. Found: C, 59.00; H, 7.80.

**Diethyl Furan-2,3-dicarboxylate (7b).** A mixture of 160 mg (0.56 mmol) of ester **4c** and two drops of concentrated sulfuric acid in 10 mL of carbon tetrachloride was refluxed for 15 min, then cooled, and poured into 15 mL of saturated ammonium chloride solution. The aqueous layer was extracted exhaustively with methylene chloride, and the combined organic layer and extracts were washed with brine, dried ( $\text{MgSO}_4$ ), and evaporated. Medium-pressure chromatography on silica gel and elution with 4:1 hexane-ethyl acetate gave 50 mg (42%) of colorless, liquid ester **7b**: IR ( $\text{CCl}_4$ ) C=O 1712 (s), 1690 (s), C=C 1680 (m)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  1.33, 1.35 (t, 3 each,  $J$  = 6 Hz, 2 Me), 4.25, 4.35 (q, 2 each,  $J$  = 6 Hz, 2  $\text{OCH}_2$ ), 6.66 (d, 1,  $J$  = 1 Hz, H-4), 7.40 (d, 1,  $J$  = 1 Hz, H-5). Anal. Calcd for  $\text{C}_{10}\text{H}_{12}\text{O}_5$ : C, 56.61; H, 5.70. Found: C, 56.56; H, 6.26.

**2-*n*-Butoxy-2,3-dihydro-4-pyrone (11).** A solution of 850 mg (8.7 mmol) of diazomalonaldehyde (**3**) in 10 mL of *n*-butyl vinyl ether was added dropwise (1 mL/h) to 40 mL of refluxing, freshly distilled *n*-butyl vinyl ether and the refluxing mixture stirred for an additional 4 h. The solvent was evaporated under vacuum and the residue chromatographed on silica gel. Elution with 2:1 hexane-ethyl acetate afforded 1.03 g (70%) of colorless, liquid ketone **11**: bp 89 °C (1 Torr); IR ( $\text{CHCl}_3$ ) C=O 1690 (s), C=C 1601 (m)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  0.85 (t, 3,  $J$  = 6 Hz, Me), 1.2–1.7 (m, 4, methylenes), 2.6–2.7 (m, 2, C-3 Hs), 3.4–3.9 (m, 2,  $\text{OCH}_2$ ), 5.30 (d, 1,  $J$  = 6 Hz, H-5), 5.4–5.5 (m, 1, H-2), 7.18 (d, 1,  $J$  = 6 Hz, H-6);  $^{13}\text{C NMR}$   $\delta$  13.3 (Me), 18.8 (butoxy C-3), 31.0 (butoxy C-2), 42.4 (C-3), 69.0 (butoxy C-1), 101.4 (C-2), 107.2 (C-5), 159.2 (C-6), 190.4 (C=O). Anal. Calcd for  $\text{C}_9\text{H}_{14}\text{O}_3$ : C, 63.51; H, 8.29. Found: C, 63.42; H, 8.18.

**$\gamma$ -Pyrone (12).** A solution of 200 mg (1.2 mmol) of ketone **11** and 0.1 mL of concentrated sulfuric acid in 20 mL of tetrahydrofuran was refluxed for 25 min. It was poured into 20 mL of saturated sodium bicarbonate solution and extracted exhaustively with ether. The extract was washed with brine, dried, and evaporated. Chromatography of the residue on Florisil and elution with 2:1 hexane-ethyl acetate gave 105 mg (96%) of liquid ketone **12**, spectrally identical with an authentic sample.

**Supplementary Material Available:**  $^1\text{H NMR}$  spectra for **4b**, **6**, **8**, **9**, and **i** (ref 9),  $^{13}\text{C NMR}$  spectra for **6**, **9**, and **i**, and IR spectra for **4b** (16 pages). Ordering information is given on any current masthead page.