

THE REACTIONS OF NITROSOBENZENE WITH DIETHYL METHYLENEMALONATE
AND 1,1-DIPHENYLETHYLENE

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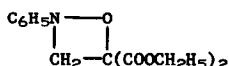
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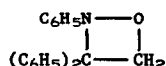
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(Received 14 June 1963)

In 1924, Ingold and Weaver reported that nitrosobenzene (I) underwent cycloaddition with diethyl methylenemalonate (II) and 1,1-diphenylethylene (III) to yield products formulated as IV and V¹;

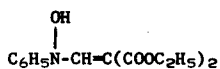


(IV)

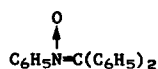


(V)

these compounds represent the only reported non-fluorinated examples of the oxazetidine ring system². In 1925, these structural assignments were criticized by Lapworth who proposed structures VI and VII for the



(VI)



(VII)

reaction products³. However, the conclusions of Ingold have been accepted by recent workers^{2,4} in the field and the criticisms of

¹ C. K. Ingold and S. D. Weaver, J. Chem. Soc. 125, 1456 (1924).

² D. A. Barr, R. N. Haszeldine and C. J. Willis, J. Chem. Soc. 1351 (1961).

³ G. N. Burkhardt and A. Lapworth, J. Chem. Soc. 127, 1748 (1925); G. N. Burkhardt, A. Lapworth and J. Walkden, J. Chem. Soc. 127, 2458 (1925).

⁴ B. G. Gowenlock and W. Luttke, Quarterly Revs. 12, 321 (1958); J. Harner and A. Macaluso, Tetrahedron Letters No. 6, 381 (1963).

Lapworth have been overlooked. Because cycloadditions are atypical of the reactions between I and mono-olefins⁵ and because the evidence cited in support of structures IV, V and VI, VII was equivocal, the reactions of I with II and III have been reinvestigated in an effort to resolve these discrepancies.

Reaction of I and II in refluxing chloroform led to the formation of a product with the reported properties^{1,3}; the analytical data was consistent with both IV and VI⁶. The adduct absorbed at 3215 cm.^{-1} (bonded hydroxyl), 1701 cm.^{-1} (ester carbonyl) and 1600 cm.^{-1} (olefinic); these absorptions are consistent only with structure VI. The structural assignment was supported by the ultraviolet absorption spectrum ($\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 224, 317 $\text{m}\mu$) of the adduct; the oxazetidine (IV) would be expected to absorb as a typical anilino compound ($\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 230, 280 $\text{m}\mu$). Finally, confirmation of the structure was provided by the NMR spectrum⁷ of the adduct, in which the presence of all the structural features of VI could be readily discerned:

(i) a sharp singlet (relative intensity by integration:

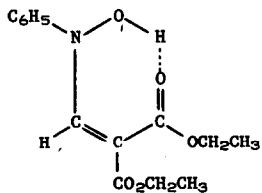
1) at $\tau = -2.46$, assignable to the strongly hydrogen-bonded hydroxyl proton as in structure VIa:

⁵ L. Alessandri, *Gazz. chim. ital.* 54, 426 (1924) and earlier papers.

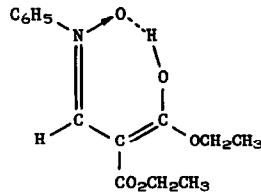
⁶ Two nitronic products, $\text{C}_6\text{H}_5\text{N(O)=C(COOC}_2\text{H}_5)_2$ and $\text{C}_6\text{H}_5\text{N(O)=CHCH(COOC}_2\text{H}_5)_2$ must be considered as possible for the adduct on the basis of the work of Alessandri⁵. Both are cleanly eliminated by the infrared and NMR studies, the latter being referred to in the text.

⁷ All NMR spectra were obtained at 60 mc. on a carefully calibrated Varian Associates model A-60 spectrometer; sample temperature $37 \pm 1^\circ\text{C}$. All spectra were determined using dilute solutions in CDCl_3 . Chemical shifts are reported as τ -values⁸, and are precise to ± 0.008 or better, except where otherwise noted.

⁸ G. V. D. Tiers, *J. Phys. Chem.* 62, 1151 (1958).



(VIa)



(VIb)

(ii) a singlet (relative intensity: 1) at $\tau = 1.62$, a not unreasonable chemical shift for the olefinic proton in view of its position at the highly electron-deficient terminus of this α,β -unsaturated carbonyl system; the attachment of the electro-negative nitrogen to the olefinic carbon atom also contributes to the low τ -value observed for this proton.

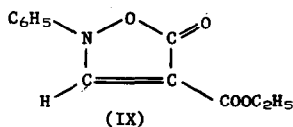
(iii) complex, but over-all relatively narrow, absorption (relative intensity: 5) in the region of $\tau \sim 2.58$, assignable to the five aromatic protons. Unpublished model compound studies in our laboratories indicate that the small observed shifts of the aromatic proton resonances (from each other) strongly favors formulation VIa over the inherently much less likely VIb, since we have observed that in the latter type of structure, the resonances of the ortho protons are chemically shifted considerably more from those of the meta and para protons than in a structure of type VIa, causing a more complex, wider-spread pattern to be obtained⁹.

(iv) a pair of quartets (total relative intensity: 4) at $\tau = 5.66$ and $\tau = 5.78$, and a pair of triplets (total relative intensity: 6) at $\tau = 8.63$ and 8.71 (all splittings 7.0 ± 0.2 cps), clearly indicative of the presence of two magnetically non-equivalent ethoxy groups attached to some additional unsaturation.

⁹ A more detailed account of these two types of spectra will be published elsewhere.

Thus the structure proposed by Lapworth is confirmed, and VI represents the first non-nitronic product formed by reaction of I and a simple mono-olefin⁵.

The adduct was reported by Ingold to undergo thermal transformation to yield dicarbethoxyacetanilide (VIII), a product inconsistent with an oxazetidine structure in view of the more recent studies of Haszeldine². Refluxing a solution of VI in dioxane or heating a melt of VI to 140° led to the formation of a material (IX) with approximately the same properties as reported¹ for VIII; IX could also be isolated from the residues of the reaction of I and II. The analysis of IX



indicated the loss of a molecule of ethanol from VI; ester (1701 cm^{-1}), five-membered lactone (1795 cm^{-1}) and olefinic (1603 cm^{-1}) absorptions were observed, but amide bands were absent. The ultraviolet spectrum ($\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 211, 311 $\text{m}\mu$) was quite similar to that of VI, but inconsistent with that expected for VIII. A cyclic structure, 2-phenyl-3-carbethoxy-5-isoxazolone, was consistent with the data; IX could be formed readily from VI by a transesterification process. Support for the postulated structure was provided by a comparison of the physical and chemical properties of IX with those of its known N-methyl analog (X)¹⁰. The infrared spectrum of IX is almost identical to that of X, and IX underwent basic hydrolysis to give the monoanilide of malonic acid in analogy to the behavior of X¹⁰. The postulated structure for IX was confirmed by its NMR spectrum, which showed the following four groups of resonances similar to those observed in the spectrum of VI:

¹⁰ H. Ulrich, J. N. Tilley and A. A. Sayigh, J. Org. Chem. 27, 2160 (1962).

(i) a singlet (relative intensity: 1) at $\tau = 1.08$ for the olefinic proton. The "extra" lowering of this resonance position over that observed for the analogous proton of VI ($\tau = 1.68$) is probably due largely to the different spatial orientation of the (lactone-type) carbonyl group in IX. In this structure, the olefinic proton is now fixed in a position (a) in the plane of, and (b) "behind", the lactone carbonyl group, circumstances well-known to result in marked extra de-shielding.

(ii) a five-proton complex from the aromatic hydrogens at $\tau \sim 2.53$, similar to that observed for VI, but again here at slightly lower fields, possibly due to a small effect similar to that discussed above for the olefinic resonance.

(iii) a two-proton quartet ($\tau = 5.68$) and a three-proton triplet ($\tau = 8.67$), splitting ~ 7.2 cps, now indicating the presence of only one ethoxy group, as required by structure IX.

The reaction of I and III in chloroform at room temperature led to the isolation of a product possessing the reported^{1,3} physical properties. The analytical results did not allow differentiation between the proposed structures (V and VII)¹¹. The ultraviolet spectrum. ($\lambda_{\max}^{95\% \text{ EtOH}}$ 232, 308 m μ) corresponded closely to that reported for benzylidene-N-phenylnitrone¹² (XI, $\lambda_{\max}^{95\% \text{ EtOH}}$ 232, 314 m μ); for V only anilino absorption should be observed. Lithium aluminum hydride

¹¹ By analogy with VI, a vinyl hydroxylamine structure was also considered for this product, but was eliminated by the lack of hydroxyl and olefinic absorptions in the infrared. A second nitronic structure, $\text{C}_6\text{H}_5\text{N}(\text{O})=\text{CHCH}(\text{C}_6\text{H}_5)_2$ was also considered but was eliminated by comparison with an authentic sample of the material prepared by the reaction of β,β -diphenylacetaldehyde with phenylhydroxylamine.

¹² M. J. Kamlet and L. A. Kaplan, *J. Org. Chem.* 22, 576 (1957).

reduction of the product gave a hydroxylamine (XII, O-H bond at 3333 cm.^{-1}) which was identical in all respects to the product formed by the addition of phenylmagnesium bromide to XI. XII could be oxidized readily to VII with hydrogen peroxide. Thus, the structure proposed by Lapworth is confirmed and this reaction follows the general behavior established by Alessandri⁵.

With the refutation of the oxazetidine formulations for these products, the fluorinated compounds² remain as the only authentic examples of this ring system.

This study was supported in part by a grant (RG 6811) from the Division of General Medical Sciences, Public Health Service.