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PREPARATION OF KETONES BY A NOVEL DECARBALKOXYLATION OF β-KETO ESTERS: STEREOELECTRONIC ASSISTANCE TO C-C BOND FISSION

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ABSTRACT: Reaction of β-keto esters with the sodium derivative of propane-1,2-diol in an excess of anhydrous propane-1,2-diol causes facile decarbalkoxylation to ketones in excellent yields.

Alkyl β-ketocarboxylates are important intermediates in the synthesis of ketones.[1] Conversion of β-keto esters to ketones is achieved either by the classical sequence of alkaline hydrolysis, acidification and thermal decarboxylation[2], or by decarbalkoxylation effected by heating in wet DMSO above 140°C for several hours.[3]

We have been studying the chemistry of glycerol esters of carboxylic acids, especially the glycerides of edible fats and oils, with nucleophilic reagents.[4] Some extraordinary chemistry of β-keto carboxylic acid esters in this group has provided the basis for a preparative route to ketones. We report on this new simple procedure which converts alkyl β-keto carboxylates into ketones in excellent yields, on the intermediates involved in decarbalkoxylation, and on plausible reasons for the course of the reaction.

General Procedure. The β-keto ester is heated at 60-85°C for 15 to 30 minutes with the sodium (or potassium) derivative of propane-1,2-diol in an excess of propane-1,2-diol (prepared by preheating anhydrous propane-1,2-diol with NaOMe or similar strong base). After cooling, the product is extracted into an inert solvent such as toluene and, if necessary, purified by crystallization or other appropriate procedure.

The simplicity of the procedure is illustrated by the preparation of 12-tricosanone (laurone) which is described at the end of this communication. Identical results were obtained with NaOMe, NaOEt or NaH (60% suspension in hydrocarbon oil). If moisture was present or if KOH was used as the base, some lauric acid accompanied 12-tricosanone. Use of ethylene glycol or glycerol gave similar results but offered no advantage over propane-1,2-diol. Yields of ketones from several β-keto esters were over 95% (Table 1).

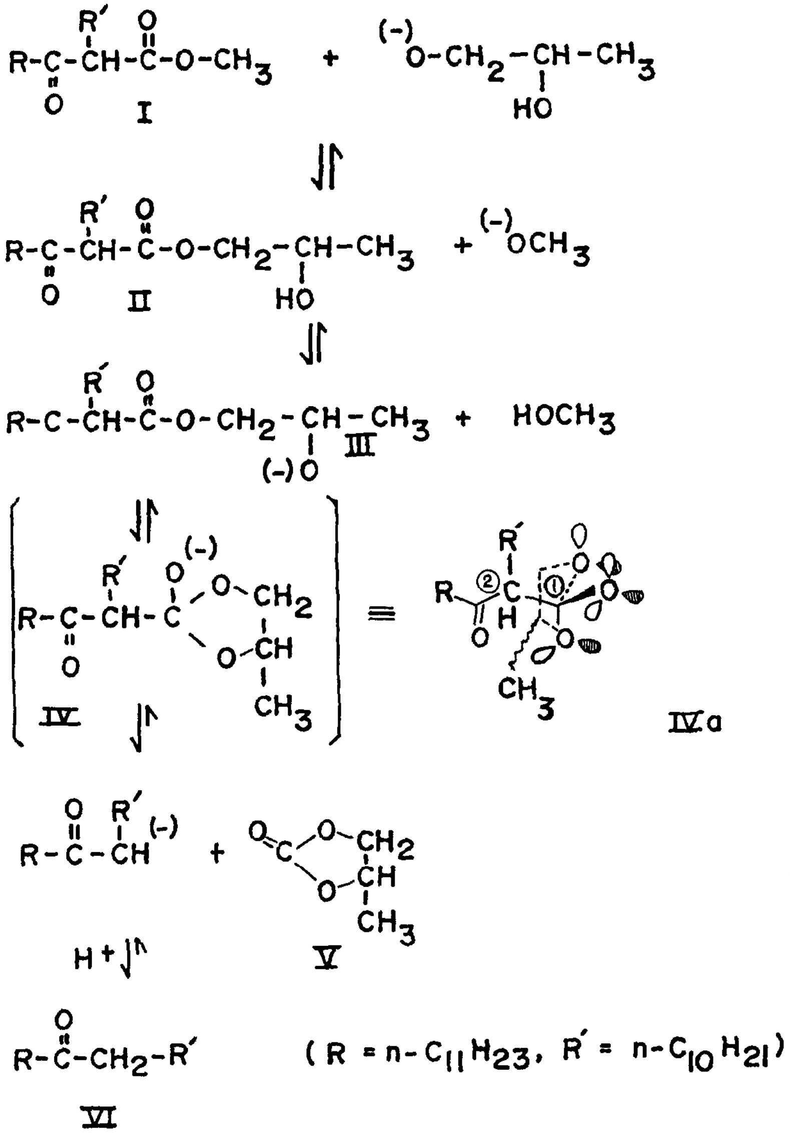
Table 1. Reactions of β-keto esters with sodio-propane-1,2-diol in anhydrous propane-1,2-diol at 80-85° for 30 minutes.

β-Keto Ester	Product	Yield[a]
Ethyl α-dodecyl acetoacetate	2-Pentadecanone	95%
Methyl α-lauroyl laurate (I)	12-Tricosanone (VI)	96%
Methyl α-palmitoyl palmitate	16-Hentriacontanone	96%
Methyl α-stearoyl stearate	18-Pentatricontanone	98%
2-Carbethoxy cyclooctanone	Cyclooctanone	95%
2-Carbethoxy cyclopentanone	Cyclopentanone	65%

[a] Quoted for chromatographically pure products.

Monitoring the reaction of methyl α-lauroyl laurate[5] (I) at successive time intervals showed that propane-1,2-diol α-lauroyl laurate (II + minor quantity of its secondary alcohol ester isomer) is formed initially but decreases in concentration as the quantity of 12-tricosanone[5] increases. The sodium derivative[6] III of II, decomposed readily at 85°C/0.25 Torr, yielding mainly 12-tricosanone (II) and propane-1,2-diol cyclic carbonate (V)[7]. In comparative experiments, reactions of I with octanol and octadecanol yielded octanyl laurate and octadecanyl laurate respectively (with a small quantity of 12-tricosanone).

In summary, base catalysed reaction of β-keto esters with monohydric alcohols involves the expected alcoholysis cum retro-Claisen fission to give two molecules of alkyl carboxylates[1]. In marked contrast, reaction with 1,2-diols leads exclusively to decarbalkoxylation. The sequence of reactions shown in Scheme 1 appears to be involved. The large excess of the reagents propane-1,2-diol and its oxygen anion ensures that the alcoholysis reaction gives a high dynamic concentration of the reactive intermediate III. Intramolecular addition of the internal oxygen anion to the ester carboxyl group in III involves a five atom ring geometry and is therefore expected to be favored over intermolecular (and intramolecular) attack on the ketonic carbonyl group. Moreover, in each of the two conformations which can be adopted by the cyclic hemi-ortho ester function in the intermediate IV, at least two non-bonded electron-pairs on different oxygens can be simultaneously antiperiplanar to the C(1)-C(2) bond, and in fact, in the conformation IVa, all three oxygens carry electron pairs in such orientation. Deslongchamps has suggested[8] that his theory of stereoelectronic control of carbon-heteroatom bond cleavage in the tetrahedral intermediates of hydrolysis of esters and amides may be applicable also to carbon-carbon bond cleavage. Therefore, it is reasonable to infer that the stereoelectronic configuration of the cyclic hemi-ortho ester IV≡IVa provides powerful assistance to C-C bond fission, and in conjunction with the intramolecular pathway to this intermediate, ensures preferential cleavage of C(1)-C(2) bond and domination by decarbalkoxylation over the normal



SCHEME 1

retro-Claisen fission.[9] We are testing this inference, inter alia, using comparative reactions with epimeric pairs of conformationally rigid 1,2-diols.

The decarbalkoxylation procedure described here complements the existing methods,[1-3] and apart from its simplicity and efficiency, offers additional advantages inherent in low-temperature, short-time reactions. It has general applicability to alkyl β-keto carboxylates and potential for application to alkyl carboxylates with other electron-with drawing β-substituents.

Preparation of 12-tricosanone. A mixture of anhydrous propane-1,2-diol (2 ml, excess; dried over Molecular Sieve 4A) and NaOMe (50mg, excess) was heated at 85°C for 15 minutes in a vial fitted with a teflon-lined screw cap. Methyl α-lauroyl laurate[5] (I) (100 mg) was added and heating continued for 30 minutes. The mixture was cooled to room temperature and extracted with anhydrous toluene (4 x 2 ml). The combined toluene extract was washed with anhydrous propane-1,2-diol (2 ml), then with water (3 x 5 ml), dried over anhydrous sodium sulphate and evaporated to dryness under reduced pressure. The residue crystallized from ethanol as colorless, shining plates (84 mg, 96%), pure by TLC and identical in TLC, IR, M.P. and mixed M.P. with authentic 12-tricosanone[5] (VI).

REFERENCES AND NOTES

1. H. O. House, Modern Synthetic Reactions, 2nd Ed., W. A. Benjamin, Inc., 1972, p. 492.
2. See J. R. Johnson and F. D. Hager in Organic Synthesis, Coll. Vol. 1, H. Gilman and A. H. Blatt, Editors, J. Wiley, New York, 1941, pp. 351.
3. See A. P. Krapcho, Synthesis, 805 (1982) and references therein.
4. R. Aneja, A. P. Davies, A. Harkes and J. A. Knaggs, J. C. S. Chem. Comm., 963 (1974) and references therein; R. Aneja, A. P. Davies, Chem. Phys. Lipids, in press; R. Aneja and W. M. Hollis, unpublished.
5. R. R. Briese and S. M. McElvain, J. Am. Chem. Soc., 55, 1697 (1933).
6. Prepared in-situ by reaction of NaH and II (isolated by preparative TLC of the crude reaction product from I, propane-1,2-diol and NaOMe at 55°C for 5 minutes).
7. H. Najer, P. Chabrier and R. Guidicelli, Bull. Soc. Chem. France, 1142 (1954); C.A., 49, 12303 (1955).
8. P. Deslongchamps, (a) Tetrahedron, 31, 2463 (1975); (b) Heterocycles, 7, 1271 (1977).
9. The concept of stereoelectronic control of C-C bond cleavage[8], and conversely of C-C bond formation, may well offer opportunities for designing new methods of C-C bond synthesis; we are exploring some of these opportunities.

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