

DECARBALKOXYLATIONS OF GEMINAL DIESTERS, β -KETO ESTERS AND α -CYANO ESTERS
EFFECTED BY SODIUM CHLORIDE IN DIMETHYL SULFOXIDE

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(Received in USA 16 January 1973; received in UK for publication 10 February 1973)

We wish to report that decarbalkoxylations of geminal diesters, β -keto esters, and α -cyano esters to the corresponding esters, ketones, and nitriles can be effected in excellent yields by sodium chloride in wet dimethyl sulfoxide at temperatures of 140-186°. This novel salt-solvent system avoids the hazardous use of sodium cyanide previously reported by us to effect decarbalkoxylations of geminal diesters (1,2).

A variety of mono- and disubstituted diethyl malonates have been decarboxylated by NaCl-wet DMSO and the results are tabulated in Table I. In all cases the yields of the esters are in the 90-95% range. The applicability of the NaCl-wet DMSO system for the decarbalkoxylation of β -keto esters and α -cyano esters is illustrated by the reactions summarized in Table II. Again excellent yields of products are obtained.

Carbon dioxide and ethanol are produced in the reaction. The loss of carbon dioxide served as a convenient probe for determining the minimum reaction temperature necessary to initiate the decarboxylation. Water is necessary to effect the reaction since use of anhydrous DMSO leads to little or no reaction.

General Procedure: The DMSO (Fisher certified grade) was used as received. Approximately 2 moles of water per mole of substrate was added to the DMSO. A slight excess of sodium chloride was used in most of the reactions. Sterling commercial uniodized table salt is satisfactory. The reaction mixture is magnetically stirred and the apparatus is fitted with an internal thermometer and a condenser. A trap containing a solution of barium hydroxide is connected to the apparatus through the top of the condenser. The reaction mixture is heated using an oil bath until no further evolution of carbon dioxide can be detected.

TABLE I

DECARBALKOXYLATIONS OF GEMINAL DIESTERS BY NaCl IN WET DMSO

$$RR_1C(CO_2Et)_2 \longrightarrow RR_1CHCO_2Et + CO_2 + CH_3CH_2OH$$

<u>DIESTER</u> \longrightarrow <u>ESTER</u> ^a	<u>TEMP (HRS)</u> ^b
R = R ₁ = H ^c	140-165 (6)
R = H, R ₁ = CH ₃ ^c	153-175 (4)
R = H, R ₁ = CH ₃ CH ₂ ^d	153-165 (4)
R = H, R ₁ = CH ₃ (CH ₂) ₁₅ ^e	158-170 (5)
R = H, R ₁ = CH ₃ (CH ₂) ₂₁ ^e	154-170 (6)
R = H, R ₁ = \emptyset ^c	135-170 (2)
R = H, R ₁ = \emptyset CH ₂ ^e	155-170 (3)
R = H, R ₁ = CH ₂ =CHCH ₂ ^e	153-165 (4)
R = R ₁ = CH ₃ ^e	175-180 (6)
R, R ₁ = CH ₂ CH ₂ CH ₂ ^f	178-183 (4)

^aEsters were isolated in 90-95% yields except in entries 1, 2, and 3 where the yields were calculated to be 85-95% from nmr analysis of the crude products. Ethanol was difficult to remove from these low boiling esters.

^bThe minimum temperature is the point at which carbon dioxide evolution commenced. The temperature was then slowly raised to the maximum temperature listed over the period of time given in parenthesis.

^c0.10 moles of diester, 0.11 moles NaCl, 0.20 moles of water in 50 ml DMSO.

^d0.07 moles diester, 0.006 moles NaCl, 0.10 moles of water in 50 ml DMSO.

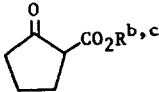

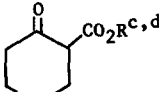
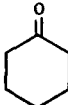
^e0.04 moles diester, 0.05 moles NaCl, 0.15 moles of water in 30-40 ml DMSO.

^f0.04 moles diester, 0.07 moles NaCl, 0.11 moles of water in 80-90 ml DMSO.

The isolation procedure depends on the properties of the product. Low boiling substrates (entries 1, 2, 3 in Table I and all entries of Table II) were distilled from the reaction. No further attempt was made to remove the co-distilled alcohol from these products. The higher boiling esters (entries 6 through 10 in Table I) were isolated by addition of water to the reaction mixture and separation of the ester layer. The aqueous layer was extracted with ether and the ester purified by distillation. The solid esters (entries 4 and 5 in Table I) were filtered from the cool reaction mixture and dissolved in ether. The ethereal solution was washed with water, dried, and the ether removed. The ester was recrystallized from ethanol.

TABLE II

DECARBETHOXYLATIONS OF β -KETO ESTERS AND α -CYANO ESTERS

REACTANT	PRODUCT ^a	TEMP (HRS)
		120-150 (5)
		130-150 (2)
$\text{CH}_3(\text{CH}_2)_3\underset{\text{CO}_2\text{Et}}{\underset{ }{\text{CH}}}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3^c$	$\text{CH}_3(\text{CH}_2)_4-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$	153-165 (5)
$\text{NCCH}_2\text{CO}_2\text{Et}^e$	CH_3CN^f	135-165 (2)
$\text{CH}_3(\text{CH}_2)_3\underset{\text{CO}_2\text{Et}}{\underset{ }{\text{CH}}}\text{CHCN}^e$	$\text{CH}_3(\text{CH}_2)_4\text{CN}$	152-168 (2)

^aIsolated in yields of 85-95%.

^bArapahoe Chemicals sample which by nmr analysis contains 35% and 65% methyl and ethyl esters, respectively.

^c0.065 moles of β -keto ester, 0.07 moles NaCl, 0.20 moles of water in 30-50 ml DMSO.

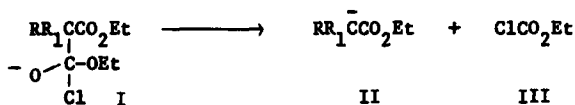
^dArapahoe Chemicals sample which by nmr analysis contains equal amounts of the methyl and ethyl esters.

^e0.09 moles α -cyano ester, 0.03 moles NaCl, 0.20 moles of water in 60 ml DMSO.

^fContaminated with ethanol and a little DMSO.

The effect of NaCl is catalytic as can be noted from entry 3 of Table I where a 10-fold molar excess of the diester over that of the salt was used and a 90% yield of the ester was obtained. For the diesters reported in Table I, diethyl phenylmalonate undergoes the most facile decarbethoxylation while diethyl dimethylmalonate and diethyl cyclobutanedicarboxylate undergoes the slowest decarbethoxylation. It, therefore, seems reasonable to propose from the limited data at hand that the decarbethoxylation proceeds via a nucleophilic catalysis mechanism. The nucleophilic attack of chloride ion, which is expected to be a strong nucleophile in a dipolar aprotic solvent such as DMSO (3), on one of the ester groups would lead to an intermediate such as I. Cleavage of the

C-C bond would lead to the carbanion II and ethyl chloroformate (III). Protonation of II by water



would lead to the ester and hydrolysis of III would regenerate the chloride ion and liberate alcohol and carbon dioxide. The decarbethoxylation ease of the diesters follows the carbanion stability of II.

Successful decarbethoxylation have been accomplished using alkali metal fluorides, bromides, chlorides, sodium azide, and sodium phosphate. Other dipolar aprotic solvents such as dimethyl formamide (bp 153°) have been utilized successfully. The decarbethoxylation of diethyl phenylmalonate with DMF-NaCl-water proceeds in an excellent yield. However, in less reactive substrates such as diethyl dimethylmalonate longer heating times must be employed because of the lower boiling point of DMF to that of DMSO (bp 189°).

Detailed studies on the above salts, other dipolar aprotic solvents, and additional substrates will be reported in the near future in a full paper.

Acknowledgment The authors are indebted to The Humphrey Chemical Company, North Haven, Connecticut 06473, for their interest in this research and partial financial support.

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