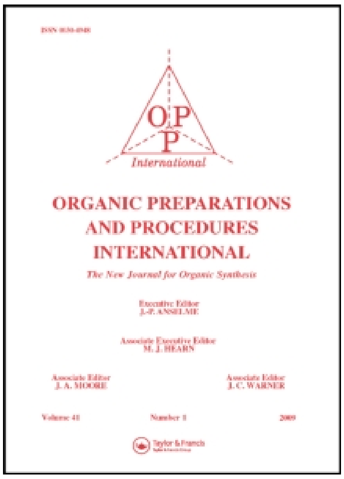

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DIMETHYL 4-NITROPHENYLMALONATE

M. A. E. Bowman[a]; R. E. Bowman[a]
[a] Department of Pharmaceutical Chemistry, University of Wales College of Cardiff, Cardiff, UNITED KINGDOM

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DIMETHYL 4-NITROPHENYLMALONATE

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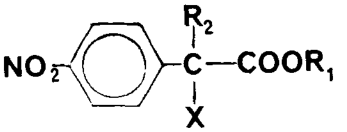
M. A. E. Bowman and R. E. Bowman*

Department of Pharmaceutical Chemistry,
University of Wales College of Cardiff,
Cardiff, CF1 3NU, UNITED KINGDOM

A simple high-yielding preparation of the title compound 1a and its facile C-methylation to the



a) $R_1 = Me; R_2 = H; X = CO_2Me$
b) $R_1 = R_2 = Me; X = CO_2Me$
c) $R_1 = X = H; R_2 = Me$

diester 1b is described. Hydrolysis of the latter furnished the propionic acid 1c thus providing a relatively simple new route to 2-alkyl/arylalkyl-2(4'-nitrophenyl)acetic acids.

Dialkyl 4-nitrophenylmalonates have obvious synthetic uses which have only so far been reported on three occasions.[1] The dimethyl ester 1a was described[2] as a solid, mp. 95°, the single crystalline product obtained in small yield from the nitration (H_2SO_4/HNO_3) of dimethyl phenylmalonate. Careful repetition of this work, however, yielded a number of crystalline crops with melting points ranging from 67-78°; fractional crystallization did yield a small amount of a nitroester of mp. 90.5-91°, which was not homogeneous (^{1}H NMR).

An attempt to prepare the title compound by carbomethoxylation of methyl 4-nitrophenylacetate with dimethyl carbonate[3] only yielded a viscous red oil. Alkylation of trimethyl sodiomethanetricarboxylate[4] with 1-bromo-4-nitrobenzene in dimethyl sulfoxide at 100° for 20 hrs led only to the recovery of starting bromo compound in high yield; there was some evidence however, that reaction of the corresponding 1-fluoro compound under similar conditions, did occur to a small extent. A more recent report[5] has claimed, on the basis of HPLC analysis, facile alkylation of diethyl sodiomalonate with the above bromo compound in the presence of copper (I) bromide; in our hands, only dark viscous oils were obtained.

Finally, we turned our attention to the direct alkylation of dimethyl malonate with 1-chloro-4-nitrobenzene (0.5 mol) previously reported for the diethyl ester by Bourdais and Mahieu[6] and which we avoided on account of the absence of detailed work-up procedures. Their method employed dimethyl sulfoxide as solvent and sodium hydride as base, a procedure potentially hazardous on the larger scale. We now report that a similar reaction employing commercially available potassium t-butoxide in the same solvent at 95-105° for 3 hrs followed by pouring the reaction mixture into a mixture of ice and hydrochloric acid, affords the essentially pure ester 1a directly in 88% yield, nearly double that reported for the corresponding diethyl ester;[6] attempts to improve the yield by lengthening the reaction time or employment of methanolic sodium methoxide, proved unrewarding.

Treatment of 1a with iodomethane in acetone solution in the presence of anhydrous potassium carbonate, readily yielded the C-methyl derivative 1b which was converted by hydrolysis to the known 2-(4-nitrophenyl)propanoic acid 1c.

EXPERIMENTAL SECTION

Dimethyl 4-Nitrophenylmalonate (1a).- Dimethyl malonate (57 mL, 0.5 mol) was added to a part solution of t-BuOK (56.2 g, 0.5 mol) in anhydrous DMSO[7] (300 mL) followed by 1-chloro-4-nitrobenzene (40 g, 0.25 mol) and the stirred mixture heated at 95-105° for 3 hrs. The cooled mixture was then poured with vigorous stirring into a mixture of ice-water (1.5 L) and 12M HCl (50 mL) and the resulting crystalline material was collected, washed with water and dried to give 55.8 g (88%) of the nearly colorless diester 1a, mp. 125-127°. Crystallization from acetonitrile yielded the pure diester as colorless rectangular plates, mp. 126-127°, IR:1735 (CO), 1520, 1350 and 845 ($ArNO_2$) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.78 (s, 6H), 7.78 (s, 1H), 7.62 (d, 2H) and 8.25 (d, 2H).

Anal. Calcd for $C_{11}H_{11}NO_6$: C, 52.17; H, 4.38; N, 5.53. Found: C, 52.21; H, 4.38; N, 5.53

Dimethyl 2-Methyl-2-(4'-nitrophenyl)propane-1,3-dioate (1b).- A mixture of anhydrous K_2CO_3 (3 g), dimethyl 4-nitrophenylmalonate (1.52 g, 6 mmol), acetone (20 mL) and CH_3I (3 mL) was heated with stirring for 3 hrs at 80°; the initially dark red mixture which had turned pale grey was then filtered. The filtrate was evaporated and the residue extracted into dichloro-methane (20 mL) and water (20 mL). The organic layer was dried and the solvent removed in vacuo to yield the diester as a viscous oil (1.5 g); IR: 1735 (CO), 1525, 1350 and 855 ($ArNO_2$) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.92 (s, 3H), 3.8 (s, 6H), 7.62 (d, 2H) and 8.25 (d, 2H).

2-(4'-Nitrophenyl)propanoic Acid (1c).- A mixture of 1.9 g of 1b, 10 mL of acetic and 20 mL of 5M HCl was refluxed for 3 hrs and the solution evaporated to dryness. The residual oil was dissolved in dichloromethane and the solution, after washing with water, was evaporated to dryness to yield 1.2 g of 1c as a solid, mp. 83-87°; recrystallization from carbon tetrachloride yielded the pure acid, mp. 87-88°, undepressed by authentic material.[8] IR: 1710, 1520, 1350 and 860 cm^{-1}.

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7. Dried by contact with 4Å molecular sieves at 25° for 24 hrs prior to use.
8. Supplied by Aldrich Chemical Co.

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