Stabilization of Singlet Ethoxycarbonylnitrene by 1,4-Dioxan. Part 3.[1] Stereospecificity for the Addition to 4-Methylpent-2-ene of the Nitrene generated from Ethyl Azidoformate

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The addition to *cis*-4-methylpent-2-ene of ethoxycarbonylnitrene generated by the photolysis of ethyl azidoformate was carried out in 1,4-dioxan–cyclohexane. Both the stereospecificity of addition and the sum of all singlet nitrene products increase with an increase in the concentration of 1,4-dioxan. The relative yield of *cis*- to *trans*-aziridine is proportional to the concentration of 1,4-dioxan, and the total triplet nitrene products stay practically constant. This suggests that increased concentration of the singlet state by 1,4-dioxan corresponds to increased concentration of a singlet 1,4-dioxan–nitrene complex, not the free singlet nitrene. For addition using *trans*-4-methylpent-2-ene in place of the *cis*-isomer, there was a smaller increase in the stereospecificity induced by 1,4-dioxan. On the other hand, for addition of the nitrene generated by thermolysis, the stereospecificity was almost independent of the concentration of 1,4-dioxan.

In previous papers[1,2] we showed from the relative reactivity of insertion into C–H bonds that 1,4-dioxan stabilizes the singlet state of ethoxycarbonylnitrene and a singlet complex is formed between the nitrene and 1,4-dioxan. It has recently been observed that dichloromethane[3-5] and hexafluorobenzene[6,7] also stabilize the singlet state upon C–H insertion. For dichloromethane, singlet stabilization by chlorine atoms is counterbalanced by intersystem crossing by the solvent.[3,5] Therefore, if the dichloromethane–nitrene interaction which causes singlet stabilization is more unfavourable than interaction of nitrene with olefin, singlet stabilization would be prevented in the presence of an olefin.[5] Singlet stabilization by dichloromethane is not found for addition to olefins.[8-10] Thus 1,4-dioxan which does not have any heavy atoms can be expected to stabilize the

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[1] Part 2, H. Takeuchi, Y. Kasamatsu, M. Mitani, T. Tsuchida, and K. Koyama, preceding paper.

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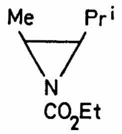
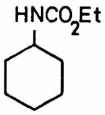
singlet state of ethoxycarbonylnitrene upon addition to olefins. Furthermore, study of the stereospecificity for addition in the presence of 1,4-dioxan may give some information on the concentrations of the singlet and triplet species.

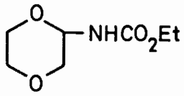
RESULTS AND DISCUSSION

Addition to 4-*Methylpent*-2-*ene of Ethoxycarbonylnitrene generated Photochemically from Ethyl Azidoformate*.—A mixture of ethyl azidoformate (I) and *trans*-4-methylpent-2-ene in the molar ratio *ca.* 1 : 10 was dissolved in

N_3CO_2Et
(I)


(II)
a; *trans*
b; *cis*


(III)


(IV)

cyclohexane or 1,4-dioxan, and irradiated under the conditions described in the Experimental section. The yield of products, *trans*- and *cis*-*N*-ethoxycarbonyl-2-isopropyl-3-methylaziridines (IIa and b), ethyl *N*-cyclohexylcarbamate (III), and ethyl 1,4-dioxan-2-ylcarbamate (IV), was determined by g.l.c. analysis (Table 1).

TABLE 1

Photochemical reactions of ethyl azidoformate with *trans*-4-methylpent-2-ene in cyclohexane or in 1,4-dioxan

Solvent	Olefin (mole %)	Aziridine yield (%)	Fraction *trans* (%)	(III) Yield (%)	(IV) Yield (%)
Cyclohexane	7	31.4	80.5	37.1	0
1,4-Dioxan	7	39.7	84.3	0	42.3
Cyclohexane	10		83.8		
1,4-Dioxan	10		87.8		

The data for 10 and 7 mole % olefin show that the stereospecificity of the addition is somewhat higher in 1,4-dioxan than in cyclohexane. Since addition affords an aziridine mixture with a high proportion of *trans*-isomer, the fraction of *trans*-product will vary to only a small extent even if singlet stabilization occurs in 1,4-dioxan.

In contrast, the use of *cis*-4-methylpent-2-ene would be anticipated to favour investigation of the solvent effect of 1,4-dioxan. For this reason, photolysis of azide (I) in the presence of the *cis*-olefin (7 mole %) was carried out under conditions similar to those above (Table 2). As Table 2 shows, addition is more stereospecific the higher the 1,4-dioxan concentration, and the effect of 1,4-dioxan is a little larger by comparison with that for the *trans*-olefin. As noted in the Experimental section, the olefins and aziridines do not isomerize under our experimental conditions. Therefore the results clearly show singlet stabilization of the nitrene by 1,4-dioxan. We have postulated previously that the interaction of the singlet nitrene with 1,4-dioxan causes such a singlet stabilization.[2] We have also reported that the formation of a 1,4-dioxan–nitrene complex which has some reactivity towards C–H bonds is responsible for singlet stabilization.[1]

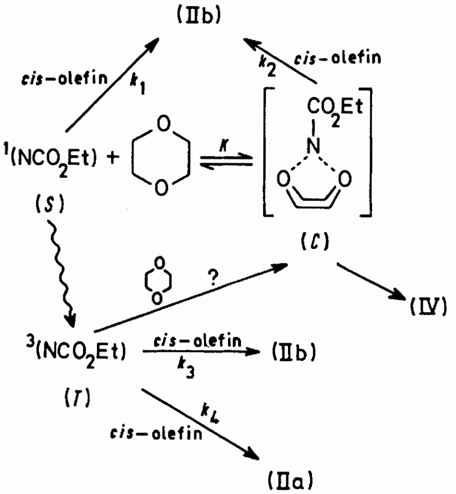
TABLE 2

Photochemical reactions of ethyl azidoformate with *cis*-4-methylpent-2-ene in 1,4-dioxan–cyclohexane

1,4-Dioxan (mole %)	Yield (%)									
	Aziridines									
	Total	*cis*	*trans*	Fraction of *cis* (%)	From triplet[a] (%)	From singlet[b] (%)	(III)	(IV)	Singlet products	Triplet products
0	37.0	16.3	20.7	44.1	25.9	11.1	41.9	0	53.0	25.9
23.8	32.5	15.7	16.8	48.3	21.0	11.5	37.8	7.5	56.8	21.0
46.4	36.4	18.4	18.0	50.6	22.5	13.9	26.6	14.6	55.1	22.5
70.1	35.4	19.3	16.1	54.6	20.1	15.3	18.7	27.2	61.2	20.1
92.7	43.1	25.1	18.0	58.3	22.5	20.6	0	44.2	64.8	22.5

[a] *trans*-yield × 1.25. [b] Total aziridine minus aziridine from triplet.

Here we assume that the singlet-like complex besides free singlet nitrene reacts stereospecifically with olefin



SCHEME

(Scheme 1). In this case, when the complex is formed with the equilibrium constant *K* as illustrated in the Scheme, the relative yield (Y_r) of *cis*- (IIb) with respect to *trans*-aziridine (IIa) can be found from equation (1).

$$Y_r = d[(IIb)]/d[(IIa)] = (k_1[S] + k_2[C] + k_3[T])/(k_4[T]) \quad (1)$$

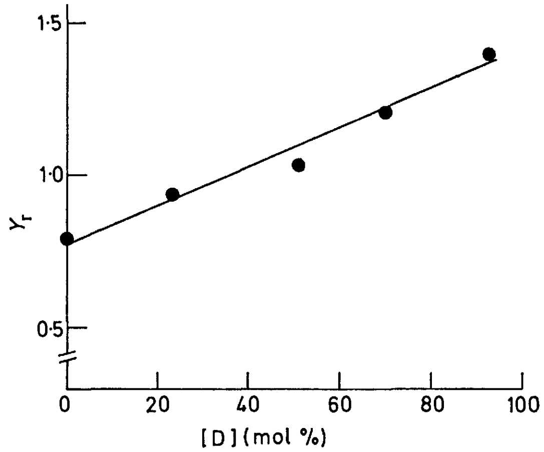
In this expression, [C], [S], and [T] are the concentrations of the complex, the singlet, and the triplet nitrene and k_1—k_4 are the rate constants shown in the

Scheme. When the concentration of 1,4-dioxan [D] is zero, the relative yield is given by equation (2). Using the relationship [C] = K(S)[D], combination of equations (1) and (2) gives (3). A linear plot of the value Y_r

$$Y_0 = k_3/k_4 + (k_1/k_4)([S]/[T]) \qquad (2)$$

$$Y_r = Y_0 + K(k_2/k_4)([S]/[T])[D] \qquad (3)$$

against [D] is obtained (Figure), indicating that [S]/[T] is independent of the concentration of 1,4-dioxan, Therefore, on the basis of the above assumption, we reach the conclusion that the increased stereospecificity by 1,4-dioxan results from the increased concentration of the singlet complex, not the free singlet nitrene.



Relative yield of *cis*- (IIb) to *trans*-aziridine (IIa) (Y_o) against mole % 1,4-dioxan in cyclohexane for the addition of ethoxycarbonylnitrene generated photochemically from ethyl azidoformate to *cis*-4-methylpent-2-ene

We can separate singlet and triplet products as follows. Since the olefin efficiently traps the triplet nitrene, the formation of ethyl carbamate which is the triplet nitrene product [2,11] is inhibited in the presence of 7 mole % *cis*-olefin. Both carbamates (III) and (IV) are therefore classified as singlet products. For the aziridines, applying the value k_3/k_4 0.25 [10] *cis*-aziridine is formed from the triplet nitrene in one-quarter of the yield of *trans*-aziridine. The sums of all singlet and triplet nitrene products are added up as indicated in Table 2. From the results, we can demonstrate without recourse to kinetics that the total singlet product yields behave very much like the yield of stereospecificially formed *cis*-aziridine, and that the total triplet products stay constant at a level of 22.4 ± 2.0%.

From the study of selectivity towards C–H insertion,[1] we found that the nitrene–1,4-dioxan complex is reactive towards C–H bonds. Thus our assumption that the complex can react with olefins seems reasonable. The complex might be regarded as being reactive to both C–H bonds and olefins, since for steric reasons it does not tend towards formation of carbamate (IV).[2] In contrast, an ylide or complex formed by interaction of the nitrene with an ether, such as tetrahydrofuran or tetrahydropyran, rapidly gives ethyl tetrahydrofuran- or tetrahydropyran-2-carbamate without reacting with other species. Thus tetrahydrofuran or tetrahydropyran do not stabilize the singlet state of nitrene.[2]

The statement that the free singlet : triplet ratio is constant at various 1,4-dioxan–cyclohexane ratios seems difficult to understand at first sight if cyclohexane traps the singlet nitrene with a rate constant different from that for 1,4-dioxan. However, these trapping rates may be almost identical since the percentage of singlet nitrene trapped by cyclohexane [the yield of carbamate (III) in cyclohexane)] and by 1,4-dioxan [the yield of carbamate (IV) in 1,4-dioxan], 50 and 45%, respectively, in photolysis are nearly the same according to our unpublished data. The yields are 42 and 44% for photolysis even at an olefin concentration of 7 mole % (Table 2).

The small influence of 1,4-dioxan on the stereospecificity for addition to the *trans*- by comparison with the *cis*-olefin shows that k_2/k_4 in the former addition is a little lower than that in the latter.

Currently, we cannot exclude the alternative possibility in which the complex is formed very quickly by interaction between the triplet nitrene and 1,4-dioxan, and equilibrates with both the singlet nitrene and 1,4-dioxan. This is under investigation.

Addition of Ethoxycarbonylnitrene generated Thermally from Ethyl Azidoformate to cis-*4-Methylpent-2-ene*.—A solution containing the same components as for the photolysis was heated at 120° for 2 h (Table 3). Stereospecificity for addition is almost independent of the concentration of 1,4-dioxan. The olefin and aziridines do not isomerize under the conditions described in the Experimental section.

TABLE 3

Thermal reactions of ethyl azidoformate with *cis*-4-methylpent-2-ene in mixtures of 1,4-dioxan and cyclohexane

1,4-Dioxan (mole %)	Aziridine yield (%)	Fraction *cis* (%)	(III) Yield (%)	(IV) Yield (%)
0	30.8	62.4	52.2	0
23.8	29.4	62.1	44.6	6.6
46.4	35.2	61.4	39.7	16.0
70.1	35.6	59.8	21.5	31.2
92.7	41.2	65.3	0	54.9

These findings show a low value for Kk_2/k_4 in equation (3). All nitrene generated thermally from azide (I) is initially in the singlet state, whereas *ca.* 30% nitrene formed by photolysis is in the triplet state,[10] so that the concentration of triplet nitrene in thermloysis is considerably lower than that in photolysis. However, as indicated in Tables 2 and 3, the yield of *trans*-aziridine formed through reaction with the triplet nitrene does not differ much between photolysis and thermolysis. Therefore the value of k_4 corresponding to thermolysis seems to be much greater than that corresponding to photolysis. The different magnitude of k_4 might be attributable to the temperature difference of 100°. We have no direct evidence for the magnitude of K and k_2, but K in thermolysis is presumably small in comparison with photolysis due to the temperature difference. The value of k_2

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is likely subject to steric influence because of the crowded transition state. It appears to have little temperature dependence.

EXPERIMENTAL

Determination of the amount of ethyl azidoformate (I) decomposed, and quantitative analysis of the products, *trans*- and *cis*-*N*-ethoxycarbonyl-2-isopropyl-3-methylaziridines (IIa and b), ethyl *N*-cyclohexylcarbamate (III), and ethyl 1,4-dioxan-2-ylcarbamate (IV), were carried out as described previously.[1] Cyclohexane and 1,4-dioxan were purified by standard methods before use. Both *trans*- and *cis*-4-methylpent-2-ene were purified by distillation, b.p. 56—59 and 55—56°, respectively, of commercial materials (Wako, reagent grade). Azide (I),[12] b.p. 45—46° at 35 mmHg, and *trans*- and *cis*-aziridines (IIa and b),[9] b.p. 56—60° and 54—55° at 3 mmHg, respectively, were obtained by literature methods.

Photochemical Reactions and Analyses.—Azide (I) and *trans*-4-methylpent-2-ene in the molar ratio *ca.* 1 : 10 were placed in a quartz vessel (25 cm × 1.8 cm). Cyclohexane or 1,4-dioxan was added, resulting in a 10.0 ml solution with an olefin concentration of 10 or 7 mole %. After purging with dry nitrogen for 1 h, the mixture was irradiated with an external 200 W low pressure Hg lamp at 20° for 2 h. The consumption of azide (*ca.* 100%) was determined by means of i.r. bands at 2 185 and 2 137 cm^{-1}. The products (II)—(IV) were analysed by g.l.c. using a glass column (2 m × 3 mm) packed with 10% polyethylene glycol on 60—80 Diasolid L, and the amounts were then calculated from the g.l.c. peak areas in the usual manner.

Experiments using *cis*- in place of *trans*-4-methylpent-2-ene were carried out at a concentration of 7 mole % in various mixtures of 1,4-dioxan and cyclohexane under the same conditions. The yields of the products (II)—(IV) were determined as above.

Non-photolysed mixtures did not produce (II)—(IV). None of the g.l.c. peaks of the starting materials and products overlapped. Further irradiation for 0.5, 1, and 2 h in the presence of the *cis*-olefin at 46.4 mole % 1,4-dioxan resulted in 61, 100, and 100% decomposition of azide, respectively, but g.l.c. analyses of the ratios of *cis*-aziridine to total aziridines agreed within <1%. This indicates that the olefins and aziridines hardly isomerize at all under our experimental conditions.

Thermal Reactions and Analyses.—A solution (2.0 ml) of the same composition as for photolysis using *cis*-olefin was placed in a sealed glass tube, and heated at 120° for 2 h, resulting in 100% decomposition of azide. The yield of products (II)—(IV), was determined by using a g.l.c. glass column (1 m × 3 mm) packed with 15% silicone SE 30 on 60—80 Uniport KS in the same manner as above.

No overlap of the g.l.c. peaks of the products was found using methods similar to these of the photochemical case. The isomerization of the olefins and aziridines probably does not occur under these conditions since at 46.4 mole % 1,4-dioxan, the ratio of *cis*-aziridine to total aziridines upon thermolysis for 0.5 h (37% decomposition of azide) is the same as that for 2 h within <1%.

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