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Intermolecular disproportionation between dimethyl (2-furylmethylidene)malonate and 4-methoxybenzylamine

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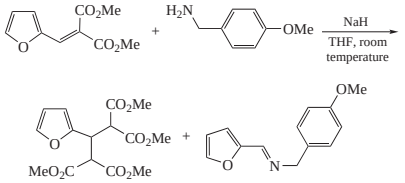
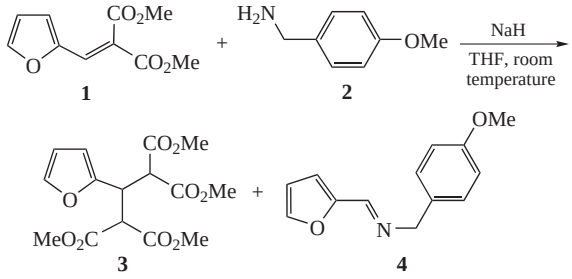
Sodium hydride-promoted disproportionation of the title compounds affords tetramethyl 2-(2-furyl)propane-1,1,3,3-tetracarboxylate and furfural *N*-(4-methoxybenzyl)imine.



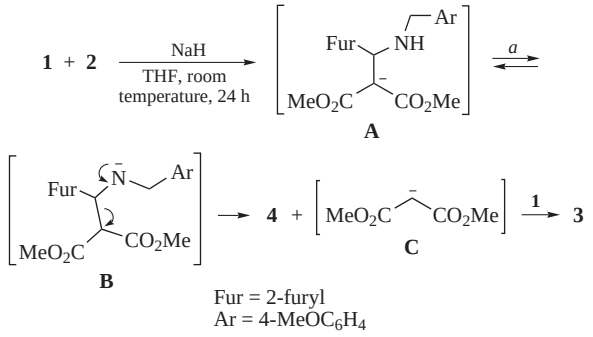
In a study of NaH-promoted aza-Michael reaction of equimolar amounts of unsaturated malonate **1**[1] with 4-methoxybenzylamine **2** with incomplete consumption of the reactants, we observed that two unexpected products were formed, namely, tetraester **3** and imine **4** (Scheme 1). Obviously, compounds **3** and **4** are the products of intermolecular disproportionation of the starting compounds **1** and **2**.



Scheme 1

Formally, this reaction starting from 2 moles of malonate **1** and 1 mole of amine **2** should have given 1 mole of tetraester **3** and 1 mole of imine **4**. However, the reaction of **1** and **2** in 2 : 1 molar ratio and with 1.67 equiv. NaH afforded a reaction mixture containing not only **3** and **4** but also the original compounds **1** and **2**. Each of the components **1**, **2**, **3**, and **4** was isolated in pure form in 35, 36, 7, and 56% yields, respectively, by column chromatography on SiO_2.†

We assume the following stage-by-stage routes of formation of compounds **3** and **4** (Schemes 2 and 3). Carbanion **A** generated after addition of amine **2** to the activated double bond of **1** can be consumed in two ways. In pathway *a*, carbanion **A** undergoes a prototropic shift to produce a more stable anion **B**. Fragmentation of the latter by β-elimination with release of malonate anion **C** leads to imine **4**. The resulting anion **C** reacts with diester **1** available in the solution to give tetraester **3**.

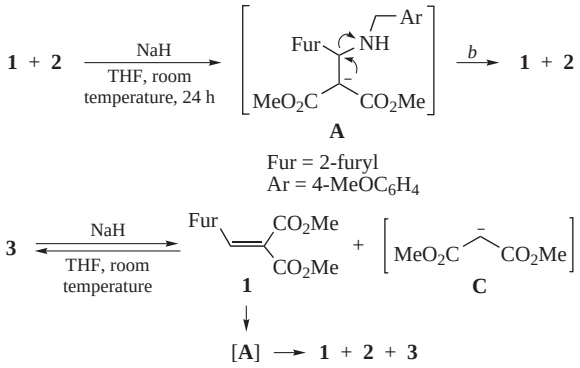


Scheme 2

† IR spectra of samples were obtained in thin layer using an IR Prestige-21 Shimadzu spectrometer. ^{1}H and ^{13}C spectra were recorded on Bruker AM-300 (300.13 and 75.47 MHz, respectively) and Bruker AVANCE-500 (500.13 and 125.77 MHz, respectively) spectrometers using Me_4Si as the internal standard. The reaction was monitored by TLC on Sorbfil plates (Russia). Compounds were visualized by wetting the plates with a solution of anisic aldehyde and sulfuric acid in ethanol followed by heating at 120–150 °C. The products were isolated by column chromatography on silica gel (30–60 g of the adsorbent per 1 g of the compound).

Reaction of malonate **1** *with 4-methoxybenzylamine*. A solution of 4-methoxybenzylamine **2** (78 mg, 0.57 mmol) in THF (3 ml) was added dropwise under argon to a suspension of NaH (40 mg, 1.67 mmol) in anhydrous THF (30 ml) stirred at room temperature. The mixture was stirred for 15 min, then malonate **1** (240 mg, 1.14 mmol) in THF (3 ml) was added and the mixture was stirred for 24 h. The solution was then concentrated and the residue was separated on a column with SiO_2 using light petroleum–ethyl acetate (4 : 1) as the eluent to give 80 mg of the starting malonate **1**, 40 mg of a **1**:**3**:**4** mixture in the ratio 1 : 1 : 4 (^{1}H NMR), 30 mg of tetraester **3**, 50 mg of imine **4**, and 30 mg of 4-methoxybenzylamine **2**. Repeated chromatography of the mixed fraction gave 20 mg of imine **4**, 5 mg of tetraester **3**, and 5 mg of malonate **1**. Eventually, taking the components of the mixed fraction into account, starting from 240 mg (1.14 mmol) of **1** and 78 mg (0.57 mmol) of **2**, we obtained 35 mg (7%) of tetraester **3**, 85 mg (35%) of diester **1**, 70 mg (56%) of imine **4**, and 30 mg (36%) of amine **2**.

Dimethyl (2-furylmethylidene)malonate **1**. IR (ν/cm^{-1}): 2954, 1728, 1713, 1634, 1475, 1438, 1367, 1356, 1257, 1224, 1207, 1084, 1064, 1021, 757, 593. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.83 (s, 3H, OMe), 3.91 (s, 3H, OMe), 6.50 (dd, 1H, H^4_{fur}, *J* 1.8 and 3.5 Hz), 6.77 (d, 1H, H^3_{fur}, *J* 3.5 Hz), 7.48 (d, 1H, CH=), 7.52 (d, 1H, H^5_{fur}, *J* 1.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 52.58 (OMe), 112.67 (C^3_{fur}), 118.28 (C^4_{fur}), 121.18 (=C^2), 128.22 (=CH), 146.37 (C^5_{fur}), 148.88 (C^2_{fur}), 164.55 and 166.74 (CO_2Me). Found (%): C, 57.42; H, 4.52. Calc. for $C_{10}H_{10}O_5$ (%): C, 57.14; H, 4.80.



Scheme 3

In the alternative pathway *b* (Scheme 3), the 'primary' carbanion **A** undergoes a prototropic shift into **B** along with decomposition into the original compounds **1** and **2** by the retro-Michael scheme. As a result, the observed 'mutation' is caused by parallel reactions of formation of **3** and **4** (pathway *a*) and 'recovery' of **1**, **2** (pathway *b*) occurring *via* carbanion **A**. Note that the content of tetraester **3** in the mixture is noticeably lower than that of imine **4**, which is explained by its easy retro-Michael decomposition under the conditions of our experiment. The resulting compound **1** is consumed in the formation of both **A** and **3**. The chain of reactions involving compound **3** recurs and its content in the mixture decreases in symbate way. As expected, model tests have shown that on treatment with NaH in THF, tetraester **3** comes into equilibrium with **1**. In this regard, a publication[2] should be noted, in which zinc- and indium-promoted reactions of ethenetricarboxylates with *N*-propargylamines to afford methylenepyrrolidines are considered.

In total, the transfomation herein described is particularly interesting from a mechanistic standpoint, since products **3** and **4** are readily available using standard techniques. It should be also emphasized that this reaction is unusual and unprecedented among the numerous examples of inter- and intramolecular disproportionations (for selected publications, see refs. 3–7).

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Tetramethyl 2-(2-furyl)propane-1,1,3,3-tetracarboxylate **3**. Mp 64–66 °C. IR (ν/cm^{-1}): 2997, 1757, 1737, 1717, 1462, 1455, 1334, 1297, 1288, 1262, 1239, 1217, 1189, 1174, 1142, 165. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.59 (s, 6 H, OMe), 3.72 (s, 6 H, OMe), 4.08 (d, 2 H, H^3, H^1, J 8.2 Hz), 4.35 (t, 1H, H^2, J 8.1 Hz), 6.23 (m, 2 H, H^4_{fur}, H^3_{fur}), 7.27 (d, 1H, H^5_{fur}, J 0.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 37.85 (C^2), 52.62 and 52.74 (OMe), 52.90 (C^1, C^3), 108.87 (C^3_{fur}), 110.39 (C^4_{fur}), 142.05 (C^5_{fur}), 150.59 (C^2_{fur}), 167.68 and 167.99 (CO_2Me). Found (%): C, 52.88; H, 5.18. Calc. for $C_{15}H_{18}O_9$ (%): C, 52.63; H, 5.30.

N-*[(1*E*)-2-Furylmethylidene]*-N-*(4-methoxybenzyl)amine* **4**. R_f 0.22 (light petroleum–ethyl acetate, 4 : 1). IR (ν/cm^{-1}): 1645, 1610, 1511, 1247, 1175, 1034, 822, 751. ^{1}H NMR (500 MHz, acetone-d_6) δ: 3.76 (s, 3 H, OMe), 4.67 (s, 2 H, CH_2), 6.55 (q, 1H, H^3_{fur}, J 1.7 Hz), 6.87–6.88 (m, 1H, H^4_{fur}), 6.89 (d, 2 H, H_{Ar}, J 8.7 Hz), 7.25 (d, 2 H, H_{Ar}, J 8.7 Hz), 7.67 (d, 1H, H^5_{fur}, J 0.9 Hz), 8.25 (s, 1H, CH=N). ^{13}C NMR (125 MHz, acetone-d_6) δ: 54.57 (OMe), 64.17 (CH_2), 111.65 (C^3_{fur}), 113.13 (C^4_{fur}), 113.65 (CH_{Ar}), 129.18 (CH_{Ar}), 131.62 (C_{Ar}), 144.72 (C^5_{fur}), 149.89 (CH=N), 152.35 (C^2_{fur}), 158.77 (C_{Ar}). Found (%): C, 72.41; H, 6.15; N, 6.61. Calc. for $C_{13}H_{13}NO_2$ (%): C, 72.54; H, 6.09; N, 6.51.

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