Reaction of Benzoylacetaldehyde and of Benzoylacetone with Hydroxylamine. Acetylation of the Resulting "Oximes"

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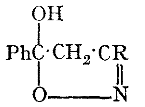
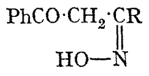
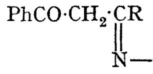
Summary Reaction of hydroxylamine with benzoylacetaldehyde gives a derivative which, in solution, is a mixture of (I; R = H), (II; R = H), and (III; R = H), whereas that from the reaction with benzoylacetone is, exclusively, (I; R = Me); acetylation of the former gives (VI) and true diacetates (V; R = H), whereas that of the latter gives only true diacetates (V; R = Me).

THE spectral properties of the known solid mono-oxime of benzoylacetaldehyde,[1] m.p. 85—7°, are only interpretable by accepting that, in solution, it exists as an *equilibrium* mixture of the two open oximes (II) and (III; R = H) and the "cyclo-oxime" (I; R = H). This is the first time we have found such an (n.m.r. observable) equilibrium mixture of open and cyclic forms in derivatives of this kind.[2] *Spectral properties*: i.r.: 3200 (broad band; associated OH), 1672 (C=O), and 1640 cm.$^{-1}$ (C=N) (KBr); 3600 (free OH) and 1695 cm.$^{-1}$ (C=O) (high dilution in CCl_4). U.v.: λ_{max} 243 nm. (ϵ 3600) (MeOH). N.m.r.: τ 2·0 [complex band: *ortho*-hydrogens in (II) and (III; R=H)], 2·6 (complex band; other phenyl hydrogens and vinyl hydrogens), 6·0 (d, *J* 5 Hz.) and 6·2 (d, *J* 6 Hz.) [methylene hydrogens in (II) and (III; R = H), respectively[3]]; 6·57, 6·86, 6·92, and 7·21 [AB system of split bands, *J* 2 Hz.; methylene hydrogens in (I; R = H)] ($CDCl_3$) (in CD_3COCD_3, similar spectrum plus OH signal at τ 4·5).

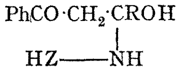

(I)


(II)

$PhCO\cdot CH_2\cdot CR{=}N{-}OH$


(III)

$PhCO\cdot CH_2\cdot CR{=}N{-}OH$

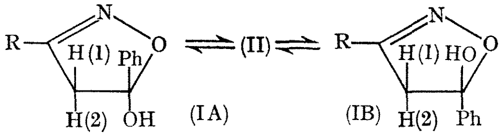

(IV)

$PhCO\cdot CH_2\cdot CROH(-NH-ZH)$

Initially, the doublet at τ 6·2 was hardly observable, but after a few minutes it was almost as intense as that at τ 6·0. In our view, in the reaction between β-dicarbonyl compounds and carbonyl reagents, intramolecular interaction in the nonisolable intermediates of type (IV) means that the isomers formed upon dehydration are those with a *cis*-relationship between the ZH group (Z = NX, O) and the carbonyl moiety.

The mono-oxime of benzoylacetone has been described[4] as an oily substance, but working in heterophase conditions, in dioxan–water, we have succeeded in isolating it (32% yield) as a solid derivative, m.p. 70—71°. According to its spectral properties, this derivative is the "cyclo-oxime" (I; R = Me); i.r.: 3200 (broad band; associated OH) and 1630 cm.$^{-1}$ (C=N) (KBr); u.v.: $\lambda_{\max}$ 250—257 nm. (ϵ 950) (EtOH); n.m.r.: τ 2·7 (complex band; 5H; phenyl hydrogens), 6·95 (2H; methylene hydrogens), 8·07 (3H; methyl hydrogens) (CCl_4) (in CD_3COCD_3, similar spectrum plus OH signal at τ 3·95; in $CDCl_3$, the spectrum was that of 3-methyl-5-phenylisoxazole).

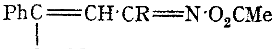
The methylene group in the "cyclo-oxime" (I; R = Me), in contrast with that in the "cyclo-oxime" (I; R = H), *does not* give rise to an AB system; this can be explained by accepting that compounds (I; R = H) and (I; R = Me)are, respectively, slow and fast (n.m.r. time-scale) equilibrating mixtures of the two enantiomers (IA and IB).



(IA) (IB)

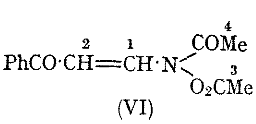
Acetic anhydride–pyridine acetylation of (I; R = Me) afforded (79% yield) a crude product from which a pure component was isolated by preparative t.l.c. Analysis and spectral properties of this substance were consistent with its being one of the four possible stereoisomers with structure (V; R = Me); i.r.: 1760 (vs), 1640 (s), and 1200 cm.$^{-1}$ (vs) (KBr); u.v.: $\lambda_{\max}$ 282 nm. (ϵ 13,500) (EtOH); n.m.r.: τ 2·55 (rather narrow band; phenyl hydrogens), 3·19 (vinyl hydrogen); 7·74, 7·81, and 7·89 (methyl resonances) (CCl_4). The i.r. spectrum of the crude product was very similar to that of the pure substance, thus showing that it was essentially a mixture of stereoisomers.

Acetic anhydride–pyridine acetylation of the oxime of benzoylacetaldehyde afforded (23% yield) the reported[1,5] "diacetate," m.p. 113—115°, whose spectral properties are widely different from those of compounds (V; R = Me) and are best interpreted on the basis of an *NO*-diacetylhydroxylamine structure (VI).[6] *Spectral properties*: i.r.: 1810, 1710, and 1680 cm.$^{-1}$ (carbonyl groups) (KBr); u.v.: $\lambda_{\max}$ 297 nm. (ϵ 17,500) (MeOH); n.m.r.: τ 1·38, 1·60 (doublet, *J* 13·7 Hz.; rather broad bands; 1-H), 1·9 (complex bands; *ortho*-hydrogens), 2·4 (complex band; other phenyl hydrogens), 3·17, 3·39 (doublet, *J* 13·7 Hz; 2-H), 7·5 [methyl (3)], and 7·68 [broad singlet; methyl (4)] (CD_3COCD_3). Spectral analysis of the crude product showed the presence of true diacetates.



$\mathrm{Ph\underset{\displaystyle O_2CMe}{C}{=}CH{\cdot}CR{=}N{\cdot}O_2CMe}$

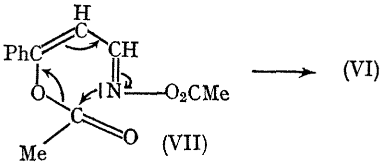
(V)



$\mathrm{PhCO{\cdot}\overset{2}{C}H{=}\overset{1}{C}H{\cdot}N{<}^{\overset{4}{C}OMe}_{O_2CMe\ 3}}$

(VI)

These acetylation results can be rationalized as follows: the solution of the oxime of benzoylacetaldehyde is an equilibrium mixture in which the two stereoisomeric open oximes are present, and thus acetylation can conceivably give the four true diacetates of structure (V; R = H). Of these diacetates, the isomer (VII), which is one of the two formed from the *trans*-oxime, has the correct configuration to undergo an *ON*-acetyl migration[7] which will lead to compound (VI). On the other hand, acetylation of the "cyclo-oxime" (I; R = Me) must take place through the intermediacy of the small (n.m.r. unobservable) amount of open *cis*-oxime present in equilibrium with the cyclic isomer, thus leading to diacetates of the wrong spatial arrangement for an *ON*-acyl migration to occur.



(VII)

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