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THERMAL AND BASE-CATALYZED REARRANGEMENTS OF DIACYL CARBINOLS[1]

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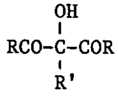
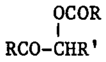
Diacyl carbinols undergo facile thermal and base-catalyzed rearrangements to α-ketol esters.

Over forty years ago Blatt and Hawkins[2] reported that attempted distillation of dibenzoyl carbinol (1a) resulted in rearrangement to the benzoate (2a) of α-hydroxyacetophenone. This result was later reproduced by Karrer et al[3] and twenty years ago two additional examples of this type of reaction (1b → 2b, 1c → 2c) were reported by House and Gannon.[4] Karrer et al also observed rearrangement of 1a to 2a in aqueous methanolic sodium bicarbonate; stronger base afforded cleavage products.[5]



$RCO-\underset{R'}{\overset{OH}{C}}-COR$

1



$RCO-\overset{OCOR}{C}HR'$

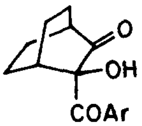
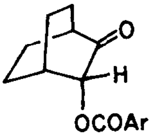
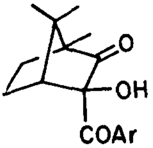
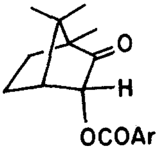
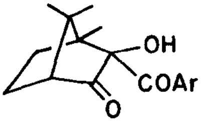
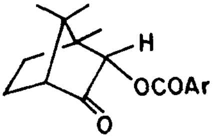
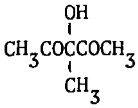
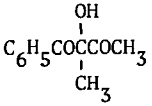
2

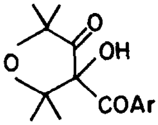
a, R = C_6H_5, R' = H b, R = C_2H_5, R' = CH_3 c, R = CH_3, R' = $C_6H_5CH_2$

In the course of investigations of photochemical reactions of cyclic α-diketones with aldehydes,[1,6] we encountered additional examples of this type of reaction. In fact, rearrangement was so facile that both gas chromatographic analysis (200°C) and column chromatography on Florisil afforded the α-ketol esters analogous to 2 quantitatively; the α-hydroxy-β-diketones actually present in the mixture were not detected. Fortunately, rearrangement was not effected by silica gel (or dilute acid) so that analysis and separation of mixtures was feasible. As a result we were led to examine the behavior of a number of compounds containing the -CO-C(OH)-CO moiety and wish to report that rearrangement of this system is quite general and may proceed with great facility both thermally and with catalysis by base.

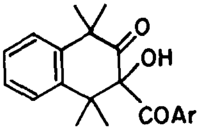
The systems examined are summarized in the table where it can be seen that both base-catalyzed and thermal reactions can be observed in all cases; cyclic systems were more reactive thermally than open chain analogues. The regio- and stereospecificity observed in the bornane system (compounds 5, 7) are particularly noteworthy and provide support for the mechanism suggested by earlier workers.[3,4] This is illustrated below for the base-catalyzed process;

Rearrangements of Diacyl Carbinols[i]

Compound	Product(s)	Conditions	Yield or Ratio
 3a, Ar=C_6H_5 b, p-ClC_6H_4 c, p-$CH_3C_6H_4$ d, p-$CH_3OC_6H_4$	 4a-d	200°, 1 min GC injector block (200°) Florisil, $CHCl_3$, RT, 1 hr $5x10^{-3}$ N KOH/CH_3OH, RT, 10 min	100%
 5a-d	 6a-d	As above	100%
 7a-d	 8a-d	As above	100%
 $CH_3CO\overset{OH}{\underset{CH_3}{C}}COCH_3$ 9	$CH_3COCH(OCOCH_3)CH_3$ 10 $CH_3COCH(OH)CH_3$ 11	200°, 30 min Florisil, $CHCl_3$, RT, 24 hr $1.4x10^{-2}$ N KOH/CH_3OH, RT, 1 min	25% of 10 N.R. 10 + 11
 $C_6H_5CO\overset{OH}{\underset{CH_3}{C}}COCH_3$ 12	$CH_3COCH(OCOC_6H_5)CH_3$ 13 $C_6H_5COCH(OCOCH_3)CH_3$ 14 $CH_3COCH(OCOCH_3)C_6H_5$ 15	210°, 2 hr NaH, ether, RT, 10 min	13:14:15=1:2:1 13+14+15



16[ii]



17[ii]

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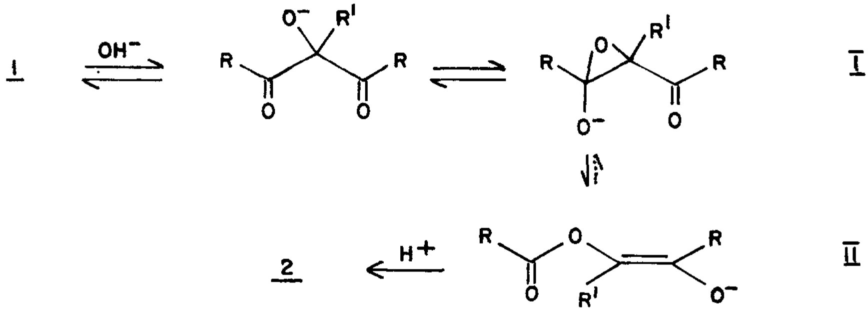
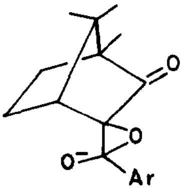
i. Preparation and characterization of compounds is described in ref. 1. Cf also ref 6.

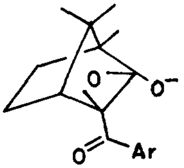
ii. Both gas and Florisil chromatography resulted in efficient rearrangement in these systems as well.



a similar mechanism has been proposed for the thermal reactions. Steric requirements for addition to carbonyl groups[8] are believed to account for regiospecificity in formation of the epoxide I[9]; thus, for example, III will be formed in preference to IV in the case of 5. Intermediacy of the enolate ion (or enol) II accounts nicely for the stereochemistry observed with 5 since such enolates have been shown[11] to undergo preferential ketonization from the *exo* side of the molecule.

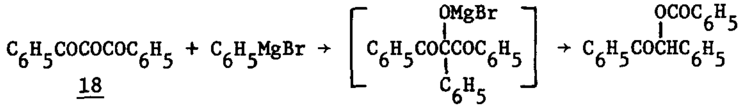


III



IV

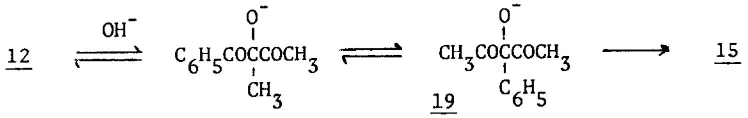
Early reports of rearranged products formed in reactions of diphenyl triketone[12] (18) with phenyl magnesium bromide[13] or active methylene compounds[14] can now be rationalized readily by assuming that initial attack of the reagent at the central carbonyl group of the trione generates a diacyl carbinol derivative. This is illustrated for the Grignard reaction. Similar



$$\underset{\mathbf{18}}{C_6H_5COCOCOC_6H_5} + C_6H_5MgBr \rightarrow \left[C_6H_5CO\overset{\overset{\displaystyle OMgBr}{|}}{\underset{\underset{\displaystyle C_6H_5}{|}}{C}}COC_6H_5 \right] \rightarrow C_6H_5CO\overset{\overset{\displaystyle OCOC_6H_5}{|}}{C}HC_6H_5$$

rearrangement might be involved in observation of α-ketol esters in photochemical reactions of cyclopropyl conjugated 1,2-diketones.[15]

The unsymmetrical compound, acetyl benzoyl methyl carbinol (12) was originally chosen to examine "relative migratory aptitudes" of acyl *vs* aroyl groups but provided an unexpected result, as shown in the Table. In addition to the two expected products, 14 (acetyl group migration) and 13 (benzoyl group migration), a third product (15) was isolated in significant quantity from both thermal[16] and base-catalyzed reactions. A possible mechanism for formation of 15 is illustrated below in which the anion of starting diacyl carbinol (12) undergoes isomerization to anion of diacetyl phenyl carbinol (19) in a process analogous to the benzilic acid rearrangement of α-diketones. A similar process has been established for



$$12 \xrightleftharpoons{OH^-} C_6H_5CO\overset{O^-}{\underset{CH_3}{C}}COCH_3 \rightleftharpoons \underset{19}{CH_3CO\overset{O^-}{\underset{C_6H_5}{C}}COCH_3} \longrightarrow 15$$

certain α-hydroxy-β-ketoesters[17] and for vic-triketones.[12] It should be noted, however, that rapid acyl group migration in the intermediate enolate ion II (or enol) could also account for formation of 15. Further evidence that rearrangement of the type 12→19 does, in fact, occur, will be presented elsewhere.

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