Stabilization of Singlet Ethoxycarbonylnitrene by 1,4-Dioxan. Part 2.† Selectivity for Insertion into C–H Bonds

By **Hiroshi Takeuchi,* Yukiko Kasamatsu, Michiharu Mitani, Teruko Tsuchida,** and **Kikuhiko Koyama,** Department of Synthetic Chemistry, Faculty of Engineering, Shinshu University, 500 Wakasato, Nagano 380, Japan

The selectivity for insertion of ethoxycarbonylnitrene generated thermally or photochemically from ethyl azidoformate into the tertiary, secondary, and primary C–H bonds of iso-octane, cyclohexane, and n-octane were determined at various concentrations of 1,4-dioxan. The relative selectivity for secondary and primary C–H bonds is almost independent of the 1,4-dioxan concentration, whereas that for tertiary and primary C–H bonds decreases with an increase in the quantity of 1,4-dioxan. The tendency for this decrease is greater in photolysis than thermolysis. The results are explained in terms of steric hindrance in the transition state of the reaction between the crowded tertiary C–H bonds and a nitrene–1,4-dioxan complex. The variation of the selectivity with temperature supports formation of this complex.

NITRENES generated in solution from various precursors are initially in the singlet state, and are then partly deactivated to the triplet state due to intersystem crossing. Since nitrenes with different spin states usually have different chemical behaviour, solvent effects on the

---

† Part 1, ref. 6.

electronic state of nitrenes are therefore of great interest. It has been found recently that dichloromethane,[1-3] hexafluorobenzene,[4,5] and 1,4-dioxan [6] possess a stabilizing effect on the singlet state of ethoxycarbonylnitrene during C–H insertion. These observations can be explained by stabilization of the singlet nitrene by interaction with the lone pair electrons of solvents.

In the case of dichloromethane, it has been proposed that part of the singlet stabilization by the electrons of chlorine is balanced against intersystem crossing induced by the solvent.[1,3] If this is true, then 1,4-dioxan should be much more advantageous for singlet stabilization since it does not promote intersystem crossing as do solvents having atoms such as chlorine.

However, it has not been established so far whether the solvent–nitrene interactions described above cause an increase only in the singlet concentration of free nitrene or whether some or all the increase corresponds to the formation of a singlet complex. If the selectivity for insertion into the C–H bonds of alkanes varies with the concentration of 1,4-dioxan, this would be evidence for the formation of a complex. On the other hand, if the selectivity is independent of the concentration of 1,4-dioxan, this would support an increase in the concentration of free nitrene.

RESULTS AND DISCUSSION

Selectivity for Insertion of Ethoxycarbonylnitrene into C–H *Bonds.*—A given amount of a solution containing ethyl azidoformate, iso-octane, cyclohexane, and n-octane in the molar ratio 1 : 12.9 : 4.3 : 12.9 was diluted with varying amounts of a solution of 1,4-dioxan and ethyl azidoformate (30 : 1 molar ratio), and irradiated or heated as described in the Experimental section. The relative reactivities for insertion of ethoxycarbonylnitrene into tertiary (3°), secondary (2°), and primary (1°) C–H bonds at different concentrations of 1,4-dioxan were determined by means of g.l.c. on the basis of the yields of the products, 2-*N*-ethoxycarbonylamino-2,4,4-trimethylpentane (I), ethyl *N*-cyclohexylcarbamate (II), and 1-*N*-ethoxycarbonylamino-octane (III) [equations (1)—(3)]. The total absolute yields for products (I)—(III)

$$\text{iso-C}_8\text{H}_{18} + \text{N}_3\text{CO}_2\text{Et} \xrightarrow[\text{or }\Delta]{h\nu} \underset{\text{(I)}}{\text{Me}_3\text{CCH}_2\text{C(Me)}_2\text{NHCO}_2\text{Et}} \qquad (1)$$

$$\text{C}_6\text{H}_{12} + \text{N}_3\text{CO}_2\text{Et} \xrightarrow[\text{or }\Delta]{h\nu} \underset{\text{(II)}}{\text{C}_6\text{H}_{11}\text{NHCO}_2\text{Et}} \qquad (2)$$

$$\text{n-C}_8\text{H}_{18} + \text{N}_3\text{CO}_2\text{Et} \xrightarrow[\text{or }\Delta]{h\nu} \underset{\text{(III)}}{\text{n-C}_8\text{H}_{17}\text{NHCO}_2\text{Et}} \qquad (3)$$

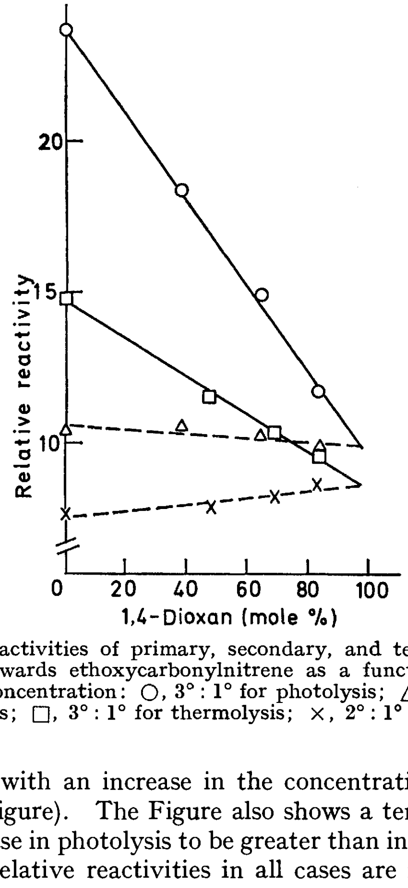
with no dilution were *ca.* 20% in both thermolysis and photolysis. The relative reactivities are summarized in Table 1. We can rule out the possibility that there is selective destruction of some of these products during the reactions since the relative ratios of the products scarcely vary under the reaction conditions (see Experimental section).

TABLE 1

Relative reactivities of tertiary, secondary, and primary C–H bonds towards ethoxycarbonylnitrene diluted with 1,4-dioxan

1,4-Dioxan (mole %)	Photolysis			Thermolysis		
	3°	2°	1°	3°	2°	1°
0	23.7	10.4	1.0	14.8	7.6	1.0
38	18.4	10.5	1.0			
47				11.5	7.8	1.0
64	14.9	10.2	1.0			
68				10.3	8.2	1.0
83	11.7	9.7	1.0	9.6	8.6	1.0

In both photolysis and thermolysis, the selectivity for 2° : 1° C–H bonds is almost independent of the concentration of 1,4-dioxan, while that for 3° : 1° C–H bonds decreases with an increase in the concentration of 1,4-dioxan (Figure). The Figure also shows a tendency for the decrease in photolysis to be greater than in thermolysis; the relative reactivities in all cases are nearly the same at 100% 1,4-dioxan.



Relative reactivities of primary, secondary, and tertiary C–H bonds towards ethoxycarbonylnitrene as a function of 1,4-dioxan concentration: ○, 3° : 1° for photolysis; △, 2° : 1° for photolysis; □, 3° : 1° for thermolysis; ×, 2° : 1° for thermolysis

From these results, it is concluded that a singlet complex between the nitrene and 1,4-dioxan coexists with the free nitrene, and that the reaction of the complex with the crowded 3° C–H bonds is retarded by steric

---

[1] R. C. Belloli, M. A. Whitehead, R. H. Wollenberg, and V. A. LaBahn, *J. Org. Chem.*, 1974, **39**, 2128.

[2] P. A. Tardella and L. Pellacani, *J. Org. Chem.*, 1976, **41**, 2034.

[3] H. Takeuchi, N. Murata, Y. Nakagawa, T. Tsuchida, and K. Koyama, *J.C.S. Perkin II*, 1977, 80.

[4] D. S. Breslow and E. I. Edwards, *Tetrahedron Letters*, 1972, 2041.

[5] R. C. Belloli and V. A. LaBahn, *J. Org. Chem.*, 1975, **40**, 1972.

[6] H. Takeuchi, K. Kinoshita, S. M. A. Hai, M. Mitani, T. Tsuchida, and K. Koyama, *J.C.S. Perkin II*, 1976, 1201.

hindrance in the transition state. Complex formation is usually favoured at low temperature, thus explaining the comparative results for photolysis and thermolysis. On the other hand, the 2° : 1° selectivity probably reflects nothing more than the absence of any steric effects. Furthermore, the convergence of the reactivities for both 3° : 1° and 2° : 1° insertions in 100% 1,4-dioxan is presumably due to an increase in the formation of the complex. The temperature dependence for selectivity in the photochemical case is discussed later.

Belloli *et al.* have also reported on the existence of complexes of ethoxycarbonylnitrene with dichloromethane [1] and hexafluorobenzene [5] on the basis of studies in which the selectivity (% tertiary product) for insertion of the nitrene into *trans*-1,2-dimethylcyclohexane decreases on dilution with solvent, accompanied by high stereospecificity and an increase in the absolute yield of insertion products. In contrast, Tardella and Pellacani [2] have found that high selectivity (ratio of methine: methylene reactivity) for insertion into *cis*- and *trans*-decalin, *cis*- and *trans*-1,2-dimethylcyclohexane, or methylcyclohexane is displayed by triplet nitrene. This is perhaps because the triplet nitrene is particularly reactive in cases where highly stable tertiary radicals, such as decalinyl, *etc.*, are involved, giving products of apparent insertion *via* hydrogen abstraction and recombination. They conclude that the singlet stabilization resulting in an increase of only the singlet concentration of the free nitrene may cause a decrease in the selectivity on dilution with dichloromethane regardless of the existence of any nitrene–dichloromethane complex.

Since the tertiary radicals derived from the hydrocarbons used in our systems are not so stable as the tertiary decalinyl radical, the tertiary product in our case may not be formed on reaction with the triplet nitrene. This would be consistent with Belloli's evidence that no more than 16% of the tertiary insertion product is formed *via* a triplet path,[1] and that the insertion of the nitrene into the tertiary C–H bonds of optically active 3-methylhexane proceeds with 100% retention of configuration.[7] Therefore our conclusion is reasonable.

Evidence that the increased concentration of the singlet state induced by 1,4-dioxan corresponds to increased formation of the nitrene–1,4-dioxan complex has been reported elsewhere.[8] It has also been established that the selectivity for hydrogen abstraction by chlorine increases when it forms a complex with the solvent.[9] The difference between insertion of nitrene and abstraction by chlorine atom therefore suggests that the transition state for insertion is considerably different from that for abstraction.[10]

Effect of Temperature on the Selectivity of Insertion.—The selectivity for insertion in photolysis was determined at different temperatures in the presence (83 mole %) or absence of 1,4-dioxan (Table 2). As Table 2 indicates, the selectivity in the absence of 1,4-dioxan decreases somewhat with an increase in temperature, whereas in the presence of 1,4-dioxan it is almost uninfluenced by variations in temperature.

TABLE 2

Effect of temperature on relative reactivities of tertiary and primary C–H bonds in the presence and absence of 1,4-dioxan (83 mole %)

	Absence of dioxan			Presence of dioxan		
T/°C	3°	2°	1°	3°	2°	1°
55.0	19.8	8.7	1.0	11.7	9.2	1.0
40.0	21.1	10.5	1.0	11.2	8.4	1.0
25.0	23.7	10.5	1.0	11.7	9.7	1.0
15.0				12.6	10.1	1.0

The results for the absence of 1,4-dioxan indicates that the nitrene becomes more active or indiscriminate at higher temperatures. This is also obvious from the fact that selectivity upon dilution in photolysis is greater than in thermolysis (Figure). On the other hand, in the presence of 83 mole % 1,4-dioxan, it seems that the influence of temperature on complex formation for tertiary insertion is counterbalanced by the temperature effect since complex formation is favoured at lower temperatures. The convergence of the 3° : 1° reactivity ratio in 100% 1,4-dioxan in both photolysis and thermolysis (Figure) supports this conclusion.

EXPERIMENTAL

G.l.c. for quantitative analyses was carried out with Shimazu GC-6A unit using two glass columns (1 m × 3 mm): A, 10% polyethylene glycol 20M in 60—80 Uniport KS and B, 15% silicone SE-30 in 60—80 Uniport KS. The carrier gas was nitrogen, and air and hydrogen were used for combustion in the flame ionization detector. I.r. and n.m.r. spectra were recorded as described previously.[6] Mass spectra were obtained with a Hitachi RMU-6M spectrometer. Molecular weights were measured with a Hitachi–Perkin-Elmer 115 molecular weight apparatus. Photolyses were carried out in a quartz vessel (25 × 1.8 cm) by use of a high pressure Halōs PIH lamp (300 W).

Cyclohexane, 1,4-dioxan, iso-octane, and n-octane were purified by standard methods before use. Ethyl azidoformate and ethyl *N*-cyclohexylcarbamate (II) were obtained as described in the literature.[11]

Preparation of 2-N-*Ethoxycarbonylamino*-2,4,4-*trimethylpentane* (I).—To a solution of 1,1,3,3-tetramethylbutylamine (100 mmol; Wako reagent grade) in anhydrous ether (75 ml) was added dropwise with constant stirring and cooling (ice-bath) ethyl chloroformate (50 mmol) in anhydrous ether (50 ml). The precipitate (amine hydrochloride) was filtered off and washed with anhydrous ether, and the combined filtrates were evaporated to dryness on a rotary evaporator. The desired product was purified by recrystallization from ethanol–water, m.p. 17—18.5°, $\nu_{max.}$(neat) 3 340 (NH), 2 950 (C–H), 1 710 (C=O), 1 530 (C–N), 1 270 (C–O), and 1 100 cm^{-1} (C–O), τ(CCl$_4$) 5.5br (1 H, NH), 6.0 (2 H, q, OCH$_2$), 8.3 (2 H, s, CH$_2$), and 8.6—9.1 (18 H, m, CH$_3$), *m/e* 201 (*P*), 186, 131, 130, 97, 90, 86, 58, 57, and 41, mol. wt.

---

[7] J. M. Simson and W. Lwowski, *J. Amer. Chem. Soc.*, 1969, **91**, 5107.

[8] H. Takeuchi, T. Igura, M. Mitani, T. Tsuchida, and K. Koyama, following paper.

[9] G. Russell, *J. Amer. Chem. Soc.*, 1957, **79**, 2277; 1958, **80**, 4987.

[10] W. Lwowski and T. J. Maricich, *J. Amer. Chem. Soc.*, 1965, **87**, 3630.

[11] W. Lwowski and T. W. Mattingly, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 1947.

212 (in benzene) (Found: C, 65.4; H, 11.75; N, 7.05. $C_{11}H_{23}NO_2$ requires C, 65.65; H, 11.5; N, 6.95%).

Preparation of 1-N-*Ethoxycarbonylamino-octane* (III).—This compound was prepared by use of n-octylamine (Wako reagent grade) in place of 1,1,3,3-tetramethylbutylamine as described above. The product was recrystallized from ethanol–water, m.p. 9—10°, $\nu_{max.}$(neat) 3 330 (NH), 2 930 (C–H), 1 710 (C=O), 1 530 (C–N), and 1 260 cm^{-1} (C–O), $\tau(CCl_4)$ 5.15br (1 H, NH), 5.95 (2 H, q, OCH_2), 6.9 (2 H, q, NCH_2), 8.4—8.8 (12 H, m, CH_2), and 8.8—9.3 (6 H, m, CH_3), *m*/*e* 202 (*P* + 1), 201 (*P*), 74, 41, 30, and 29, mol. wt. 218 (in benzene) (Found: C, 65.65; H, 11.65; N, 6.85. $C_{11}H_{23}NO_2$ requires C, 65.65; H, 11.5; N, 6.95%).

Reactions and Analyses.—A fixed amount of a solution consisting of ethyl azidoformate, iso-octane, cyclohexane, and n-octane (1 : 12.9 : 4.3 : 12.9 molar ratio) was diluted with varying amounts of a solution containing 1,4-dioxan and ethyl azidoformate in the molar ratio 30 : 1 to give a total volume of 10.0 ml. The mixture was placed in a quartz vessel. After purging with dry nitrogen for 1.5 h, it was irradiated for 6 h at a given temperature, resulting in *ca.* 40% decomposition of the azide. The consumption of azide was followed by means of the i.r. bands at 2 185 and 2 137 cm^{-1}. When the reaction was carried out at high dilution $\geqslant$50% 1,4-dioxan), the product mixture was concentrated by removing three-quarters of the solvent. The relative yields of (I) and (II) to (III) in the mixture were determined by g.l.c. under conditions which gave satisfactory separation. The yields were calculated from the g.l.c. peak areas following standard procedures. The reactivity values were derived from the yields thus obtained. The results are based on two or three runs with an error of ±4 or ±6% for the 3° : 1° insertion concentrations of 1,4-dioxan lower or higher than 50 mole % and ±3% for the 2° : 1° insertion.

For the thermal reactions, a solution (2.0 ml) containing the same components as described for the photolysis was placed in a sealed tube, and heated at 120° for 2 h. The determination of selectivity was done by similar methods. The experimental error was almost identical with that in the photochemical case.

Compounds (I)—(III) were not produced under the g.l.c. conditions, and none of the g.l.c. peaks of the starting materials and products overlapped. A solution containing (I) (2×10^{-3}M), (II) (1.1×10^{-2}M), and (III) (5.3×10^{-3}M) in 1,4-dioxan–cyclohexane (68 : 32 v/v) was heated at 120° for 1 h, but the relative ratios, (I) : (III) and (II) : (III) are in accord with those of the starting solution within $<2\%$. The above solution was also irradiated for 2 h under the normal photochemical conditions. The ratios of (I) and (II) to (III) after irradiation agreed with those before within 3 and 7%. Thus the possibility that selective destruction of products (I)—(III) occurs under the reaction conditions can be eliminated.

We thank Dr. S. M. A. Hai, Pakistan C.S.I.R. Laboratories, and Professor P. S. Skell, Department of Chemistry, The Pennsylvania State University, for comments and discussion.

[7/734 *Received, 2nd May,* 1977]