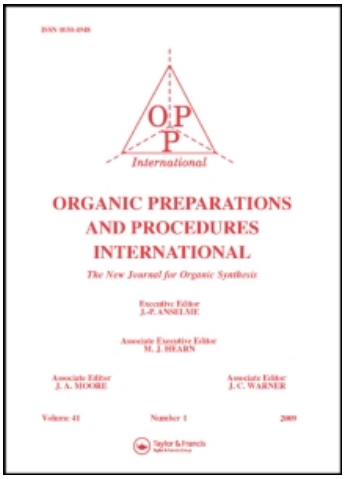

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A CONVENIENT SYNTHESIS OF β-KETO DIESTERS

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A CONVENIENT SYNTHESIS OF β-KETO DIESTERS

Submitted by (05/11/87) **Hans-Werner Schmidt* and Manfred Klade**

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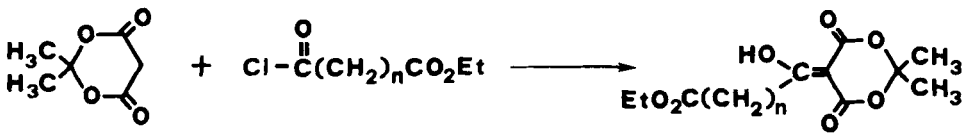
In connection with our studies of the reaction of ethoxymethylenemalononitrile with active methylene compounds,[1,2] we had need for a convenient and general synthesis of ω-carbethoxy β-keto esters. In 1978, Yonemitsu and coworkers[3] described a general and versatile method for the preparation of β-keto esters. In this method, Meldrum's acid 1 is acylated in the presence of pyridine with an acyl chloride to give the C-acylated derivative, which usually exists largely in the enol form (see 3). When heated under reflux with an alcohol, the acyl derivative is rapidly converted into the β-keto ester. We report herein the preparation



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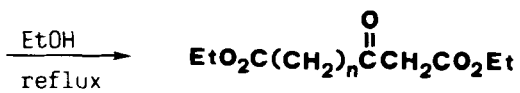

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of a variety of ω-carbethoxy β-keto esters (see Table) by this method using the ω-carbethoxy carboxylic acid chlorides 2a-f[4] as acylating agents. Compared with known methods (ref. of Table) the procedure outlined here offers a particularly attractive route to β-keto diesters.

TABLE. Diethyl 3-Oxoalkanedioates 4a-f

Cmpd	n	Yield (%)	bp. (°C/mm Hg)	Ref.
4a	2	80	110-113/1.0	5-7
4b	3	64	99-104/0.01	8,9
4c	4	40	120-125/0.5	10,11
4d	5	33	119-124/0.1	12
4e	6	51	130-134/0.08	
4f	7	36	137-142/0.15	

EXPERIMENTAL SECTION

^{1}H-NMR spectra were determined on a Varian EM-360L spectrometer.

Diethyl 3-Oxoalkanedioates (4a-f). General Procedure.- To a stirred solution of Meldrum's acid (1) (7.2 g, 50 mmol) in dichloromethane (100 ml) and dry pyridine (8 ml) was added dropwise under nitrogen the corresponding ω-carbethoxy carboxylic acid chloride (2) (55 mmol) at 0°.

After stirring for 0.5 hr at 0° and 1 hr at room temperature, the reaction mixture was washed with 2N hydrochloric acid and water, dried over anhydrous $MgSO_4$ and evaporated. The residue was dissolved in abs. ethanol (50 ml) and heated to reflux for 2 hrs. Removal of the ethanol and vacuum distillation of the resulting oil afforded the diethyl 3-oxoalkanedioates 4a-f (See Table).

4e: ^{1}H-NMR (CCl_4): δ 1.03-1.85 (m, 14H, CH_3,CH_2), 1.95-2.65 (m, 4H, $COCH_2$), 3.25 (s, 4H, $COCH_2CO$), 4.05 (m, 4H, $O\underline{CH_2}CH_3$), 4,80 (s, CH enol); IR(KBr): 3000-2860, 1740, 1720 cm^{-1}.

Anal. Calcd. for $C_{14}H_{24}O_5$: C, 61.76; H, 8.82. Found: C, 61.52; H, 8.41

4f: ^{1}H-NMR (CCl_4): δ 1.02-1.75 (m, 16H, $\underline{CH_3}CH_2$), 1.95-2.95 (m, 4H, $COCH_2$), 3.30 (s, 4H, $COCH_2CO$), 4.05 (m, 4H, $O\underline{CH_2}CH_3$), 4.83 (s, CH enol); IR(KBr): 3000-2860, 1740, 1720 cm^{-1}.

Anal. Calcd. for $C_{15}H_{26}O_5$: C, 62.94; H, 9.09. Found: C, 62.89; H, 9.04

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SYNTHESIS OF METHYL

trans-2-PHENYLCYCLOPROPANE CARBOXYLATES

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As part of our ongoing synthetic program in designing new adrenergic agents, a series of substituted trans-2-phenylcyclopropane carboxylates was desired. Although the cyclopropanation of ethyl cinnamate using a palladium acetate catalyst has been reported as a preliminary communication,[1] there is no systematic study of the influence of aromatic substituents on the success of the reaction. We have now confirmed that palladium(II) acetate is suitable for the cyclopropanation of a variety of cinnamic acids or their esters with diazomethane under very mild conditions.

The nature of the substituents studied has little effect on the