Stabilization of Singlet Ethoxycarbonylnitrene by 1,4-Dioxan. Part 4.[1] Yield of Nitrene Products in 1,4-Dioxan–Cyclohexane and Effect of Cyclohexane-1,2-dione on C–H Insertion

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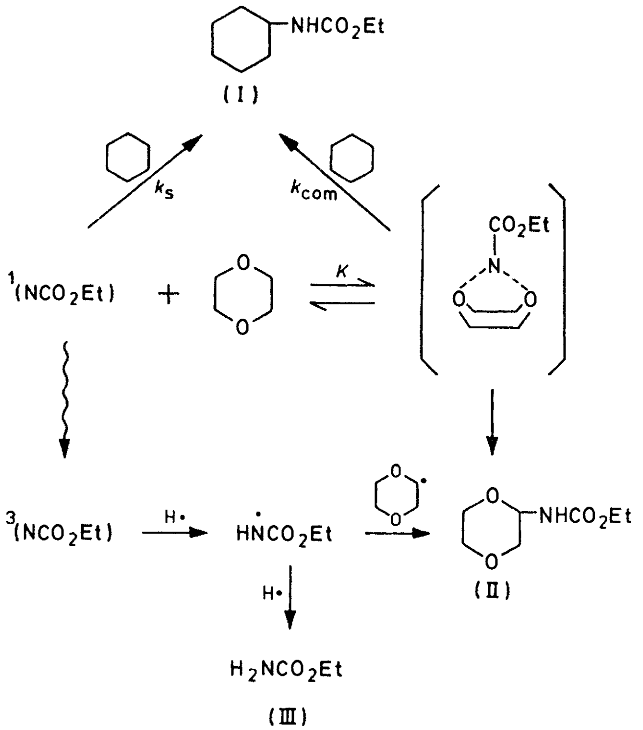
A study of the yield of ethoxycarbonylnitrene products for the thermolysis and photolysis of ethyl azidoformate in 1,4-dioxan–cyclohexane shows that the singlet state of the nitrene is stabilized by 1,4-dioxan. The results for the effect of added cyclohexane-1,2-dione both on the yield and on the selectivity for the insertion of nitrene suggest that the dione predominantly traps the triplet rather than the singlet nitrene to give 3-ethoxycarbonylimino-2-hydroxycyclohexanone, and that a complex which can react with the C–H bonds of cyclohexane is formed by interaction of 1,4-dioxan with the singlet, not the triplet nitrene.

It has recently been observed that dichloromethane [2-4] and hexafluorobenzene [5,6] stabilize the singlet state of ethoxycarbonylnitrene upon C–H insertion. We have shown from the relative reactivity of insertion into ether C–H bonds that 1,4-dioxan stabilizes the singlet state,[7] and that the stabilization is caused by the formation of a singlet 1,4-dioxan–nitrene complex which is reactive to C–H bonds of alkanes.[8] We have also shown that an increased concentration of the singlet state upon addition of 1,4-dioxan results in an increased quantity of the singlet complex, not the free singlet nitrene, from our study of the addition of the nitrene to *cis*- and *trans*-4-methylpent-2-ene.[1] This paper deals with both the singlet stabilization based on the yield for the nitrene products in 1,4-dioxan–cyclohexane and the mechanism for the stabilization.

RESULTS AND DISCUSSION

Stabilization of Singlet Ethoxycarbonylnitrene in 1,4-*Dioxan–Cyclohexane.*—The thermolysis and photolysis of ethyl azidoformate were carried out in 1,4-dioxan–cyclohexane. The molar ratio azide: mixed solvent was kept nearly constant (1 : 35—40). The quantity of products, ethyl *N*-cyclohexylcarbamate (I), ethyl 1,4-dioxan-2-ylcarbamate (II), and ethyl carbamate (III), was determined by g.l.c. analysis. The yield was calculated from the above quantity on the basis of the azide consumed as described in the Experimental section (Tables 1 and 2). The yields agree within <2% for two or three runs. The data are presented in graphical forms in Figures 1 and 2. The plots of yields for carbamates (I) and (II) against 1,4-dioxan concentration show upward and downward curvatures, respectively, whereas the yield for carbamate (III) is almost independent of 1,4-dioxan concentration.



SCHEME 1

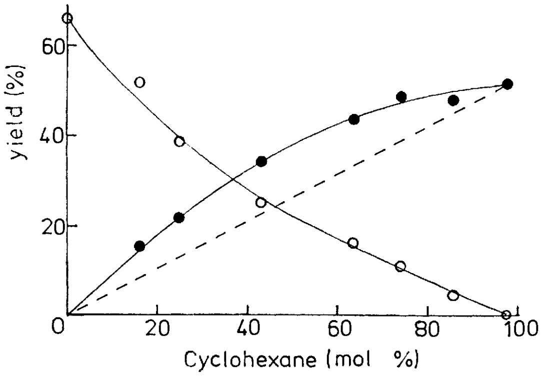


FIGURE 1 Thermolysis of ethyl azidoformate in 1,4-dioxan–cyclohexane: ●, yield of ethyl *N*-cyclohexylcarbonate (I); ○, yield of ethyl 1,4-dioxan-2-ylcarbamate (II)

It has been reported that the quantities of free singlet and triplet nitrenes are independent of 1,4-dioxan concentration in cyclohexane.[1] The decomposition rate of azide, V, may be constant in 1,4-dioxan–cyclohexane since the rate constant (k_{decomp} 4.4 × 10^{-3} s^{-1} at 120°) in 1,4-dioxan is equal to that in cyclohexane. Thus the yield for carbamate (I) formed on reaction with the free

TABLE 1

Yields for the thermolysis of ethyl azidoformate in 1,4-dioxan–cyclohexane in the presence and absence of cyclohexane-1,2-dione (0.5 molar ratio with respect to azide)

Cyclohexane (mol %)	Yield (%)					
	Absence of dione			Presence of dione		
	(I)	(II)	(III)	(I)	(II)	(III)
97.6	51.4	0	29.9			
96.2				50.9	0	5.2
85.6	47.7	4.4	30.3			
74.1	48.6	10.9	34.5			
73.1				46.7	6.8	8.8
63.5	43.6	16.1	32.5			
43.1	34.0	25.0	26.3			
42.5				33.6	19.6	11.4
24.9	21.6	38.8	27.5			
16.1	15.3	51.7	26.6			
15.6				18.2	34.8	12.8
0	0	65.7	25.0			

TABLE 2

Yields for the photolysis of ethyl azidoformate in 1,4-dioxan–cyclohexane in the presence and absence of cyclohexane-1,2-dione (0.5 molar ratio with respect to azide)

Cyclohexane (mol %)	Yield (%)					
	Absence of dione			Presence of dione		
	(I)	(II)	(III)	(I)	(II)	(III)
97.2	49.2	0	17.8			
68.2	41.8	10.7	18.2			
55.4	35.4	16.4	18.0			
52.8				25.3	10.5	4.2
40.4				19.9	14.9	8.0
40.0	24.1	16.8	18.4			
12.0	10.0	28.7	18.8			
0	0	44.8	20.8			

singlet nitrene (S_s), Y_S, should increase linearly with an increase in cyclohexane concentration, as shown in the dotted lines in Figures 1 and 2 [equation (1)]. Therefore $Y_{obs} - Y_S$ may be equal to Y_{com}, where Y_{obs} and Y_{com}

$$Y_S = k_s[\text{Cyclohexane}][S_s]/V \qquad (1)$$

are the yield for (I) observed experimentally and that for reaction with a singlet complex (S_{com}) which equilibrates between the nitrene and 1,4-dioxan,[1] respectively [equation (2)]. In these equations, k_s and k_{com} are the rate constants shown in Scheme 1. Using the relationship $[S_{com}] = K[S_s][D]$ where K is the equilibrium

$$Y_{com} = Y_{obs} - Y_S = k_{com}[\text{Cyclohexane}]\,[S_{com}]/V \qquad (2)$$

constant shown in Scheme 1, and [D] is the concentration of 1,4-dioxan, equation (3) can be derived from (1) and

$$Y_{com}/Y_S = (k_{com}\,K/k_s)[D] \qquad (3)$$

(2). Linear plots of the ratio Y_{com}/Y_S against [D] is obtained (Figure 3), suggesting that the assumptions made are reasonable.

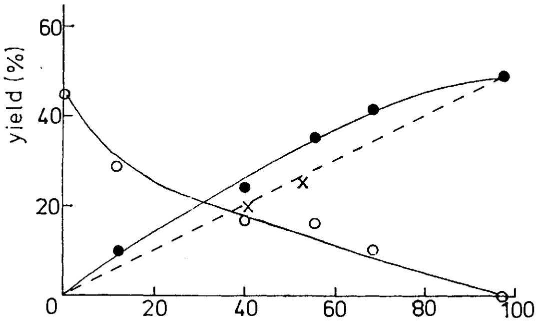


FIGURE 2 Photolysis of ethyl azidoformate in 1,4-dioxan–cyclohexane: ●, yield of ethyl *N*-cyclohexylcarbamate (I); ○, yield of ethyl 1,4-dioxan-2-ylcarbamate (II); ×, yield of (I) in the presence of cyclohexane-1,2-dione

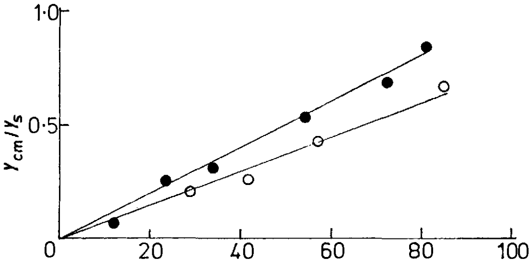


FIGURE 3 Relationship between Y_{com}/Y_s and mol % 1,4-dioxan in cyclohexane on the decomposition of ethyl azidoformate: ●, for thermolysis; ○, for photolysis

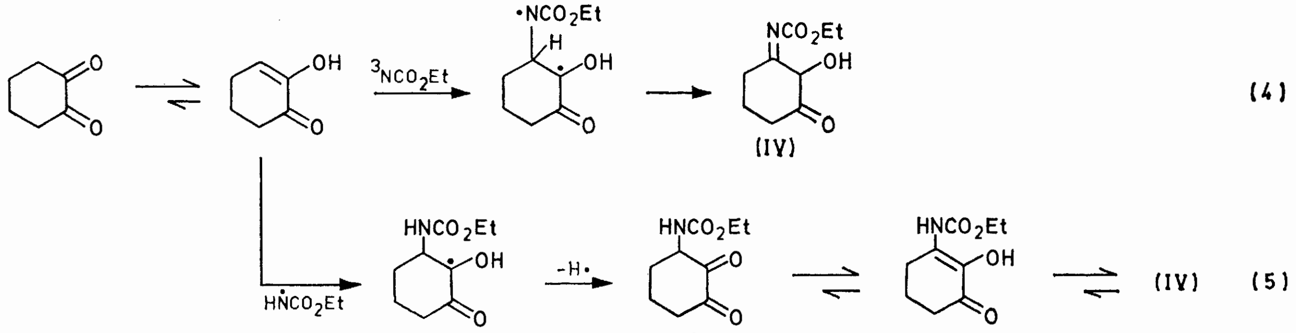
The slope of the line for photolysis is somewhat low compared with that for thermolysis (see Figure 3). This probably means that k_{com} for the former is lower than that for the latter since the values K and k_s for photolysis are greater and smaller than those for thermolysis, respectively.[1,8] The difference for k_{com} suggests that the components (the nitrene and 1,4-dioxan) of the complex are tightly combined in photolysis (lower temperature) compared with thermolysis.

As seen in Scheme 1, the reaction of the complex with cyclohexane competes with the formation of (II) *via* the complex. Consequently, the complex may persist for a short time during the reaction. This is in good agreement with our earlier observation that the complex can react with olefins [1] and the C–H bonds of ethers [7] or alkanes,[8] resulting in the singlet stabilization induced by 1,4-dioxan.

*Effect of Cyclohexane-*1,2*-dione on the* C–H *Insertion of the Nitrene.*—We cannot exclude the possibility that the complex is formed *via* the triplet nitrene, and readily equilibrates with both the singlet nitrene and 1,4-dioxan. The following study is concerned with the pathway of complex formation.

The thermolysis and photolysis were carried out in 1,4-dioxan–cyclohexane in the presence of cyclohexane-1,2-dione of 0.5 molar ratio with respect to the azide (Tables 1 and 2 and Figure 2). As for the thermolysis, the addition of the dione remarkably lowered the yield for the triplet nitrene product, carbamate (III), but hardly varied the yield for the singlet nitrene product, carbamate (I). This indicates that the dione acts as a good scavenger for the triplet nitrene or ethoxycarbonylamino radical, since (III) is formed stepwise by hydrogen abstraction of the triplet nitrene.[9]

3-Ethoxycarbonylimino-2-hydroxycyclohexanone (IV) was found for the thermal decomposition of ethyl azidoformate in the presence of cyclohexane-1,2-dione. Two possible pathways may be expected with regard to its formation (Scheme 2). However, the process shown in equation (5) is ruled out by the following result. When the dione was absent, the yield for (III) was very low upon thermolysis in dichloromethane relative to cyclohexane on account of the difficulty in abstracting hydrogen atoms from dichloromethane, but the yield for (IV) did not decrease in dichloromethane compared with cyclohexane (Table 3). Table 3 also indicates that cyclohexane-1,2-dione can very effectively scavenge the triplet nitrene in the reaction system as indicated by the yield for (IV).



SCHEME 2

TABLE 3

Thermolysis of ethyl azidoformate in cyclohexane or in dichloromethane (CH_2Cl_2) in the presence and absence of cyclohexane-1,2-dione (0.5 molar ratio with respect to azide)

		Yields (%)	
Solvents	Decomposition yield of azide (%)	Absence of dione (III)	Presence of dione (IV) [a]
Cyclohexane	96.3	29.9	
Cyclohexane	65.5		19
CH_2Cl_2	59.2	6.2	
CH_2Cl_2	19.6		68
CH_2Cl_2	38.8		57
CH_2Cl_2	79.2		20

[a] The yield for (IV) is based on the azide decomposed.

Cyclohexane-1,2-dione which is in almost completely enolic form[10] scavenges the triplet nitrene to give a diradical in which the tertiary and nitrogen radicals are conjugated with the carbon–oxygen double bond, yielding (IV) after a [1,2] shift of a hydrogen atom [see equation (4)].

The formation of (IV) through a triazoline intermediate was excluded by the fact that the yield for the triplet relative to singlet nitrene product markedly decreases in the presence of the dione. Further, product (IV) should not be formed thermally *via* the triplet azide since the azide is in the singlet ground state.

These results indicate that complex formation is not suppressed even in the presence of the efficient triplet scavenger. Therefore, it is concluded that the complex is formed by interaction of 1,4-dioxan with the singlet, not the triplet nitrene.

On the other hand, the photochemical study shows that the yield of (I) decreases to some extent in the presence of the scavenger (see Figure 2), so that the result gives us no information on the pathway of complex formation.

We have previously reported that the selectivity for insertion of the nitrene into tertiary and primary C–H bonds decreases with an increase in the concentration of 1,4-dioxan as the result of steric hindrance in the reaction between the crowded tertiary C–H bonds and the 1,4-dioxan–nitrene complex.[8] If the complex results from only the interaction of the singlet nitrene with 1,4-dioxan, the selectivity should not vary in the presence of the triplet nitrene scavenger since the insertion practically occurs *via* the pathway involving only the singlet state of nitrene.[11]

The relative reactivities for insertion of the nitrene into tertiary and primary C–H bonds in 60% 1,4-dioxan in the presence or absence of cyclohexane-1,2-dione were determined on the basis of the yields of products, 2-*N*-ethoxycarbonylamino-2,4,4-trimethylpentane (V) and 1-*N*-ethoxycarbonylamino-octane (VI) as noted before[8] [equations (6) and (7)]. The results are based on two

$$\text{iso-}C_8H_{18} + N_3CO_2Et \xrightarrow[\text{or }\Delta]{h\nu} Me_3CCH_2C(Me)_2NHCO_2Et \quad (6)$$

$$\text{n-}C_8H_{18} + N_3CO_2Et \xrightarrow[\text{or }\Delta]{h\nu} \text{n-}C_8H_{17}NHCO_2Et \quad (7)$$

or three runs with an error of ±5%. The data are summarized in Table 4.

As Table 4 shows, the relative reactivities for tertiary : primary insertion at 60% 1,4-dioxan are smaller than those at 0% 1,4-dioxan, and the selectivity is almost independent of the addition of cyclohexane-1,2-dione. The result supports the idea that the complex is formed by the interaction between 1,4-dioxan and the singlet nitrene only, although Gleiter and Hoffmann[12] has proposed the theory that nitrene singlet states are stabilized by interaction of the triplet nitrene with the lone pair electrons of NH_3, H_2O, halogeno-compounds, *etc.* Probably the vacant orbital of the singlet nitrene plays an important role in complex formation.[7]

TABLE 4

Relative reactivities for the insertion of ethoxycarbonylnitrene into C–H bonds in the absence or presence of cyclohexane-1,2-dione (0.5 molar ratio with respect to azide)

1,4-Dioxan (mol %)	Relative reactivities (tertiary : primary)	
	Thermolysis	Photolysis
60	10.8	17.7
	(9.3)	(17.0)
0	14.8 [a]	23.7 [a]

The values in parentheses are the relative reactivities in the presence of cyclohexane-1,2-dione; the others are the values in the absence of the dione.

[a] From ref. 8.

In this case, the addition of cyclohexane-1,2-dione brings about a slight decrease in the selectivity. This may be because a very small amount of the tertiary insertion product is formed *via* a triplet path,[2] or the free singlet nitrene relative to the complex is more intercepted by the dione in spite of their low reactivities towards the dione.

EXPERIMENTAL

Determination of the amount of ethyl azidoformate decomposed, and quantitative analysis of the products, ethyl *N*-cyclohexylcarbamate (I), ethyl 1,4-dioxan-2-ylcarbamate (II), ethyl carbamate (III), 2-*N*-ethoxycarbonylamino-2,4,4-trimethylpentane (V), and 1-*N*-ethoxycarbonylamino-octane (VI), were carried out as described in previous papers.[1,8] Cyclohexane, 1,4-dioxan, iso-octane, n-octane, and dichloromethane were purified by standard methods before use. Ethyl azidoformate,[13] b.p. 45—46° at 35 mmHg, and cyclohexane-1,2-dione,[14] b.p. 75—79° at 16 mmHg, were obtained by literature methods.

I.r., mass, and n.m.r. spectra and molecular weights were measured with the apparatus described previously.[1,8] U.v. spectra were obtained with a 124 type Hitachi recording spectrometer.

Preparation of 3-*Ethoxycarbonylimino*-2-*hydroxycyclohexanone* (IV).—A mixture of cyclohexane-1,2-dione (60.8 mmol) and ethyl azidoformate (30.4 mmol) was heated at 120° for 3 h, resulting in *ca.* 100% decomposition of azide on the basis of evolved nitrogen gas. After the mixture was cooled, carbon tetrachloride (5 ml) and cyclohexane (5 ml) were added and left in a refrigerator overnight. The precipitate was filtered off and washed with a small amount of carbon tetrachloride. The yield of the crude compound (IV) was 0.99 g (16.3% based on the azide employed). The *product* was purified by recrystallization from carbon tetrachloride, plates, m.p. 122—123°, $\nu_{max.}$ (Nujol) 3 350 (O–H), 1 740 (C=O), 1 610 (N=C), 1 510 (N–C), 1 180 (C–O), and 1 140 cm^{-1} (C–O); δ(CDCl$_3$) 1.3 (3 H, t, CH$_3$), 2.0 (2 H, m, 5-H$_2$), 2.2 (1 H, s, CH), 2.5 (2 H, t, 4-H$_2$), 3.1 (2 H, t, 6-H$_2$), 4.2 (2 H, q, OCH$_2$), and 6.4br (1 H, OH); *m/e* 199 (*P*), 98, 73, 45, and 29; molecular weight 191 (in benzene), $\lambda_{max.}$ (EtOH) 297 nm (log ε 4.30) (Found: C, 54.0; H, 6.55; N, 7.0. $C_9H_{13}NO_4$ requires C, 54.25; H, 6.55; N, 7.05%).

Photolysis and Thermolysis of Ethyl Azidoformate in the Absence and Presence of Cyclohexane-1,2-*dione*.—A fixed amount of a solution consisting of ethyl azidoformate and cyclohexane (1 : 35) was mixed with various amounts of a solution containing ethyl azidoformate and 1,4-dioxan (1 : 35) to give a total volume of 10.0 ml. The solution was placed in a quartz vessel (25 cm × 1.8 cm). After purging with dry nitrogen for 1 h, it was irradiated with an external 300 W high pressure Halōs mercury lamp at 25° for 3 h, resulting in *ca.* 40% decomposition of azide. The quantity for products (I)—(III) was analysed by g.l.c. as described before.[1,8] The yields for these products were calculated on the basis of the azide consumed.

Non-photolysed mixtures did not produce (I)—(III). None of the g.l.c. peaks of the starting materials and products overlapped.

For thermolysis, a solution (1.0 ml) was made by similar ways shown in the photolysis, but the molar ratio of azide to solvent was *ca.* 1 : 40. The solution was placed in a sealed glass tube, and heated at 115° for 4 h. The consumption of azide was *ca.* 100%. The yields were obtained as described in the photolysis.

The photolysis and thermolysis of ethyl azidoformate in 1,4-dioxan–cyclohexane in the presence of cyclohexane-1,2-dione (0.5 mol. equiv. relative to azide) were conducted as indicated above. Photolysis was, however, carried out for 20 h. The yields were also obtained by the above methods.

The thermolysis of ethyl azidoformate in dichloromethane or cyclohexane was performed at 110—120° for 2 h by heating a solution which contains azide (2.3 mmol) and dichloromethane (10 ml) in the absence or presence of cyclohexane-1,2-dione (1.15 mmol). The yield for (III) was obtained as described above. The yield for (IV) was determined by g.l.c. using a glass column (1 m × 3 mm) packed with 10% silicone SE-30 in 60—80 Uniport KS.

Relative Reactivities for Insertion of Ethoxycarbonylnitrene into the Tertiary and Primary C–H *Bonds in the Presence and Absence of Cyclohexane*-1,2-*dione*.—A solution containing ethyl azidoformate, n-octane, iso-octane, and 1,4-dioxan (total 10.0 ml) in the molar ratio *ca.* 1 : 4.8 : 4.4 : 18.2 was made in the absence and presence of cyclohexane-1,2-dione (0.5 mol. equiv. relative to azide), and irradiated or heated as described earlier.[8] The relative reactivity for insertion of the nitrene into the tertiary and primary C–H bonds of iso-octane and n-octane were obtained by similar methods described in the previous paper.[8]

Measurement of Decomposition Rate Constants of Ethyl Azidoformate.—A solution (2.0 ml) consisting of ethyl azidoformate and 1,4-dioxan or cyclohexane in the molar ratio *ca.* 1 : 30 was placed in a sealed glass tube. Six identical mixtures were made up and analysed at various times for reaction at 120°. The consumption of azide was followed by means of i.r. spectra.[1,8]

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