A Simple Synthesis of 4-Substituted 5,5-Diethoxycarbonyl-3-formyl-2,3-dihydrofurans

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Polyfunctional 2,3-dihydrofurans are of interest for the synthesis of natural compounds[1] and potentially physiologically active compounds. 4-Substituted 5,5-diethoxycarbonyl-3-formyl-2,3-dihydrofurans **5** have not been prepared previously. We have found that substituted methylenemalonic aldehydes **3**[2] react with bromomalonic ester **1** under phase transfer catalysis to give compounds **5** in satisfactory yields (51–75%).

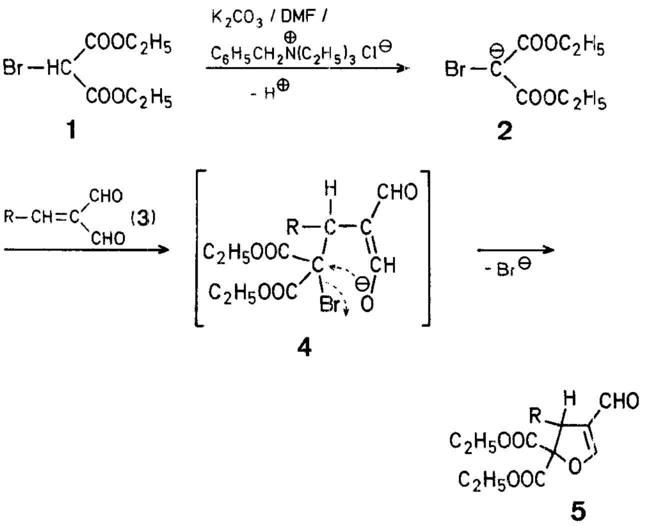
Of the simple α,β-unsaturated aldehydes, only acrolein reacts with **1** under the above conditions. However, instead of the corresponding dihydrofuran derivative, 1,1-diethoxycarbonyl-2-formylcyclopropane is formed[3].

The formation of compounds **5** may be explained by the generation of the carbanion **2** which is added to the activated double bond of **3**. Intramolecular substitution of the bromine in intermediate **4** with simultaneous cyclization

Table. Compounds **5** prepared

Product No.	R	Yield [%]	b.p. [°C]/torr or m.p. [°C]	n_D^{20}	Molecular formula[a]	U.V. (C_2H_5OH) λ_{max} (ε_{max})	I.R. (CCl_4) ν[cm^{-1}]	^{1}H-N.M.R. (CCl_4/TMS) δ[ppm]
1a	C_6H_5	51	158–160°/0.5	1.5375	$C_{17}H_{18}O_6$ (318.3)	255 (13444), 220 (13711), 201 (23111)	1622, 1672, 1745	0.75 (t, 3H, J = 7 Hz, CH_3); 1.27 (t, 3H, J = 7 Hz, CH_3); 3.52 (m, 2H, CH_2); 4.23 (m, 2H, CH_2); 5.1 (d, 1H, J = 2 Hz, 4-H); 7.15 (s, 5H_{arom}); 7.45 (d, 1H, J = 2 Hz, 2-H); 9.5 (s, 1H, CHO)
1b	4-Cl—C_6H_4—	60	197–199°/0.5	1.5345	$C_{17}H_{17}ClO_6$ (352.8)	255 (13044), 223 (13528), 201 (26631)	1623, 1673, 1745	0.84 (t, 3H, J = 7 Hz, CH_3); 1.28 (t, 3H, J = 7 Hz, CH_3); 3.16 (m, 2H, CH_2); 4.28 (m, 2H, CH_2); 5.15 (d, 1H, J = 2 Hz, 4-H); 7.00–7.35 (m, 4H_{arom}); 7.55 (d, 1H, J = 2 Hz, 2-H); 9.5 (s, 1H, CHO)
1c	4-H_3CO—C_6H_4—	74	69–70°	–	$C_{18}H_{20}O_7$ (348.3)	255 (10385), 230 (10513), 201 (25236)	1620, 1670, 1740	0.8 (t, 3H, J = 7 Hz, CH_3); 1.2 (t, 3H, J = 7 Hz, CH_3); 3.6 (m, 2H, CH_2); 4.2 (m, 2H, CH_2); 4.65 (s, 3H, H_3CO); 5.1 (d, 1H, J = 2 Hz, 4-H); 6.6–7.1 (m, 4H_{arom}); 7.5 (d, 1H, J = 2 Hz, 2H); 9.4 (s, 1H, CHO)
1d	C_6H_5—CH=CH— (*trans*)	55	111–112°	–	$C_{19}H_{20}O_6$ (344.4)	256 (21962), 204 (18155)	1620, 1675, 1745	1.1 (t, 3H, J = 7 Hz, CH_3); 1.3 (t, 3H, J = 7 Hz, CH_3); 4.1 (q, 2H, J = 7 Hz, CH_2); 4.3 (q, 2H, J = 7 Hz, CH_2); 4.8 (dd, 1H, J = 8 Hz, 2 Hz, 4-H); 5.9 (dd, 1H, J = 16 Hz, 8 Hz, C_6H_5—CH=C$\underline{H}$—); 6.6 (d, 1H, J = 16 Hz, C_6H_5—C$\underline{H}$=CH—); 7.25 (s, 5H_{arom}); 7.4 (d, 1H, J = 2 Hz, 2-H); 9.7 (s, 1H, CHO)
1e	2-thienyl	75	170–175°/0.5	1.5313	$C_{15}H_{16}O_6S$ (324.4)	285 (11071), 241 (11596), 202 (22116)	1620, 1670, 1740	0.9 (t, 3H, J = 7 Hz, CH_3); 1.3 (t, 3H, J = 7 Hz, CH_3); 3.75 (q, 2H, CH_2, J = 7 Hz); 4.25 (q, 2H, CH_2, J = 7 Hz); 5.4 (d, 1H, J = 2 Hz, 4-H); 6.7–7.2 (m, 3$H_{thienyl}$); 7.5 (d, 1H, J = 2 Hz, 2-H); 9.5 (s, 1H, CHO)
1f	H_3C—$(CH=CH)_2$— (*trans*, *trans*)	60	210–215°/0.5	1.5085	$C_{16}H_{20}O_6$ (308.3)	255 (13862), 233 (20793)	1620, 1672, 1747	1.22 (t, 3H, J = 7 Hz, CH_3); 1.30 (t, 3H, J = 7 Hz, CH_3); 1.72 (d, 3H, J = 6 Hz, CH_3); 4.15 (q, 2H, J = 7 Hz, CH_2); 4.20 (q, 2H, J = 7 Hz, CH_2); 4.54 (d, 1H_{olef}, J = 8 Hz); 5.15 (dd, 1H, J = 8 Hz, 14 Hz, 4-H); 5.6–6.25 (m, 3$H_{olef.}$); 7.4 (d, 1H, J = 2 Hz, 2-H); 9.54 (s, 1H, CHO)

[a] Satisfactory microanalysis obtained: C ± 0.41; H ± 0.21; Cl ± 0.23; S ± 0.34.



yields products **5**. Thus, this reaction sequence represents the first example for the formation of the 2,3-dihydrofuran ring as the result of a Michael addition at the double bond of α,β-unsaturated aldehydes.

The purity of liquid products **5** has been checked by G. L. C. (LHM-8 MD-5 gas chromatograph; glass column with 5% SE-30 on Chromaton N-AW-DMCS) and the purity of crystalline products has been checked by T.L.C. (Silufol plates; 1/20 ethyl acetate/benzene).

4-Substituted 5,5-Diethoxycarbonyl-3-formyl-2,3-dihydrofurans 5; General Procedure:

A solution of **1** (2.39 g, 0.01 mol) and **3** (0.01 mol) in dimethylformamide (2.5 ml) is added to a suspension of potassium carbonate (1.38 g, 0.01 mol) and a catalytic amount of benzyltriethylammonium chloride (0.23 g, 0.001 mol) in dimethylformamide (2.5 ml) at room temperature with efficient stirring. After stirring for 2 h, filtration, and evaporation of the solvent under reduced pressure, the residue is distilled or recrystallized from *n*-hexane (Table).

Received: December 19, 1983
(Revised form: April 10, 1984)

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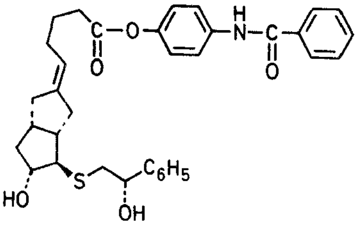
[1] Y.S. Rao, *Chem. Rev.* **76**, 625 (1976).

[2] Z. Arnold, V. Král, D. Dvořák, *Tetrahedron Lett.* **23**, 1725 (1982).

[3] G.V. Kryshtal, N.I. Shtemenko, L.A. Yanovskaya, *Izv. Akad. Nauk SSSR Ser. Khim.* **1980**, 2420; *C.A.* **94**, 46812 (1981).

R.F. Newton, S.M. Roberts, R.J.K. Taylor, *Synthesis* **1984** (6), 449–478:

The structure of compound **305** (p. 475) should be:



305 (EMD 46335)

H. Sard, R.P. Duffley, L.R. Robertson, R.K. Razdan, *Synthesis* **1984** (6), 506–509:

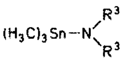
The fourth sentence in the paragraph above Scheme A (p. 507) should read:
This racemic compound could be preferentially enriched by a single recrystallization from ethanol as the (−)-dibenzoyl-L-tartrate salt **5a** (96% yield).

C.K. Ghosh, N. Tewari, A. Bhattacharya, *Synthesis* **1984** (7), 614–615:

Compounds **2a–d** should be named as 3-ethoxy-10-oxo-4,4a-dihydro-3*H*,10*H*-pyrano[4,3-*b*][1]benzopyrans.

Abstract 6925, *Synthesis* **1984** (7), 624:

The structure of reagent **5** should be:



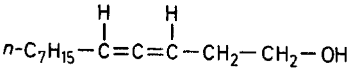
$(H_3C)_3Sn{-}N(R^3)_2$ (5)

M. Sato, N. Katsumata, S. Ebine, *Synthesis* **1984** (8), 685:

The title compound should be named 4,5-Dihydrobenzocyclobutene-4,5-dione.

R.E. Doolittle, *Synthesis* **1984** (9), 730–732:

The structure of product **3** (p. 730) should be:

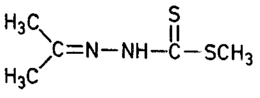


$n\text{-}C_7H_{15}{-}CH{=}C{=}CH{-}CH_2{-}CH_2{-}OH$

3

Y. Nakayama, Y. Sanemitsu, *Synthesis* **1984** (9), 771–772:

The structure of compound **6** (p. 772) should be:



6

I. Reichelt, H.-U. Reissig, *Synthesis* **1984** (9), 786–787:

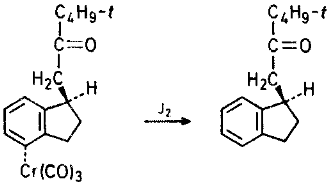
The title compounds **2** should be named as 3-oxo-2,3,4,5-tetrahydropyridazines

M. Tirant, T.D. Smith, *Synthesis* **1984** (10), 833–834

The names for products **2a** and **3a** should be bis[2-hydroxybenzylidenehydrazino] sulfide and 2-hydroxyethyl 2-hydroxybenzylidenehydrazino sulfide, respectively.

Abstract 6971, *Synthesis* **1984** (10), 892:

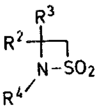
The structures of products **4** and **5** should be:



4 **5**

Abstract 6976, *Synthesis* **1984** (10), 894:

The structure of product **8** should be:



8

E.A. Mistryukov, I.K. Korshevetz, *Synthesis* **1984** (11), 947–949:

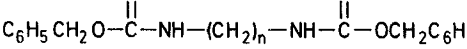
Compound **10** should be named as 1-(1-cyclohexenyl)-3-diethylaminopropyne.

Z. Arnold, V. Kral, G.V. Kryshtal, L.A. Yanovskaya, *Synthesis* **1984** (11), 974–976:

The title compounds **5** should be named as 3-substituted 2,2-diethoxycarbonyl-4-formyl-2,3-dihydrofurans.

G.J. Atwell, W.A. Denny, *Synthesis* **1984** (12), 1032–1033:

The structure of products **4a–f** (p. 1032) should be:



$C_6H_5CH_2O{-}C({=}O){-}NH{-}(CH_2)_n{-}NH{-}C({=}O){-}OCH_2C_6H_5$

4a-f

R.G. McR. Wright, *Synthesis* **1984** (12), 1058–1061:

Formula **8** should be replaced by: