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TRIANIONS (α-ANIONS OF DILITHIO MALONATES). C-ALKYLATIONS OF MONOSUBSTITUTED MALONIC ACIDS.

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Treatment of dianions of carboxylic acids (α-anions of carboxylate salts) with alkyl halides has been utilized to prepare α-alkylated carboxylic acids (1). These α-anions undergo reactions with other electrophilic reagents and readily lead to α-functionalized carboxylic acids (2) We now wish to report a method for the conversion of monosubstituted malonic acids 1 into the corresponding disubstituted malonic acids 3. This procedure involves conversion of the monosubstituted

$$\underset{\underline{1}}{RCH(COOH)_2} \xrightarrow{n\text{-BuLi}} \underset{\underline{2}}{RC(COO)_2^{-3}\ 3Li^+} \xrightarrow{R'X} \underset{\underline{3}}{RR'C(COOH)_2}$$

malonic acids 1 into the novel trianions 2 (α-anions of dilithio malonates) and treatment of 2 with alkyl halides to yield 3. This procedure by-passes the classical alkylation of malonate esters (3) as the carboxyl group can be used directly in the reaction. The results of this investigation are tabulated in Table I.

The trianions 2 (R = Me or ϕ) were prepared by treatment of THF solutions of acids 1 (R = Me or ϕ) with 3.3 equivalents of n-butyllithium at 0° for about 1 hour. In these diacids, the use of lithium diisopropylamide is unnecessary (1,2). Up to this point we have been unable to alkylate the malonic acid 1 (R = H) under the same conditions where malonic acids 1 (R = Me or ϕ) yield the trianion. Treatment of 1 (R = ϕ) with n-butyllithium followed by quenching with D_2O leads to an 85% recovery of phenylmalonic acid with a 90% incorporation of deuterium (nmr analysis) which undoubtedly arises from quenching of the trianion 2 (R = ϕ).

As can be seen from the data in Table I, good yields of disubstituted malonic acids can be obtained from primary halides but no alkylation could be detected with isopropyl bromide, iodide, or tosylate.

TABLE I

DISUBSTITUTED MALONIC ACIDS 3 PREPARED FROM TRIANIONS 2

1, R[a]	R'X	3, R	R'	% YIELD[b]
Ø	MeI	Ø	Me	88
Ø	EtI	Ø	Et	82
Ø	ØCH_2Br	Ø	ØCH_2	78[c]
Ø	IsoPrX (X = Br,I,OTs)	Ø	IsoPr	-[d]
Me	MeI	Me	Me	76
Me	ØCH_2Br	Me	ØCH_2	74
Me	IsoPrX (X = Br,OTs)	Me	IsoPr	-[d]

[a] General Procedure. To 4 mmol of 1 in 50 ml THF is added dropwise below -50° 13 mmol n-butyllithium (2.0 M in hexane). The mixture is warmed to 0° (1 hr), 8 mmol of R'X is added, and the mixture is warmed to 50° (1 hr). The mixture is washed with water and a saturated aqueous $NaHCO_3$ solution. The combined aqueous layers are washed with ether, acidified (2 M HCl), then extracted repeatedly with ether or ethyl acetate. The organic phase is dried ($MgSO_4$), decolorized, and concentrated. The solid is crystallized from ethyl acetate and pentane. All compounds had nmr spectra consistent with their structure and melting points in agreement with literature values.

[b] Yields are nearly quantitative if the workup includes a continuous extraction.

[c] A mixture of 3 and 1 in a 3.5 1 ratio as determined by nmr.

[d] Only 1 was recovered.

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