Some unusual reactions of Meldrum's acid. Synthesis of cinnamic acids, coumarins and 2-benzyl-1-indanone†‡

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The use of Meldrum's acid (**1**) in the synthesis of the substituted cinnamic acid **3** and malonic acid **4**, the coumarins **8** and **9**, and of 2-benzyl-1-indanone (**13**), is reported. The structure of benzylidene benzalmalonate is corrected to **14**.

Keywords: Meldrum's acid, cinnamic acids, malonic acids, coumarins, indan-1-ones

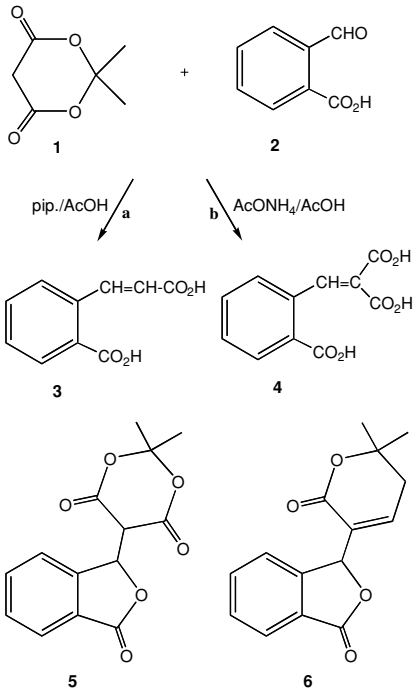
Since its discovery,[1] and especially the correct assignment of its structure,[2] Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione; isopropylidene malonate, **1**) has been widely used in organic synthesis. As it behaves as a versatile C_3O_2 synthon and contains an active methylene group (pK_a 5.1), it appears to be an attractive alternative to the synthetically well-established acyclic malonic esters.[3,4] A number of novel reactions[3,4] associated with the rigid ring structure of **1** have been identified which have no reported parallels in the chemistry of acyclic malonates.

At the simplest level, **1** can act as a methylene synthon by hydrolysis and exhaustive decarboxylation of its derivatives. As with simple malonic ester syntheses, the presence in **1** of a highly active methylene group adjacent to an ester function allows the molecule to be manipulated to give a wide range of possible products. In our work[5,6] on Meldrum's acid (**1**), the formation of some unexpected products prompted us to undertake this study separately. We now report: (i) Some Knoevenagel condensation reactions of **1** with aldehydes (**2, 7**) to give the products such as cinnamic acid (**3**) and malonic acid (**4**) (Scheme 1), and coumarins (**8, 9**) (Scheme 2), (ii) the polyphosphoric acid (PPA) cyclisation of **11** and **12** to give 2-benzyl-1-indanone (**13**) (Scheme 3), and (iii) a reaction of benzaldehyde with malonic acid, by the procedure[2] for synthesis of **1** to give **14** instead of **15** (Scheme 4).

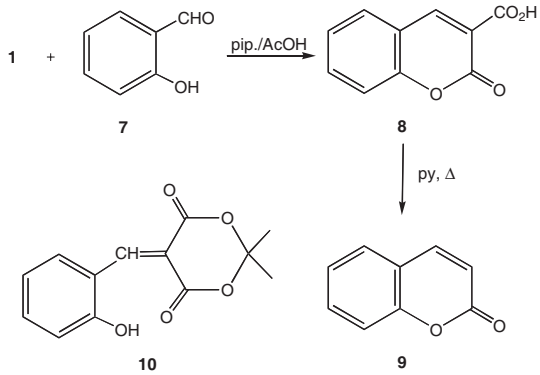
The reaction of malonic acid with benzaldehyde is reported to give different products under different conditions.[1-3,7-10] We were interested in the synthesis of phthalide Meldrum's acid (**5**), according to Scheme 1, required as an intermediate for the synthesis of a natural product, catalpalactone (**6**). Knoevenagel condensation using different reagents resulted in two different products, **3** and **4**. Furthermore, in Scheme 2 our expected product was **10**; however, coumarin-3-carboxylic acid (**8**) was obtained.

A synthesis of 2-benzyl-1-indanone was achieved via cyclisation of both dibenzyl Meldrum's acid (**11**) and dibenzylmalonic acid (**12**) using PPA (Scheme 3). The malonic acid **12** wa formed by alkaline hydrolysis of **11**.

The condensation of benzaldehyde and malonic acid in acetic anhydride using a catalytic amount of conc. H_2SO_4, according to the procedure for the preparation of Meldrum's acid[2] yielded **14** and not the expected product **15**. Michael and Weiner[8] reported the formation of β-phenyl-β-propiolactone-α-carboxylic acid (**17**), m.p. 148 °C (dec.), by Ott's method.[7] The preparation of benzylidene benzalmalonate (**14**) was also achieved by the procedure of Hedge *et al.*[10] as a byproduct in the synthesis of benzylidene malonate (**15**). Mowry[9] carried



Scheme 1



Scheme 2

out the reaction of malonic acid and benzal diacetate in acetic acid to give **14** in 5% yield, m.p. 142 °C. Though Michael and Weiner[8] assigned the correct structure for the product of malonic acid and cinnamaldehyde as cinnamylidene cinnamalmalonate (**18**), their structure for the product **17** appeared to be incorrect as it was suggested on the basis of wrong structure of Meldrum's acid, assigned by Meldrum[1] as **16**, which was then corrected by Davidson and Bernhard[2] as **1**. On the basis of the correct structure[2] for Meldrum's acid, the study of Hedge

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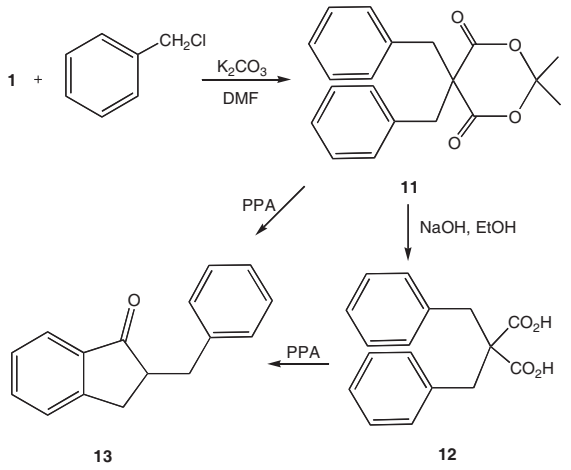


Scheme 3

et al.[10] and also by comparison of the melting points (148 °C dec.), the structure for benzylidene benzalmalonate should be **14**. This was confirmed by hydrolysis[11] of **14** with aqueous HCl-AcOH-dioxan as well as with aqueous pyridine, to afford benzaldehyde and cinnamic acid. It was also supported by PMR and IR spectral characteristics and elemental analysis.

Experimental

Meldrum's acid (**1**) was prepared as reported.[2] All other analytical grade chemicals were used.

o-Carboxycinnamic acid (**3**): A mixture of Meldrum's acid (0.008 mol), *o*-phthalaldehydic acid (**2**) (0.01mol), piperidine (0.1 ml) and acetic acid (0.25 ml) in 40 ml of dry benzene, was refluxed using a Dean-Stark apparatus for 3 h. The removal of benzene at 50 °C by rotary vacuum evaporator gave a yellowish solid, which was recrystallised from acetone – pet. ether to afford a colourless crystalline product (**3**) (93%), m.p. 217 °C [lit.[13] 217–219 °C]. ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 6.25 (d, 1H, J = 12 Hz, olefinic α-H), 7.00–8.02 (m, 4H, Ar–H), 8.35 (d, 1H, J = 12 Hz, olefinic β-H); IR (KBr): 3500–3150, 1790, 1758, 1742 1725, 1606 cm^{-1}.

o-Carboxybenzalmalonic acid (**4**): A mixture of **1** (0.02 mol), *o*-phthalaldehydic acid (**2**) (0.02 mol), ammonium acetate (0.004 mol) and acetic acid (0.94 ml) in dry benzene (60 ml) was refluxed and product was obtained as above procedure to give colourless crystalline tricarboxylic acid **4** (91%), m.p. 245 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 7.12 (s, 1H, olefinic-H), 7.75–8.05 (m, 4H, Ar–H); IR (KBr): 3500–3130, 1792, 1756, 1742, 1728, 1605, 1425, 1380, 1278, 950 cm^{-1}. Anal. Calcd. for $C_{11}H_8O_6$ C, 55.93; H, 3.38. Found C, 56.02; H, 3.35 %.

Coumarin-3-carboxylic acid (**8**): Meldrum's acid (**1**) (0.008 mol), salicylaldehyde (**7**) (0.01 mol), piperidine (0.1 ml) and acetic acid (0.25 ml) were heated to reflux in dry benzene (40 ml) and product was obtained by isolation as above to afford the slightly yellow crystalline **8** (92%), m.p. 190 °C dec. (lit.[13] 187–190 °C dec.). ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 7.20–7.88 (m, 4H, Ar–H), 8.96 (s, 1H, =CH-); IR (KBr): 3300–3050,1745,1680,1605 cm^{-1}.

Coumarin (**9**): Coumarin-3-carboxylic acid (**8**) (1 g) in dry pyridine (5 ml) was heated on water bath for 5 h. The contents were cooled, poured into 25 ml of ice-cold water and acidified with dil. HCl. It was extracted with ether (2 × 25 ml) and the ether extract was successively washed with water, $NaHCO_3$ solution, water and dried over anhydrous Na_2SO_4. Removal of ether gave a product which was recrystallised from pet. ether to afford the colourless crystalline coumarin (**9**) (95%), m.p. 70 °C [Lit.[13] 70 °C]. ^{1}H NMR ($CDCl_3$): δ 6.35 (d, 1H, olefinic H adjacent to >C=0 group), 7.15–7.60 (m, 4H, Ar–H), 7.68 (d, 1H, olefinic H). IR (KBr): 1710, 1605 cm^{-1}.

Dibenzyl Meldrum's acid (**11**): Meldrum's acid (**1**) (0.01 mol) was added in a single portion to a stirred suspension of anhydrous K_2CO_3 (0.015 mol) in dry DMF (10 ml) and stirring was continued for 15 min at room temperature. Benzyl chloride (0.021 mol) was added and the reaction mixture was stirred for 6 h and kept overnight. The reaction mixture was poured into ice-cold water (30 ml) and extracted with chloroform. The chloroform extract was washed with water and dried over anhydrous $CaCl_2$. Removal of chloroform and recrystallisation from chloroform – pet. ether yielded colourless crystalline **11** (92%), m.p. 230 °C (dec.) (Lit.[12] 230 °C dec.).

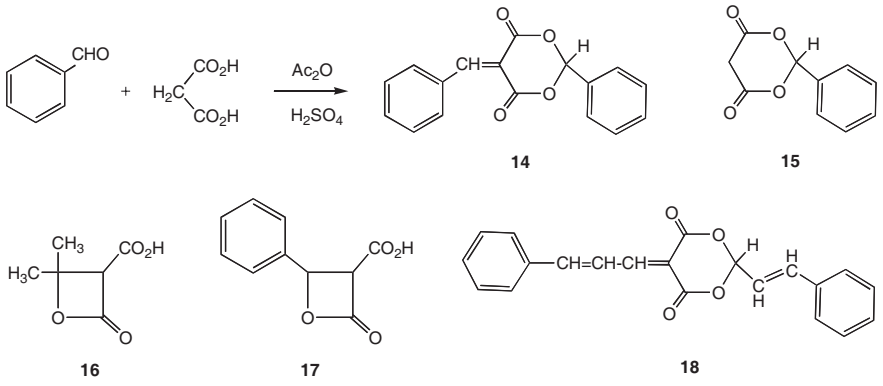
Dibenzylmalonic acid (**12**): A mixture of **11** (2.5 g), 10% aqueous NaOH (20 ml) and ethanol (20 ml) was refluxed for 5 h on a water bath. Ethanol was removed and the cooled residue was acidified with dil. HCl to give a solid product which was filtered off, washed with cold water, and dried. The crude product was recrystallised from ethanol to afford colourless crystalline **12**, 82%, m.p. 175 °C (dec.) [Lit.[13] 175–176 °C dec.].

2-Benzyl-1-indanone (**13**): (a) PPA was prepared by adding in three lots, phosphorus pentoxide (5 g) to ortho-phosphoric acid (3 ml) with stirring and stirring continued for 15 min. To this cooled reagent compound **11** (1 g) was added in a single portion with stirring and the reaction mixture was stirred and heated at 90 °C. The cooled contents were decomposed with 50 ml ice-cold water and extracted with ether. The ether extract was successfully washed with water, $NaHCO_3$ solution, water and dried over Na_2SO_4. Removal of ether yielded the product **13** (72%), as a viscous yellow liquid which was purified by TLC over silica gel using ethyl acetate : pet. ether (1 : 9). IR (CCl_4): 3010, 3000, 2996, 2887, 1705, 1602 cm^{-1}. ^{1}H NMR (CCl_4): δ 2.50–3.05 (m, 2H, benzylic CH_2 and 2H, indanone CH_2),3.05–3.62 (m, 1H,CH), 7.20–7.94 (m, 9H, Ar–H).

(b) PPA cyclisation-decarboxylation of dibenzylmalonic acid (**12**) was carried out as described above to give pure product **13** (87.5%).

Benzylidene benzalmalonate (**14**)[2]: To a suspension of malonic acid (0.125 mol) in acetic anhydride (0.15 mol) was added conc. H_2SO_4 (0.38 ml) with stirring and cooling (15–20 °C) to dissolve most of the malonic acid. To the resulting solution benzaldehyde (0.14 mol) was added with cooling to maintain the temperature below 20 °C. The reaction mixture was kept in a refrigerator overnight and the resulting crystals were filtered, washed with ice-cold water and dried, to yield crude product which was recrystallised as yellowish shining crystals of **14** (34%), m.p. 148 °C dec. [Lit.[10] 148 °C dec.] from chloroform – pet. ether. IR (KBr): 1772, 1730, 1628, 1378, 1280, 1198 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 6.65 (s, 1H, vinylic H), 7.10–8.05 (m, 10H, Ar–H), 8.25 (s, 1H, benzylic methine H). Anal. Calcd. For $C_{17}H_{12}O_4$: C, 72.85; H, 4.28. Found C, 72.82; H, 4.30 %.

Hydrolysis of benzylidene benzalmalonate (**14**)[11]: (a) *With aqueous HCl-AcOH-dioxane:* A mixture of **14** (3 g), 1 N HCl (5 ml), acetic acid (5 ml) and dioxan (20 ml) was refluxed for 2 h (or heated on



Scheme 4

a water bath for 4 h). The cooled contents were poured into 25 ml of cold water and extracted with ether. The ether extract was successively washed with water, $NaHCO_3$ solution, and water again, and dried over Na_2SO_4. The removal of ether gave benzaldehyde (83%), b.p. 181 °C (Lit.[13] b.p. 180–183 °C). The $NaHCO_3$ washings were acidified with dil. HCl to give a solid, which was filtered and dried. Recrystallisation from ethanol yielded colourless crystalline cinnamic acid (83%), m.p. 134 °C [lit.[13] m.p. 134 °C].

(b) *With aqueous pyridine:* Compound **14** (3 g) in water (2 ml) and pyridine (6 ml) was heated to reflux for 2 h. The cooled reaction mixture was poured into ice-cold water (25 ml) and acidified with dil. HCl. The products were obtained by ether extraction as described above to afford benzaldehyde, (82%) and cinnamic acid (81%).

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