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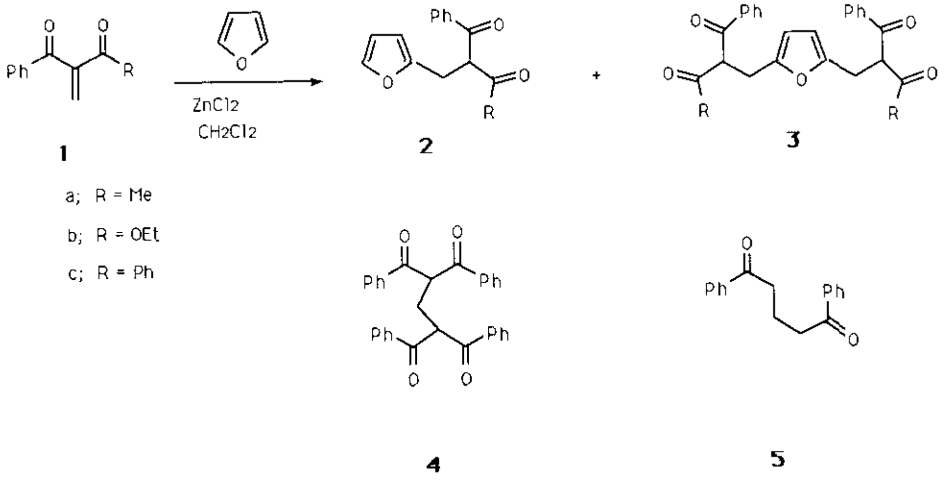
REACTIONS OF 2-METHYLENE-1,3-DICARBONYL COMPOUNDS WITH FURAN

Masashige Yamauchi,* Miwa Shirota, and Toshio Watanabe
Faculty of Pharmaceutical Sciences, Josai University,
Keyakidai, Sakado, Saitama 350-02, Japan

Abstract — The mono- and/or di-substituted furans (**2** and **3**) were synthesized by the reaction of 2-methylene-1,3-dicarbonyl compounds (**1**) with furan under moderate selectivity.

It is long established[1] that the reaction of furan with α,ß-unsaturated carbonyl compounds is different from that of cyclopentadiene. Although many α,ß-unsaturated carbonyl compounds as dienophiles fail to react with furan, it gives the Michael addition products in the presence of acidic catalysts.[2] We have reported the synthesis of 2-methylene-1,3-dicarbonyl compounds (**1**),[3] which are regarded as a α,ß-unsaturated carbonyl compound activated by electron-withdrawing α-substituent. In order to obtain more informations concerning the reactivities[4] of 2-methylene-1,3-dicarbonyl compounds (**1**) we examined the reaction of **1** with furan (Scheme 1).



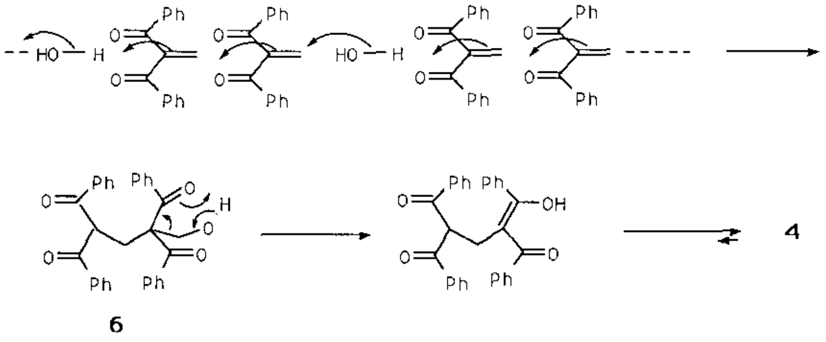
Scheme 1

1-Acetyl-1-benzoylethene (**1a**) was treated with furan in dichloromethane in the presence of zinc chloride, mono- and di-substituted products (**2a** and **3a**) were obtained. The ratio of the products depended on the addition time of furan. The stoichiometric reaction did not give desired results presumably due to volatility of furan and reactivity of mono-substituted furan. Of many attempts examined, the best conditions are (A) addition of a large excess (ca. 10 equiv.) of furan to the solution of **1** in a portion to obtain mono-substituted furan, and (B) prolonged addition (ca. 2 h) of furan (3 equiv.) to 1 to obtain di-substituted furan.

Table 1. Reaction of 2-methylene-1,3-dicarbonyl compounds (1) with furan.

Reactant	Reaction Condition[a]	Yield(%)[b]	Ratio **2** : **3**
1a	A	78	76 : 24
1a	B	68	7 : 93
1b	A	90	56 : 44
1b	B	62	5 : 95
1c	A	60	50[c] : 50
1c	B	70	2[c] : 98

a) mentioned in the text b) after column chromatography c) ratio of **4**



Scheme 2

As shown in Table 1 it is difficult to give mono-substituted product predominantly in all cases. Interestingly, 1,1,3,3-tetrabenzoylpropane (**4**) was obtained in the case of dibenzoylethene (**1c**) instead of yielding **2c**. This compound might be formed from the reaction of two molecules of unreacted starting material (**1c**) with one molecule of water, which could be present in silica gel, during chromatography. In fact **1c** was treated with silica gel in chloroform containing a few drops of water to afford **4** almost quantitatively. The structure (**4**) was confirmed by the elementary analysis, CIms, and ^{1}H nmr spectrum [δ 5.74 (t, J=7.0 Hz, two methine protons) and 2.76 (t, J=7.0 Hz, methylene protons)] and this result may be explained by the reaction mechanism shown in Scheme 2. 1,1,3,3-Tetrabenzoylethene (**4**) would be formed by decarbonylation of alcohol (**6**) which was condensation product of one molecule of water and two molecules of **1c**. Under the same conditions this type of compound could not be synthesized from 1-acetyl-1-benzoylethene (**1a**) or 1-benzoyl-1-ethoxycarbonylethene (**1b**). The fact that treatment of **4** with potassium carbonate in methanol gave 1,5-diphenylpentane-1,5-dione (**5**)[5] is additional support of structure (**4**).

Compounds (**3** and **4**) have active methine proton and further studies using these compounds are in progress in our laboratories.

EXPERIMENTAL

Mps were measured on a Yanako micromelting point apparatus and are uncorrected. Extracts were dried over anhydrous magnesium sulfate. Ir spectra of solids (KBr) and liquids (film) were recorded on a JASCO-IR-810 spectrophotometer. Mass spectra were taken on a JEOL JMS-DX300 instrument. Nmr spectra were obtained with JEOL JMN-GX 270 spectrometer (in $CDCl_3$, tetramethylsilane as internal reference).

Reaction of 2-methylene-1,3-dicarbonyl compounds (1) with furan. Method A.

To a stirred suspension of 2-methylene-1,3-dicarbonyl compounds (1 mmol) and $ZnCl_2$ (1.5 mmol) in dichloromethane (10 ml) was added at once a solution of furan (10 mmol) in dichloromethane (3 ml) at ambient temperature. After the stirring was continued for 1 h the reaction mixture was washed with water and brine. The organic layer was dried, and evaporated. The resulting residue was subjected to column chromatography on silica gel using benzene-hexane (2 : 1) as eluent to yield mono- and di-substituted furans (**2** and **3**). The yields and the ratios of **2** and **3** given in Table 1 were determined by the pure isolated products. Analytical oily samples were further purified by preparative thin layer chromatography.

Method B.

To a stirred suspension of 2-methylene-1,3-dicarbonyl compounds (**1**, 1 mmol) and $ZnCl_2$ (1.5 mmol) in dichloromethane (10 ml) was added a solution of furan (3 mmol) in dichloromethane (3 ml) at ambient temperature during a period of 2 h. The reaction mixture was stirred for additional 16 h. Work up as above gave **2** and **3**. The yields and ratios of **2** and **3** given in Table 1 were determined by the pure isolated products.

2-(2-Acetyl-2-benzoylethyl)furan (**2a**)

Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.16; H, 6.09; ir 1720, 1685, 1595, 1580 cm^{-1}; δ 2.15 (3H, s, CH_3), 3.30 and 3.36 (each 1H, each dd, J=15.4, 7.3 Hz, CH_2), 4.90 (1H, t, J=7.3 Hz, CH), 6.02 (1H, dd, J=3.0, 0.8 Hz, 3-H), 6.21 (1H, dd, J=3.0, 1.8 Hz, 4-H), 7.26 (1H, dd, J=1.8, 0.8 Hz, 5-H), 7.43-7.62 (3H, m, Ar-H), 7.90 (2H, dd, J=8.1, 1.3 Hz, Ar-2',6'-H)

2,5-Bis(2-acetyl-2-benzoylethyl)furan (**3a**)

Anal. Calcd for $C_{26}H_{24}O_5$: C, 74.98; H, 5.81. Found: C, 74.92; H, 5.97; ir 1720, 1685, 1595, 1580 cm^{-1}; ms m/z 416 (%) (M^+, 0.2), 373 (15.5), 245 (35.7), 211 (90.5), 149 (55.5), 105 (100); δ 2.11 (3H, s, CH_3), 2.12 (3H, s, CH_3), 3.12-3.33 (4H, m, CH_2), 4.76 (1H, t, J=7.0 Hz, CH), 4.79 (1H, t, J=7.0 Hz, CH), 5.85 (2H, s, 3-, 4-H), 7.45-7.63 (6H, m, Ar-H), 7.95 (4H, d, J=7.0 Hz, Ar-H).

2-(2-Benzoyl-2-ethoxycarbonylethyl)furan (**2b**)

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.68; H, 6.08; ir 1740, 1690, 1600, 1580 cm^{-1}; δ 1.15 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 3.33 and 3.38 (each 1H, each dd, J=13.5, 6.7 Hz, CH_2), 4.13 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.74 (1H, t, J=7.3 Hz, CH), 6.05 (1H, dd, J=3.0, 0.7 Hz, 3-H), 6.23 (1H, dd, J=3.0, 1.8 Hz, 4-H), 7.27 (1H, dd, J=1.8, 0.7 Hz, 5-H), 7.44-7.76 (3H, m, Ar-H), 8.00 (2H, dd, J=7.3, 1.3 Hz, Ar-2',6'-H).

2,5-Bis(2-Benzoyl-2-ethoxycarbonylethyl)furan (**3b**)

Anal. Calcd for $C_{28}H_{28}O_7$: C, 70.58; H, 5.92. Found: C, 70.77; H, 6.06; ir 1740, 1690, 1600, 1580 cm^{-1}; ms m/z (%) 476 (M^+, 2.56), 325 (2.14), 284 (17.8), 179 (8.5), 134 (25.9), 105 (100); δ 1.13 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 1.14 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 3.26 (4H, m, CH_2), 4.10 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.11 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.63 (1H, t, J=7.2 Hz, CH), 4.65 (1H, t, J=7.2 Hz, CH), 5.88 (2H, s, 3-, 4-H), 7.43-7.60 (6H, m, Ar-H), 7.96 (4H, d, J=7.4 Hz, Ar-2',6'-H).

2,5-Bis(2,2-dibenzoylethyl)furan (**3c**)

mp 144-145 °C (from benzen-hexane). Anal. Calcd for $C_{36}H_{28}O_5$: C, 79.98; H, 5.22. Found: C,80.10; H,5.30; ir 1695, 1665, 1595, 1580 cm^{-1}; δ 3.33 (4H, d, J=6.9 Hz, CH_2), 5.50 (2H, t, J=6.9 Hz, CH), 5.84 (2H, s, 3-, 4-H), 7.45-7.58 (12H, m, Ar-H), 7.85 (8H, d, J=8.0 Hz, Ar-2',6'-H).

1,1,3,3-Tetrabenzoylpropane (**4**)

A mixture of 1,1-dibenzoylethene (**1c**, 100 mg), silica gel (3 g), a few drops of H_2O, and $CHCl_3$ (10 ml) was stirred at ambient temperature for 3 h. Silica gel was filtered off, and the filtrate was evaporated. The resulting residue was subjected to column chromatography on sileca gel using benzene-hexane (2 : 1) as eluent to give 1,1,3,3-tetrabenzoylpropane (**4**, 89 mg, 91%). mp 178-179 °C (from EtOH). Anal. Calcd for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25. Found: C, 81.09; H, 5.36; CIms <u>m/z</u> 461 (M^++1); ir 1685, 1665, 1590, 1580 cm^{-1}; δ 2.76 (2H, t, J=7.0 Hz, CH_2), 5.74 (2H, t, J=7.0 Hz, COCHCO), 7.45-7.61 (12H, m, Ar-H), 8.14 (8H, d, J=7.3 Hz, Ar-2',6'-H).

1,5-Diphenylpentane-1,5-dione (**5**)

A mixture of 1,1,3,3-tetrabenzoylpropane (**4**, 200 mg, 0.43 mmol), K_2CO_3 (240 mg, 1.8 mmol), and MeOH (20 ml) was refluxed for 8 h. The solvent was distilled off. Water was added to the residue and the organic material was extracted with ether. The organic layer was washed with brine, dried, and evaporated. The resulting residue was subjected to column chromatography on silica gel using benzene-hexane (2 : 1) as eluent to yield crystalline 1,5-diphenylpentane-1,5-dione (**5**, 85 mg, 78%). mp 65.5 °C (from EtOH) (lit.,[5] mp 67.5 °C). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.63; H, 6.54; ir 1680, 1600, 1580 cm^{-1}; δ 2.21 (2H, quintet, J=6.9 Hz, CH_2), 3.13 (4H, t, J=6.9 Hz, $COCH_2$), 7.43-7.59 (6H, m, Ar-H), 7.98 (4H, d, J=7.0 Hz, Ar-2',6'-H).

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