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# The Photolysis and Thermolysis of Ethyl Azidoformate in the Presence of Ketones

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The photochemical decomposition of ethyl azidoformate (I) in an acetone solution gives the nitrene adduct, oxazirane II, whereas the thermolysis of the solution gives a C–H insertion product, III. The photolysis of I in cyclohexanone gives an α-insertion product, IX, while the thermolysis affords a β-insertion product, X, and an oxazole, XIII, in addition to IX. The multiplicity of the reactive species is examined in terms of the heavy-atom effect.

In contrast with carbene chemistry, few examples have been reported of the reactions of nitrenes with *n*-bases.[1,2] An arylnitrene has been observed to react intramolecularly with a carbonyl group to produce anthranil,[3] but the attempted intermolecular reaction of benzenesulfonylnitrene with cyclohexanone failed to afford any products arising from nitrene-addition.[4] We wish now to report that ethoxycarbonylnitrene generated by photolysis or thermolysis has been incorporated into acetone and cyclohexanone.

Table 1 lists the reaction conditions and product distributions in the reaction of ethyl azidoformate (I) with acetone. The irradiation[5] of an acetone solution of I gave 2-ethoxycarbonyl-3,3-dimethyloxazirane (II), hexane-2,5-dione (IV), and ethyl carbamate (V). The thermally labile oxazirane II polymerized upon slight heating and gave no satisfactory analyses, but the exact mass was compatible with the molecular formula of $C_6H_{11}NO_3$. The hydrolysis of II gave an

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[1] "Nitrenes," ed. by W. Lwowski, John Wiley & Sons, New York (1970).

[2] H. Nozaki, S. Fujita, H. Takaya, and R. Noyori, *Tetrahedron*, **23**, 45 (1967).

[3] P. A. S. Smith, B. B. Brown, R. K. Putney, and R. F. Reinisch, *J. Amer. Chem. Soc.*, **75**, 6335 (1953).

[4] G. P. Balabanov, Y. I. Dergunov, and V. A. Gal'perin, *J. Org. Chem. USSR*, **2**, 1797 (1966); see also Ref. 1, p. 280.

[5] Since the solution of I in acetone showed none of the UV absorptions which are absent in those of the components, the possibility of the formation of a CT-complex under the photolysis may be excluded.

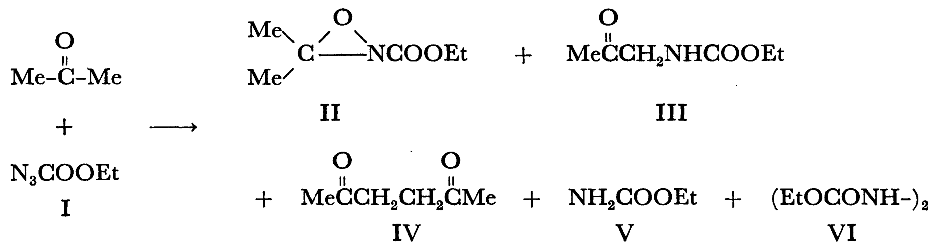
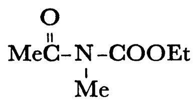


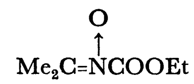
TABLE 1. PHOTOLYSIS AND THERMOLYSIS OF I IN ACETONE

| Condition | Solvent | Reaction time (hr) | Products (%)[a] | | | | |
|---|---|---|---|---|---|---|---|
| | | | II | III | IV | V | VI |
| $h\nu$[b] | none | 40 | 60 | 0 | 4 | 23 | 0 |
| $h\nu$[b] | CH$_2$Cl$_2$[c] | 45 | 0 | 27 | 0 | 15 | 0 |
| $\Delta$[d] | none | 4 | 0 | 26 | 0 | 5 | 4 |
| $\Delta$[d] | CH$_2$Cl$_2$[c] | 3 | 0 | 45 | 0 | 11 | 0 |

a) All products were isolated by column chromatography, and the isolation yields are given.
b) An 0.4 M acetone solution of I was irradiated by means of a 200-W high-pressure mercury lamp externally at room temperature.
c) An 0.4 M acetone solution of I was diluted with an equi-volume of dichloromethane.
d) Thermolysis was performed in an autoclave at 180°C.



VII

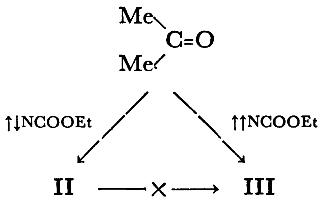


VIII

acetone identified as the 2,4-dinitrophenylhydrazone. The NMR spectrum (see Experimental section) may also be explained by two alternative structures, VII and VIII, but both are unlikely.[6]

When the photolysis was carried out in dichloromethane, ethyl acetonylcarbamate (III)[9] and V were obtained, but no trace of II was isolated (Table 1). The solvent effect[2,10] observed in the formation of II probably indicates that the formation of oxazirane II is to be ascribed to attack of the singlet nitrene on acetone. On the other hand, triplet nitrene is involved in the formation of III. The formation of IV and V can be understood in terms of the hydrogen-abstraction reaction of the triplet nitrene.

The thermal decomposition of I in acetone yielded III, V, and *N,N'*-diethoxycarbonylhydrazide (VI), while the reaction under dilution with dichloromethane resulted in increased yield of III and V (Table 1). This indicates that the carbamates are possibly derived from the triplet nitrene. As is shown in Scheme 1, we may assume that the reaction of the singlet nitrene yields oxazirane II, while the triplet nitrene gives carbamate III. The possible formation of III *via* II was excluded, as the heating of the crude II at 180°C gave no carbamate III, but only polymeric products.



Scheme 1

The reactions in a cyclohexanone solution are summarized in Table 2. Photolysis gave 2-ethoxycarbonylaminocyclohexanone (IX),[11] bicyclohexyl-2,2'-dione (XI),[12] and V, while the photoreaction in a dichloromethane solution gave 3-ethoxycarbonylaminocyclohexanone (X)[13] in addition to IX, V, and 2-(1-cyclohexenyl)cyclohexanone (XII).

The thermolysis of I in cyclohexanone yielded another novel compound, 2-ethoxy-4,5-tetramethyleneoxazole (XIII), which exhibited an IR band at 1597 cm$^{-1}$ and a UV absorption at 265 nm (log $\varepsilon$ 1.48), both characteristic of oxazoles.

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[6] An authentic sample of VII prepared from *N*-methylurethane[7] was not identical with II. Another possibility, VIII, may be rejected because a strong absorption between 1050—1200 cm$^{-1}$ due to nitrones[8] is absent in the IR spectrum of II and because the photochemistry of nitrones is known to give rise to oxaziranes. Further, the structure of VIII implies a positive charge on the nitrogen atom bearing an electronegative ethoxycarbonyl group; this is not possible.

[7] D. Ben-Ishai and E. Katchalski, *J. Org. Chem.*, **16**, 1025 (1951).

[8] R. Bonnett, V. M. Clark, and S. R. Todd, *J. Chem. Soc.*, **1959**, 2102; E. Schmitz, "Advances in Heterocyclic Chemistry," Vol. 2, ed. by A. R. Katritzky and A. J. Boulton, Academic Press, New York (1963), p. 89.

[9] J. F. W. Keana, S. B. Keana, and D. Beetham, *J. Org. Chem.*, **32**, 3057 (1967).

[10] J. M. Simson and W. Lwowski, *J. Amer. Chem. Soc.*, **91**, 5107 (1969); W. Lwowski and T. J. Maricich, *ibid.*, **87**, 3630 (1965); A. J. L. Beckwith and J. W. Redmond, *Chem. Commun.*, **1967**, 165.

[11] S. Fujita, T. Hiyama, and H. Nozaki, *Tetrahedron*, **26**, 4347 (1970).

[12] M. S. Kharasch, H. C. McBay, and W. H. Urry, *J. Amer. Chem. Soc.*, **70**, 1269 (1948).

[13] The authentic sample was obtained in an independent study by the ethoxycarbonylation of *m*-aminophenol, followed by hydrogenation and oxidation. In a similar manner, 4-ethoxycarbonylaminocyclohexanone was prepared. Details of the syntheses will be given elsewhere in the near future.

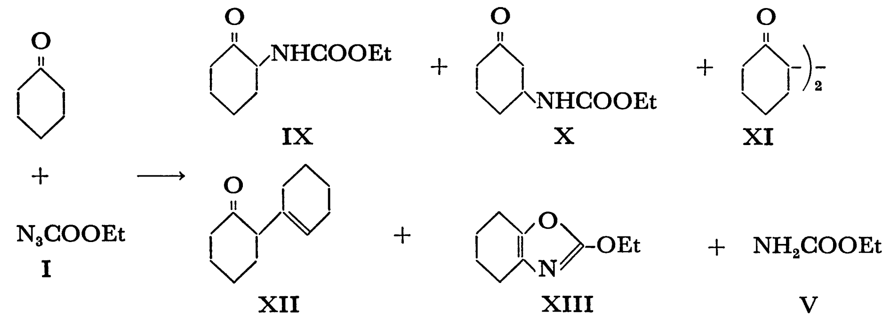
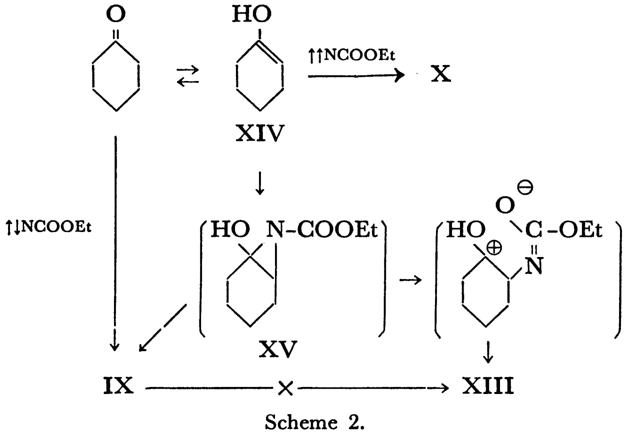


Table 2. Photolysis and thermolysis of I in cyclohexanone

| Condition | Solvent | Reaction time (hr) | Products (%)[a] | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | IX | X | XI | XII | XIII | V |
| $h\nu$[b] | none | 40 | 8 | 0 | 5 | 0 | 0 | 22 |
| $h\nu$[b] | $CH_2Cl_2$[c] | 45 | 15 | 8 | 0 | 24 | 0 | 7 |
| $\Delta$[d] | none | 2 | 29 | 11 | 2 | 0 | 17 | 4 |
| $\Delta$[e] | $CH_2Cl_2$[c] | 3 | 18 | 7 | 2 | 0 | 13 | 4 |

a) All products were isolated by column chromatography, and the isolation yields are given.
b) A 0.4 M solution of I in cyclohexanone was irradiated by means of a 200-W high-pressure mercury lamp externally at room temperature.
c) A 0.4 M cyclohexanone solution of I was diluted with an equi-volume of dichloromethane.
d) Thermolysis was performed by adding I to cyclohexanone at 156°C.
e) Thermolysis was performed in an autoclave at 150°C.

A possible account of the products is given in Scheme 2. The formation of XIII should involve the attack of I or the nitrene on the *enol* form, XIV, of cyclohexanone,[14] since IX could not be converted to XIII under thermolytic conditions. The precursor of XIII may be a 1,3-dipolar adduct, hydroxyaziridine XV, and/or a triazoline, but no conclusive data are yet available.



Scheme 2.

The observed heavy-atom effect implies that X is derived from the triplet nitrene. The absence of 4-ethoxycarbonylaminocyclohexanone in the products suggests that the allylic insertion of triplet nitrene into the enolized cyclohexanone led to X. The reactive species in the formation of IX is either singlet nitrene or hydroxyaziridine, XV.[15]

## Experimental

All the melting points are uncorrected. The infrared spectra were recorded on a Shimadzu spectrophotometer IR-27-G, the ultraviolet spectra, on a Hitachi EPS-2 spectrometer, the nuclear magnetic resonance spectra on a JEOL C-60-H spectrometer, and the mass spectra, on a Hitachi RMU-6L spectrometer.

*Photolysis of Ethyl Azidoformate in Acetone.* A mixture of acetone (20 m*l*) and ethyl azidoformate (1.00 g, 8.7 mmol) was placed in a quartz tube, degassed by bubbling nitrogen and irradiated externally at room temperature with a 200-W high-pressure mercury lamp until nitrogen evolution had ceased and the characteristic IR bands at 2185 and 2137 $cm^{-1}$ due to the azide group had disappeared (*ca.* 40 hr). After the removal of the excess acetone under reduced pressure, the yellow oily residue (1.5 g) was separated by column chromatography on silica gel. Elution with *n*-hexane, benzene, and finally with ether gave 2-ethoxycarbonyl-3,3-dimethyloxazirane (II) (0.76 g, 60%); bp 100°C (bath temperature) at 2 mmHg. IR (neat): 1715, 1400, 1375, 1327, 1212, 1004 $cm^{-1}$; NMR ($CCl_4$): $\delta$ 1.35 (t, 3H, $\underline{CH_3}CH_2$-), 1.45 (s, 3H, $C\underline{H_3}$-), 1.52 (s, 3H, $C\underline{H_3}$-), 4.12 (q,2 H, $CH_3\underline{CH_2}$); MS: *m/e* 145 (19%), 73 (100), 59 (73), 58 (72).

Found: *m/e* 145.075 ($M^+$). Calcd for $C_6H_{11}NO_3$: *m/e* 145.074.

Further elution gave hexane-2,5-dione (IV) (0.04 g, 4%) and ethyl carbamate (V) (0.18 g, 23%). Both IV and V were identified by a comparison of their infrared spectra and retention times on gas chromatography with those of authentic samples.

*Photolysis of Ethyl Azidoformate in an Acetone-dichloromethane Mixture.* A solution of ethyl azidoformate (0.50 g, 4.4 mmol) in acetone (10 m*l*) and dichloromethane (10 m*l*) was irradiated as has been described above. After concentration, the residual mixture was separated by column chro-

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14) Cyclohexanone involves several percentages of the enol form at room temperature; this form is often the reactive species.

15) The photolysis of ethyl azidoformate in 1-cyclohexenyl acetate gives the acetate of the hydroxyaziridine XV, which is transformed to IX on hydrolysis.[9]

matography on alumina. Successive elution with *n*-hexane, benzene, and ether gave ethyl acetonylcarbamate (III) (0.11 g, 27%). IR (neat): 3350, 1705, 1525, 1330, 1065 cm$^{-1}$; NMR ($CCl_4$): $\delta$ 1.26 (t, 3H, $\underline{CH_3}CH_2$-), 2.17 (s, 3H, $CH_3$-), 3.9—4.3 (m, 4H, doublet at $\delta$ 4.00, -$CH_2$-, quartet at $\delta$ 4.10, $CH_3\underline{CH_2}$-), 5.59 (broad s, 1H, NH); MS: *m/e* 145 ($M^+$, 3%), 102 (39), 78 (19), 74 (18), 62 (58), 44 (100). Ethyl carbamate (V) (0.07 g, 15%) was obtained as a by-product.

*Hydrolysis of Oxazirane II.* A mixture of 2,4-dinitrophenylhydrazine (0.70 g), concentrated sulfuric acid (3 m*l*), water (3 m*l*), and ethanol (10 m*l*) was added, drop by drop, to a solution of oxazirane (0.45 g, 3.1 mmol) in ethanol (5 m*l*). The reaction mixture was then allowed to stand at 50°C overnight, and the red crystals thus precipitated were filtered; mp 119—120°C. The mixed melting point with acetone 2,4-dinitrophenylhydrazone was 119—120°C.

*Thermolysis of Ethyl Azidoformate in Acetone.* Ethyl azidoformate (2.00 g, 17.4 mmol) dissolved in acetone (40 m*l*) was heated under a nitrogen atmosphere in an autoclave at 180°C for 4 hr. The removal of the excess acetone *in vacuo* gave a dark-colored residue (2.38 g), which then was subjected to chromatography on an alumina column. Elution with benzene and ether gave ethyl acetonylcarbamate (III) (0.67 g, 26%), *N,N'*-diethoxycarbonylhydrazide (VI) (0.12 g, 4%), and ethyl carbamate (V) (0.07 g, 5%).

*Thermolysis of Ethyl Azidoformate in Acetone-dichloromethane.* A solution of ethyl azidoformate (1.00 g, 8.7 mmol) in acetone (20 m*l*) and dichloromethane (20 m*l*) was placed in an autoclave and heated at 160—180°C for 3 hr. The subsequent separation of the crude mixture by chromatography on a column of silica gel afforded III (0.51 g, 45%), and V (0.08 g, 11%).

*Photolysis of Ethyl Azidoformate in Cyclohexanone.* Ethyl azidoformate (1.00 g, 8.7 mmol) in cyclohexanone (20 m*l*) was irradiated in a manner similar to that described above (*ca.* 40 hr). The subsequent removal of the excess cyclohexanone *in vacuo* afforded a yellow oil, which was separated by chromatography on an alumina column. Elution with benzene and ether gave bicyclohexyl-2,2'-dione (XI) (0.08 g, 5%); mp 70—71°C (*n*-hexane) (lit,[12] 70—71°C). IR (neat): 1705, 1220, 1125 cm$^{-1}$; NMR ($CCl_4$): $\delta$ 1.2—2.1 (m, 12H, methylene), 2.2—2.6 (m, 4H, methylene), 2.6—3.1 (m, 2H, methine); MS: *m/e* 194 ($M^+$, 17%), 98 (100). Further elution with ether afforded 2-ethoxycarbonylaminocyclohexanone (IX)[11] (0.14 g, 8%), IR (neat): 3330, 1710, 1510, 1257, 1052 cm$^{-1}$; NMR ($CCl_4$): $\delta$ 1.20 (t, 3H, $\underline{CH_3}CH_2$-), 1.5—2.8 (m, 8H, methylene), 4.02 (q, 2H, $CH_3\underline{CH_2}$-), 4.0—4.4 (m, 1H, methine), 5.73 (broad d, 1H, $\underline{NH}$); MS: *m/e* 185 ($M^+$, 8%), 157 (8), 141 (10), 128 (51), 62 (34), 56 (49), 44 (100), and ethyl carbamate (V) (0.15 g, 22%).

*Photolysis of Ethyl Azidoformate in Cyclohexanone-dichloromethane.* A solution of ethyl azidoformate (0.50 g, 4.4 mmol) in cyclohexanone (10 m*l*) and dichloromethane (10 m*l*) was irradiated much as has been described above. Work-up and chromatography on alumina gave 2-(1-cyclohexenyl)cyclohexanone (XII) (0.18 g, 24%), IR (neat): 3050, 1717, 1120, 678 cm$^{-1}$; NMR ($CCl_4$): $\delta$ 0.7—3.0 (m, 17H, methylene and methine), 5.4—5.5 (m, 1H, olefinic); MS: *m/e* 178 ($M^+$, 57%), 149 (100), 81 (70), 79 (69), 67 (67). Subsequent elution with ether gave 2-ethoxycarbonylaminocyclohexanone (IX) (0.12 g, 15%), 3-ethoxycarbonylaminocyclohexanone (X) (0.06 g, 8%), IR (neat): 3370, 1700, 1535, 1268, 1244, 1217, 1046 cm$^{-1}$; NMR ($CCl_4$): $\delta$ 1.22 (t, 3H, $\underline{CH_3}CH_2$-), 1.6—2.9 (m, 8H, methylene), 3.5—4.2 (m, 1H, methine), 4.04 (q, 2H, $CH_3\underline{CH_2}$-), 5.8—5.9 (broad s, 1H, NH); MS: *m/e* 185 ($M^+$, 9%), 156 (57), 128 (79), 96 (84), 43 (100), and ethyl carbamate (V) (0.02 g, 7%).

*Thermolysis of Ethyl Azidoformate in Cyclohexanone.* A mixture of ethyl azidoformate (1.00 g, 8.7 mmol) and cyclohexanone (5 m*l*) was added, drop by drop, to refluxing cyclohexanone (*ca.* 1 hr) After an additional hour of refluxing, the excess cyclohexanone was removed *in vacuo.* The subsequent work-up of the residual mixture and chromatography on an alumina column afforded 2-ethoxy-4,5-tetramethylene oxazole (XIII) (0.25 g, 17%). IR (neat): 1712, 1597, 1450, 1387, 1315, 1210 cm$^{-1}$; NMR ($CCl_4$): $\delta$ 1.40 (t, 3H, $\underline{CH_3}CH_2$–), 1.5—2.1 (m, 4H, methylene), 2.1—2.7 (m, 4H, methylene), 4.36 (q, 2H, $CH_3\underline{CH_2}$–); MS: *m/e* 167 ($M^+$, 44%), 139 (97), 111 (100), 66 (85), 55 (60); UV: $\lambda_{max}$ (EtOH) 265 nm (log $\varepsilon$ 1.48), $<$220 nm (log $\varepsilon$>2.54).

Found: C, 64.5; H, 8.1; N, 8.2%. Calcd for $C_9H_{13}NO_2$: C, 64.7; H, 7.8; N, 8.4%.

The subsequent eluants were 2-ethoxycarbonylaminocyclohexanone (IX) (0.47 g, 29%), 3-ethoxycarbonylaminocyclohexanone (X) (0.18 g, 11%), bicyclohexyl-2,2'-dione (XI) (0.04 g, 2%), and ethyl carbamate (V) (0.04 g, 4%).

*Thermolysis of Ethyl Azidoformate in Cyclohexanone-dichloromethane.* A mixture of ethyl azidoformate (1.00 g, 8.7 mmol), cyclohexanone (20 m*l*), and dichloromethane (20 m*l*) was heated at 150°C in an autoclave for 3 hr. A subsequent work-up gave the oxazole XIII (0.18 g, 13%), XI (0.03 g, 2%), IX (0.29 g, 18%), X (0.11 g, 7%), and V (0.03 g, 4%).

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