CCCLIV.—*Alkyl Derivatives of Ethyl Malonate and Ethyl Cyanoacetate.*

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In the course of some synthetic work in progress in this laboratory, the need arose for esters of the di(β-chloroethyl)-malonic or -cyanoacetic type. It was considered that these compounds would result from the action of β-chloroethyl toluene-*p*-sulphonate on ethyl sodiomalonate or -cyanoacetate respectively (compare Peacock and Tha, J., 1928, 2303). [β-Chloroethyl toluene-*p*-sulphonate and β-cyanoethyl toluene-*p*-sulphonate are referred to hereafter as ester A and ester B respectively. An improved method for the preparation of the former (compare Clemo and Perkin, J., 1922, **121**, 642) is recorded in the experimental part.] All attempts, however, to effect a satisfactory condensation of ester A and ethyl sodiomalonate in absolute alcohol, ether, or benzene have failed, the ester A being decomposed in part under the alkaline reaction conditions, giving sodium chloride and sodium toluene-*p*-sulphonate. With ester A and ethyl sodiocyanoacetate, which is alkylated in certain cases with considerably greater ease than is ethyl sodiomalonate (compare Hessler, *J. Amer. Chem. Soc.*, 1913, **35**, 990), there are indications that the highest-boiling fraction of the reaction product contains ethyl di(β-chloroethyl)cyanoacetate, but so far it has not been possible to isolate it from the unchanged ester A.

On account of these unexpected results and in view of the fact that β-cyanoethyl toluene-*p*-sulphonate, which is markedly less stable to aqueous alkalis than ester A (compare Clemo and Walton, J., 1928, 723), condenses readily with potassium pyrrole (Clemo and Ramage, this vol., p. 49), it became a matter of interest to examine the action of ester B on ethyl sodio-malonate and -cyanoacetate respectively.

Ester B reacted smoothly with ethyl sodiomalonate in either absolute alcohol or ether, and *ethyl* β-*cyanoethylmalonate* and *ethyl*

di(β-*cyanoethyl*)*malonate* could be isolated in 63% and 80% yields of the theoretical respectively. In this reaction the use of ether as a solvent favoured the formation of the di-alkylated compound.

Molecular amounts of ester B and ethyl sodiocyanoacetate reacted in alcohol so easily that only the *di*-β-*cyanoethyl* derivative could be isolated, but no reaction occurred when ether was used as the solvent.

When alcohol is used in these condensations, the sodium toluene-*p*-sulphonate separates in an easily filterable crystalline form, and its weight enables the extent of the reaction to be judged.

Of the numerous synthetical possibilities of β-cyanoethyl-malonic and -cyanoacetic esters, only a few have been investigated : for instance, ethyl di(β-cyanoethyl)malonate is a very convenient material for the preparation of pentane-1 : 3 : 3 : 5-tetracarboxylic ester, or acid, and thus of 4-ketohexahydrobenzoic acid (compare Perkin, J., 1896, **69**, 1509; Emery, *Ber.*, 1891, **24**, 283). A further obvious application is for the preparation of derivatives of barbituric acid.

EXPERIMENTAL.

β-*Chloroethyl Toluene*-p-*sulphonate*.—Toluene-*p*-sulphonyl chloride (300 g.) and anhydrous ethylene chlorohydrin (300 g.) were heated on the water-bath until evolution of hydrogen chloride ceased (24—36 hrs.). The excess of chlorohydrin (180 g.) was removed on the water-bath under reduced pressure, and the clear light brown residual liquid washed with aqueous sodium hydroxide; the ester then readily separated, without the formation of troublesome emulsions, from the aqueous layer, which was twice shaken with benzene. The benzene washings were added to the ester, and the whole was dried and fractionated, giving 270 g., b. p. 210°/21 mm.

Ethyl β-*Cyanoethylmalonate*.—Sodium (2·3 g.) was dissolved in absolute alcohol (30 c.c.), and ethyl malonate (16 g.) added, followed by a hot solution of ester B (22·5 g.) in absolute alcohol (30 c.c.). The vigorous reaction which set in was completed by refluxing for 8 hours. After cooling, the sodium toluene-*p*-sulphonate was filtered off (17·8 g.; calc., 19·4 g.). The filtrate was worked up in the usual way and fractionation gave 7·6 g. of a fragrant colourless liquid, b. p. 165°/18 mm., 135°/0·2 mm. (Found : C, 55·8; H, 6·9; N, 6·6. $C_{10}H_{15}O_4N$ requires C, 56·3; H, 7·0; N, 6·6%), and 4·8 g. of an oil, b. p. 200—205°/0·2 mm., which crystallised on cooling, m. p. 61·5°. The latter was ethyl di(β-cyanoethyl)malonate, which is best prepared as follows.

Ethyl Di(β-*cyanoethyl*)*malonate*.—The condensation of ethyl sodiomalonate with ester B was carried out as above, after 3 hours' refluxing further quantities of sodium (2·3 g.) in alcohol (30 c.c.) and of ester B (22·5 g.) were added, and the mixture was refluxed for

12 hours. After being filtered from the sodium toluene-*p*-sulphonate (36 g.; calc., 39 g.), the liquid was worked up in the usual way and gave *ethyl di*(β-*cyanoethyl*)*malonate* (21 g. or 80%), b. p. 200—205°/0·2 mm., m. p. 61·5° (Found: C, 58·5; H, 6·8; N, 10·3. $C_{13}H_{18}O_4N_2$ requires C, 58·7; H, 6·8; N, 10·5%).

Ethyl Di(β-*cyanoethyl*)*cyanoacetate.*—Ethyl cyanoacetate (2·83 g.) was treated successively with two lots of sodium (0·6 g.) and ester B (5·7 g.) in absolute alcohol (50 c.c.). The total reaction time allowed was 18 hours. When the product was worked up, 4·5 g. (86%) of a pale yellow oil were obtained, b. p. 197—202°/0·2 mm., which solidified on standing to a mass of pale yellow crystals, m. p. 38° (Found: C, 60·6; H, 5·8; N, 19·4. $C_{11}H_{13}O_2N_3$ requires C, 60·3; H, 5·9; N, 19·2%). The *ester* is readily soluble in the common organic solvents other than low-boiling petroleum.

Ethyl Propane-1 : 3 : 3-*tricarboxylate.*—Ethyl β-cyanoethylmalonate (4 g.) was refluxed for 5 hours with alcoholic hydrogen chloride (20 c.c.; 40% HCl). After cooling, ammonium chloride (0·9 g.; calc., 1·1 g.) was filtered off, and the propanetricarboxylic ester obtained (3·8 g. or 80%), b. p. 165—166°/22 mm.

Pentane-1 : 3 : 3 : 5-*tetracarboxylic Acid.*—Ethyl di(β-cyanoethyl)-malonate (2 g.) was refluxed for 3—4 hours with alcoholic potassium hydroxide (30 c.c.; 20%). Considerable separation of the potassium salt occurred and after removal of the alcohol this was decomposed by a little concentrated hydrochloric acid, and the solution extracted repeatedly with ether. The gummy mass left after removal of the ether was dissolved in the minimum amount of water and placed in a vacuum desiccator. The crystals which separated (1·0 g.) had m. p. 184° (decomp.). Perkin records the m. p. of the acid as 185—187° (Found: C, 43·8; H, 5·0. Calc. for $C_9H_{12}O_8$: C, 43·6; H, 4·8%).

Ethyl Pentane-1 : 3 : 3 : 5-*tetracarboxylate.*—Ethyl di(β-cyanoethyl)-malonate (3 g.) on hydrolysis with alcoholic hydrogen chloride (30 c.c.; 40%) as described above yielded 2·8 g. (70%) of the tetracarboxylic ester, b. p. 217—219°/20 mm.

One of the authors (C. R. S. T.) is indebted to the Council of Armstrong College for a scholarship which has enabled him to take part in this investigation.

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NEWCASTLE-UPON-TYNE. [*Received, August 1st,* 1931.]