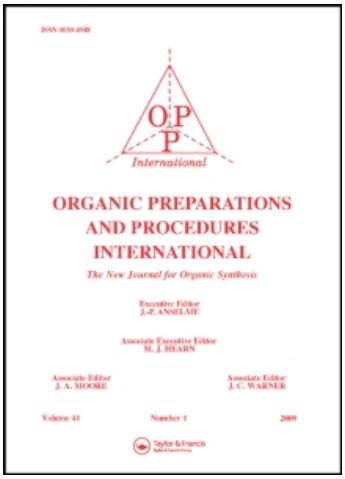

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ARYLGLYOXYLIC ESTERS VIA ARYLLITHIUM COMPOUNDS

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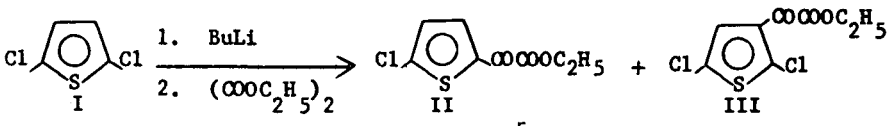
Arylglyoxylic esters may be prepared from the aroyl chlorides[1] or via a Friedel-Crafts reaction on the hydrocarbon[2]. Recently Nyberg[3] reported that while thienyl Grignard reagents reacted with dimethyl oxalate to form methyl thienylglyoxalate and methyl dithienylglycolate, 2- and 3-lithiothiophene reacted with dimethyl oxalate to form the corresponding 2,2'- and 3,3'-thenoin. In these latter reactions none of the glyoxylic esters could be detected.

We have found that the reverse addition of an aryl or heteroaryl lithium compound to an excess of an oxalate ester is a convenient method of preparing certain glyoxylic esters. 2-Lithiothiophene by this

$$Ar\text{-}Li + (COOR)_2 \longrightarrow Ar.CO.COOR + LiOR$$

method gave 84% of the ketoester. In the case of 3-lithiothiophene a mixture of the 2- and 3-glyoxylic esters resulted, probably because the temperature of the 3-lithiothiophene was not rigorously kept below -70° during the transfer into the oxalate solution[4]. An attempt to make ethyl 5-chloro-2-thienylglyoxylate from 2,5-dichlorothiophene by this method resulted in a 90% yield of a 1;1 mixture of ethyl 5-chloro-2-thienylglyoxylate II and ethyl 2,5-dichloro-3-thienylglyoxylate, III. This composition was determined by a comparison of the n.m.r. spectrum of the product with the spectra of authentic samples[2].



EXPERIMENTAL[5]

n-Butyllithium in hexane (125 ml. of a 1.6 molar soln., 0.20 mole) was added slowly to a stirred, cold (-60°) solution of the hydrocarbon (thiophene, thiazole or isothiazole) or the halo compound (2,3,5-tribromothiophene or 1-bromonaphthalene) (0.20 mole) in anhydrous THF (300 ml.) under a nitrogen atmosphere. After an additional 30 minutes at this temperature, the resulting aryllithium solution was slowly siphoned (ca. 20 minutes) into a stirred mixture of diethyl oxalate (0.60 mole) and dry ether (200 ml) while the temperature was maintained at ca. -60°. After the transfer was completed the reaction mixture was warmed to ca. -40° and then poured into 200 ml. of ice-cold 2 N hydrochloric acid. The product was extracted with ether (3 x 100 ml.). The combined organic layers were dried ($MgSO_4$), the solvent removed and the residue distilled under reduced pressure. The arylglyoxylic esters made by this route are listed in the Table.

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TABLE $ArCOCOOC_2H_5$

Ar	bp.°/mm.	Yield%	Ref.	Elemental Analysis[e]
2-Thienyl[a]	90-93/0.9	84	2	----------
2-(3,5-Dibromothienyl)[b]	135-137/0.5 mp. 65-66	75	-	C,H,Br,S
2-Thiazolyl[c]	88-90/0.4	72	-	C,H,N,S
2-Isothiazolyl[d]	105-106/0.3 mp. 19-20	71	-	C,H,N,S
1-Naphthyl	154-155/0.5	80	6	-------

a. Methyl ester. In this experiment THF was used in place of ether since dimethyl oxalate is not appreciably soluble in ether.

b. N.m.r. in $CDCl_3$: 2.80 τ (s, 1H); 5.55 τ (q, 2H); 8.58 τ (t, 3H).

c. N.m.r. in $CDCl_3$: AB type 1 proton doublets centered at ca. 1.78 τ and 2.06 τ (J=3 Hz); 5.47 τ (q, 2H); 8.57 τ (t, 3H).

d. N.m.r. in CCl_4: AB type 1 proton doublets centered at ca. 1.49 τ and 2.06 τ (J=1.8 Hz); 5.60 τ (q, 2H); 8.57 τ (t, 3H).

e. The elemental analysis were within ± 0.4% of the calculated values.

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5. The infrared spectrum of the glyoxylic esters showed two sharp strong bands in the carbonyl stretching region at 1730 to 1740 and 1670 to 1680 cm^{-1}.

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