Tetrahedron Letters No. 49, pp 4389 - 4392, 1975. Pergamon Press. Printed in Great Britain.

A NOVEL SYNTHESIS OF CYCLOPROPYL KETONES VIA DECARBOXYLATIVE RING CONTRACTIONS OF α-ACYL-γ-BUTYROLACTONES CATALYZED BY HALIDE IONS IN DIPOLAR APROTIC SOLVENTS

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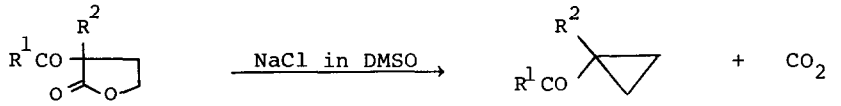
(Received in Japan 21 August 1975; received in UK for publication 20 October 1975)

While the decarboxylation of β-keto carboxylic acids has been a well-known reaction, the recent investigations by Krapcho[1] and other workers[2] enabled a direct decarbalkoxylation of β-keto esters using alkali metal halides in dipolar aprotic solvents. We now wish to report that when this new method was applied to α-acyl-γ-butyrolactones, cyclopropyl ketones were obtained in excellent yields. Namely, for example, 3-benzoyldihydro-2(3H)-furanone(α-benzoyl-γ-butyrolactone) (1a) was heated in DMSO in the presence of NaCl to yield cyclopropyl phenyl ketone(2a).

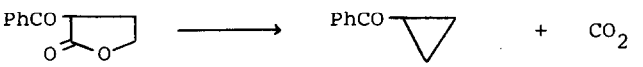


(1) (2)

Although many synthetic methods of cyclopropyl ketones are known in the literature,[3] the present method is unique in the mechanistic viewpoint and more versatile in practice. Only two cases of the ring contraction of dihydro-2(3H)-furanones(γ-butyrolactones) into cyclopropanes are documented, namely photolysis of γ-phenyl-γ-butyrolactones[4] and thermal decomposition of the phosphonium salt obtained from α-bromo-γ-butyrolactone and triphenylphosphine.[5]

Table I shows that, a) NaCl is essential for the conversion of (1a) to (2a), b) water is unnecessary for the present reaction although wet DMSO was used in the case of decarbalkoxylation of β-keto esters,[1,2] c) other alkali metal halides are also effective; among them NaBr achieves the most facile conversion of (1a) to (2a), and d) successful decarboxylative ring contraction is also accomplished using quarternary ammonium halides in DMSO or 1,4-diazabicyclo[2,2,2]octane (Dabco) in o-xylene, the latter being a reagent recently reported to cleave β-keto esters.[6]

Table I Reaction of 3-Benzoyldihydro-2(3H)-furanone in Various Solvents in the Presence of Catalysts



(1a) (2a)

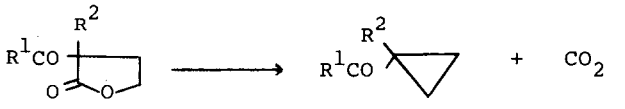
Catalyst[a]	Solvent	Yield of (2a)[b]	Reaction Conditions	
NaCl	DMSO	69 (%)	160°	6 (hr)
none	DMSO	0[c]	160	6
NaBr	DMSO	91.5	160	6
NaI	DMSO	76.5	160	6
KCl	DMSO	50.3	160	6
TMAB[d]	DMSO	57.5	160	6
NaBr	DMF	73.2	reflux	6
Dabco[e]	o-Xylene	62.3	reflux	6

a) 0.01 mole substrate (1a) and 0.011 mole catalyst were used except for Dabco. Six mole equivalents of Dabco were used. b) Isolated yield by SiO_2 column chromatography. c) (1a) was recovered. d) TMAB: Tetramethylammonium bromide. e) Dabco: 1,4-Diazabicyclo-[2,2,2]octane.

The following example represents a typical procedure of the present synthesis of cyclopropyl ketones. A mixture of 3-benzoyldihydro-2(3H)-furanone(1a) (10 mmole) and alkali metal halide(11 mmole) in DMSO(10 ml) was heated at 160° for several hours in a nitrogen atmosphere. After cooling, water was added to the reaction mixture and the resulting mixture was extracted with chloroform. The extract was washed, dried and concentrated. The residue was chromatographed over SiO_2 to give pure cyclopropyl phenyl ketone(2a): IRν(liq. film) 1670 cm^{-1} (ketone); NMR(60 MHz)$\delta(CDCl_3)$ 0.7-1.5(m. 4H cyclopropane), 2.4-2.5(m. 1H cyclopropane), 7.2-8.2(m. 5H aromatic).

The results of the decarboxylative ring contractions of other 3-acyl-3-alkyldihydro-2(3H)-furanones(1) are summarized in Table II; cyclopropyl ketones were obtained in excellent yields. With less reactive substrates, such as 3-acetyl and 3-cyclohexylcarbonyldihydro-2(3H)-furanone, longer heating was necessary. In these cases DMF was superior to DMSO as solvent probably because of the thermal stability of the former.

Table II Synthesis of Cyclopropyl Ketones from 3-Acyl-3-alkyldihydro-2(3H)-furanones

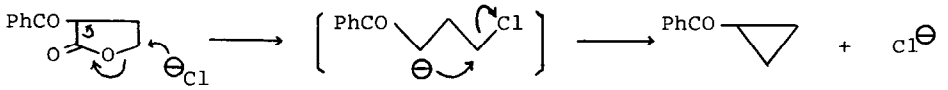


(1) (2)

Substrate	R^1	R^2	Catalyst[a]	Solvent	Yield[b] of (2)	Reaction Conditions	
(1a)	Ph	H	NaCl	DMSO	69 (%)	160°	6 (hr)
(1b)	4-Cl-C_6H_4	H	NaCl	DMSO	69	160	8
(1c)	4-Me-C_6H_4	H	NaCl	DMSO	73.5	160	9
(1d)	4-MeO-C_6H_4	H	NaCl	DMSO	6o.7	160	9
(1e)	Ph	Me	NaCl	DMSO	82.4	160	12
(1f)	Ph	$PhCH_2$	NaCl	DMSO	100	160	10
(1g)	$PhCH_2$	H	NaBr	DMSO	65	160	8
(1h)	Me	H	NaBr	DMF	51.8	reflux	59
(1i)	Cyclohexyl	H	NaBr	DMF	70	reflux	55

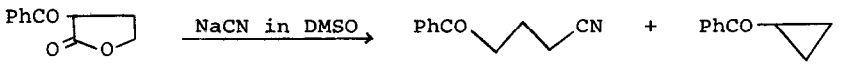
a) 1.1 mole equivalents of catalyst were used. b) (2a)-(2f) were isolated by SiO_2 column chromatography; (2g)-(2i) were purified by distillation. All the products were identified by IR and NMR spectra.

We propose the following mechanism for the present reaction. Chloride ion, which is expected to be a strong nucleophile in the dipolar aprotic solvents, would attack position 5 of (1a). Subsequent decarboxylation gives the carbanion (3),[7] which undergoes intramolecular cyclization to give (2a).



(1a) (3) (2a)

In order to get an evidence for the proposed mechanism of this ring contraction, (1a) was allowed to react with NaCN in DMSO which is also mentioned as a catalyst for decarbalkoxylation of geminal diesters.[1a] 4-Benzoylbutyronitrile (4) [IRν(liq. film 2230 cm^{-1}(nitrile), 1690 cm^{-1}(ketone); NMR(60 MHz)δ($CDCl_3$) 1.8-2.4(m. 2H methylene), 2.46(t. J=6 Hz 2H methylene), 3.10(t. J=6 Hz 2H methylene), 7.2-8.1(m. 5H aromatic)] was isolated as expected.



(1a) (4) 17 % (2a) 3.6 %

The present one-step synthesis of cyclopropyl ketones conducted in neutral conditions is of greater advantage than the classical procedure[8] which involves hydrolysis and decarboxylation of (1) under acidic conditions and subsequent intramolecular cyclization under basic conditions.

We thank Professor H.Takei, Tokyo Institute of Technology, for informing us that he obtained similar results, prior to publication.[9]

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