

Stabilization of Singlet Ethoxycarbonylnitrene. Effect of Dichloromethane on Insertion into Tetrahydrofuran and Cyclohexane

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Ratios of singlet ethoxycarbonylnitrene to total nitrene species for the insertion of the nitrene into tetrahydrofuran and cyclohexane in dichloromethane were determined by taking into consideration tetrahydrofuran-dichloromethane interactions, solvent polarity effects, and triplet quenching experiments. In the case of the nitrene generated photochemically, the ratios were almost independent of dichloromethane concentration. This probably suggests that singlet destabilization by the external heavy atom effect of dichloromethane is counterbalanced by singlet stabilization due to an interaction between the nitrene and the lone pair electrons of dichloromethane. Whereas the result for the insertion of the nitrene generated thermally reveals slightly predominant singlet destabilization compared with the photochemical case. This may also result from different temperature conditions.

SOLVENT effects on the electronic state of nitrenes have been much studied. Solvents with heavy atoms are known to promote intersystem crossing due to external heavy atom effects. A striking example of such singlet destabilization by dichloromethane is found in the addition of ethoxycarbonylnitrene to olefins.^{1,2}

It has been recently observed that dichloromethane has a stabilizing effect on the singlet state of nitrene³ as well as on alkanoylnitrene⁴ during insertion into C-H bonds. Hexafluorobenzene^{5,6} and 1,4-dioxan⁷ have also been shown to stabilize singlet ethoxycarbonylnitrene for C-H insertion. These observations are in agreement with a proposal⁸ in which singlet nitrene is stabilized by interaction with the lone pair electrons of halogens, oxygen, nitrogen, etc. The different behaviour of dichloromethane between addition to olefins, and C-H insertion aroused our interest. The activated C α -H bonds of tetrahydrofuran are reactive to both

singlet and triplet ethoxycarbonylnitrene,^{7,9} whereas the unactivated C-H bonds of cyclohexane are only reactive to the singlet nitrene.¹⁰ Therefore the relative rate constant for insertion into tetrahydrofuran to cyclohexane would depend on the relative concentration of the singlet and the triplet nitrene.

RESULTS AND DISCUSSION

Effect of Dichloromethane on the Insertion of Photochemically Generated Ethoxycarbonylnitrene in Tetrahydrofuran (THF) and Cyclohexane.—Photolysis of ethyl azidoformate was performed in THF-cyclohexane-CH₂Cl₂ (see Experimental section). The molar ratio azide : THF : cyclohexane was kept constant (1 : 20 : 20), and the concentration of CH₂Cl₂ was varied from 0 to 93 mol %. Cyclohexylurethane (1), ethyl tetrahydrofuran-2-ylcarbamate (2), and ethyl carbamate were the main products. The observed relative rate constants (k_{rel}) of cleavage of one C α -H bond of THF to one C-H

⁶ D. S. Breslow and E. I. Edwards, *Tetrahedron Letters*, 1972, 2041.

⁷ H. Takeuchi, K. Kinoshita, S. M. A. Hai, M. Mitani, T. Tsuchida, and K. Koyama, *J.C.S. Perkin II*, 1201.

⁸ R. Gleiter and R. Hoffmann, *Tetrahedron*, 1968, **24**, 5899.

⁹ H. Nozaki, S. Fujita, H. Takaya, and R. Noyori, *Tetrahedron*, 1967, **23**, 45.

¹⁰ J. M. Simson and W. Lwowski, *J. Amer. Chem. Soc.*, 1969, **91**, 5107.

¹ J. S. McConaghy, jun., and W. Lwowski, *J. Amer. Chem. Soc.*, 1967, **89**, 2357.

² J. S. McConaghy, jun., and W. Lwowski, *J. Amer. Chem. Soc.*, 1967, **89**, 4450.

³ R. C. Belloli, M. A. Whitehead, R. H. Wollenberg, and V. A. LaBahn, *J. Org. Chem.*, 1974, **39**, 2128.

⁴ G. R. Felt, S. Linke, and W. Lwowski, *Tetrahedron Letters*, 1972, 2037.

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

bond of cyclohexane were calculated using equation (1)

$$k_{rel} = \frac{d[(2)]/d[(1)]}{([Cyclohexane]_0/[THF]_0)(12/4)} \quad (1)$$

from data obtained by g.l.c. analysis. In this equation, the factor 12/4 comes from the number of hydrogens involved in the formation of products (1) and (2). Similarly the k_{rel} values of 1,4-dioxan and 1,3-dioxolan were obtained for various dilutions with CH_2Cl_2 . These data are given in Table 1 and Figure 1.

TABLE 1

Dilution effect with CH_2Cl_2 for the insertion of photochemically generated ethoxycarbonylnitrene into THF and cyclohexane

CH_2Cl_2 (mol %)		THF (mol %)	k_{rel}	k_{TS}/k_C	k_{TT}/k_C	$\frac{[S]}{[S] + [T]} \times 100$ (%)
$[D]_0$	$[D]$					
0	0	52	5.3	3.3	4.6	69
20	17	41	5.1	3.1	4.5	65
39	35	32	4.5	2.8	4.4	65
60	56	21	3.8	2.6	4.4	67
77	75	12	3.3	2.4	4.3	68
93	92	4.0	2.8	2.2	4.2	71

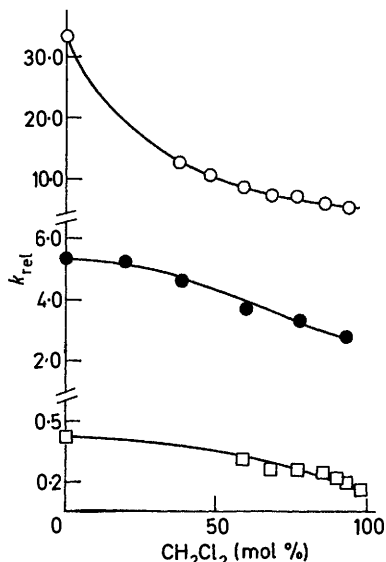
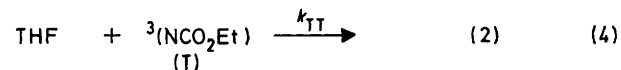
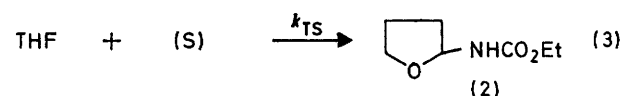
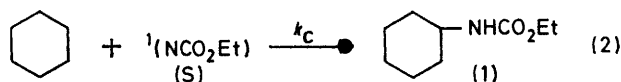


FIGURE 1 Effect of CH_2Cl_2 on the k_{rel} values of cyclic ethers: ●, THF-cyclohexane; □, 1,4-dioxan-cyclohexane; ○, 1,3-dioxolan-cyclohexane

As described previously, the unactivated C-H bonds of cyclohexane react with the singlet nitrene only¹⁰ whereas the activated C_α -H bonds of ethers such as



THF are reactive towards both the singlet (S) and triplet nitrene (T)^{7,9} [see equations (2)–(4)]. Using

k_C , k_{TS} , and k_{TT} , the rate constants in equations (2)–(4), gives the rate expression (15). Combination of

$$\frac{d[(2)]}{d[(1)]} = (4/12) \times \frac{k_{TS}[THF]_0[S] + k_{TT}[THF]_0[T]}{k_C[Cyclohexane]_0[S]} \quad (5)$$

equations (1) and (5) gives (6). Since the k_{rel} value is independent of THF concentration (see Table 2), equation (6) appears reasonable at first sight.

$$k_{rel} = (k_{TS} + k_{TT}[T]/[S])/k_C \quad (6)$$

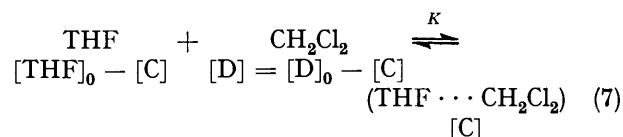
If the reaction proceeds according to equation (6), k_{rel} should increase with dilution with CH_2Cl_2 as the result of the increase in $[T]/[S]$ due to the heavy atom effect of CH_2Cl_2 . However the experimental observations (Figure 1) show a decrease in k_{rel} upon higher dilution with CH_2Cl_2 .

TABLE 2

Effect of the concentration of THF on the k_{rel} value of THF at constant dilution with CH_2Cl_2

Cyclohexane (mmol)	THF (mmol)	Ethyl azidoformate (mmol)	CH_2Cl_2 (mol %)	k_{rel}
65	37	2.5	60	3.7
45	61	2.5	59	3.8
32	80	2.7	57	3.7
27	86	2.5	57	3.8

(a) *Interaction of THF with CH_2Cl_2 .* Halogenoforms¹¹ and dichloromethane¹² undergo interaction with THF *via* hydrogen bonding ($O \cdots H-C$), so that the concentration of THF which does not interact with CH_2Cl_2 is lower at higher dilution with CH_2Cl_2 . THF molecules which interact with CH_2Cl_2 would, presumably, not be reactive to the nitrene, since insertion into the C_α -H bonds of THF occurs through an O-N ylide¹³ in which THF is co-ordinated through its oxygen to the nitrene nitrogen atom. If this model is accepted then, we can see that it is possible to visualize an equilibrium such as (7) where $[D]$ or $[C]$ is the steady state concen-



tration of CH_2Cl_2 or a complex between THF and CH_2Cl_2 . The concentration of THF which does not interact with CH_2Cl_2 , $[THF]_0 - [C]$, may be expressed in the form (8).

$$[THF]_0 - [C] = [THF]_0/(1 + K[D]) \quad (8)$$

Replacing the $[THF]_0$ term in equation (5) with this form, $[THF]_0 - [C]$, we can rewrite equation (6) as (9).

$$k_{rel} = \frac{1}{1 + K[D]} \times \frac{k_{TS} + k_{TT}[T]/[S]}{k_C} \quad (9)$$

¹¹ C. J. Creswell and A. L. Allred, *J. Amer. Chem. Soc.*, 1963, **85**, 1723.

¹² C. S. Marvel, M. J. Copley, and E. Ginsberg, *J. Amer. Chem. Soc.*, 1940, **62**, 3109.

¹³ T. Shingaki, M. Inagaki, N. Torimoto, and M. Takabayashi, *Chem. Letters*, 1972, 297.

(b) *Determination of the values k_{TS}/k_C , k_{TT}/k_C , and K , and the concentration $[D]$ by the triplet quenching and solvent polarity effects.* We have previously⁷ reported that the triplet nitrene is effectively quenched in the presence of piperylene ($\geq 0.25M$). Thus, according to equation (9), the k_{TS}/k_C value (for $[D] = 0$) becomes equal to the k_{rel} value, 3.3,⁷ in the absence of CH_2Cl_2 in the presence of piperylene of $\geq 0.25M$ (*i.e.* $[T] = 0$). In the absence of piperylene, $k_{TT}/k_C = 4.6$ (for $[D] = 0$) when $[T]/[S] = 0.44$, $[D] = 0$, $k_{rel} = 5.3$ (obtained experimentally), and k_{TS}/k_C is substituted in equation (9). Here the $[T]:[S]$ ratio of the initially formed nitrene was found by Lwowski and McConaghy² for photolysis of ethyl azidoformate.

The plots of the $\log k_{rel}$ value against the solvent polarity parameters $E_T(30)$ ¹⁴ and Kirkwood parameter $(\epsilon - 1)/(2\epsilon + 1)$ ¹⁵ of various solvents (90% v/v) in the presence or absence of piperylene has been reported earlier.⁷ Now we report further experimental data using CH_2Cl_2 as solvent (see Figures 2 and 3). In this case, the protic solvents and solvents containing halogens are not chosen, except CH_2Cl_2 , since such solvents are known to hinder¹⁶ the reactivity of the nitrene towards THF due to hydrogen bonding. They also affect the nitrene spin state. Thus the K value in these solvents with the exception of CH_2Cl_2 should be zero. As seen in Figures 2 and 3, the plots are straight lines excluding the case of CH_2Cl_2 as solvent. If the k_{rel} value in CH_2Cl_2 in the presence of piperylene is

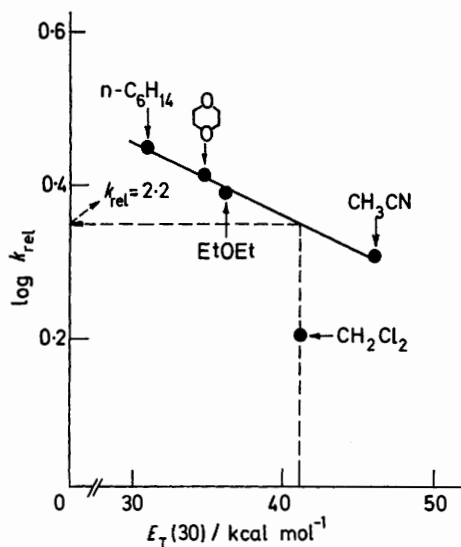


FIGURE 2 Solvent polarity effect on $\log k_{rel}$ of THF versus $E_T(30)$ values in the presence of piperylene (0.25M). The $E_T(30)$ value for 90% v/v solvents is used

assumed to fall on this line, then it has the value 2.2 (see Figure 2). Therefore, $k_{TS}/k_C = 2.2$ (for $[D] = 92$ mol %) can be calculated from substituting $k_{rel} = 2.2$, $K = 0$, and $[T] = 0$ in equation (9).

¹⁴ E. M. Kosower, 'An Introduction to Physical Organic Chemistry,' Wiley, New York, 1968, p. 305.

¹⁵ K. B. Wiberg, 'Physical Organic Chemistry,' Wiley, New York, 1966, p. 381.

Similarly, from Figure 3 in the absence of piperylene, we obtain $k_{TT}/k_C = 4.2$ (for $[D] = 92$ mol %); the relations $k_{rel} = 4.1$ (obtained from Figure 3), $K = 0$,

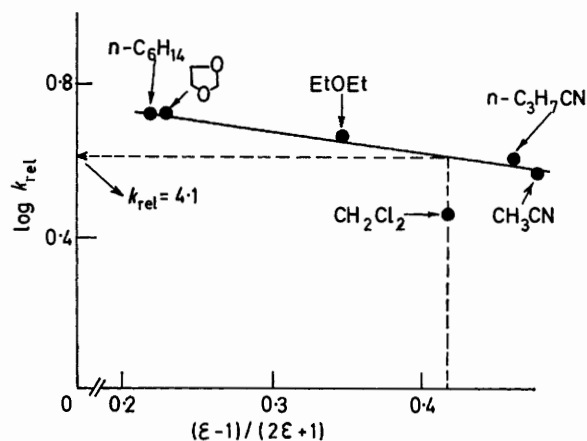


FIGURE 3 Solvent polarity effect on $\log k_{rel}$ of THF versus $(\epsilon - 1)/(2\epsilon + 1)$ in the absence of piperylene. The dielectric constant was calculated on the basis of solvent-substrate (THF-cyclohexane) 9:1

$k_{TS}/k_C = 2.2$, and $[T]/[S] = 0.44$, are substituted in equation (9).

As described above, the values k_{TS}/k_C and k_{TT}/k_C vary with the concentration of CH_2Cl_2 presumably due to the macroscopic solvent effect. Then their values on various concentrations of CH_2Cl_2 can be obtained from the assumption that a linear relationship exists between $\log(k_{TS}/k_C)$ or $\log(k_{TT}/k_C)$ and $[D]$ (Table I).

We calculated the K value on the basis of the assumption that the unusually low value for k_{rel} in CH_2Cl_2 as seen in Figures 2 and 3 possibly depends on the hydrogen bonding interaction between THF and CH_2Cl_2 as mentioned above. The relations $k_{rel} = 1.6$ (obtained experimentally), $k_{TS}/k_C = 2.2$, $[T] = 0$, and $[D] = 0.92$ mol %, are substituted in equation (9) and give $K = 0.44$ (mol fraction)⁻¹.

Additionally we should consider whether the interaction of the singlet nitrene with CH_2Cl_2 causes the low value of k_{rel} in CH_2Cl_2 . But this is disproved by the following results. (i) There is no change in the insertion selectivity for primary, secondary, and tertiary C-H bonds on dilution with CH_2Cl_2 for the thermal and photochemical decomposition of ethyl azidoformate in 3-methylhexane¹⁰ or for the reaction of 3-methylbutane¹⁷ with ethoxycarbonylnitrene generated by photolysis and α -elimination. (ii) Lwowski *et al.*⁵ have reported that CH_2Cl_2 stabilizes the singlet character of a number of alkanoylnitrenes without modifying their C-H insertion reactivity. (iii) We have previously proposed⁷ that 1,4-dioxan quite efficiently stabilizes singlet ethoxycarbonylnitrene formed photochemically from ethyl azidoformate for insertion into the C $_{\alpha}$ -H

¹⁶ E. L. Eliel and O. Hofer, *J. Amer. Chem. Soc.*, 1973, **95**, 8041.

¹⁷ W. Lwowski and T. J. Maricich, *J. Amer. Chem. Soc.*, 1965, **87**, 3630.

bonds of cyclic ethers. According to our observations, the singlet nitrene reactivity is not altered as can be seen in Figure 2.

The steady state concentration $[D]$ is obtained by using the K value determined as follows. Substituting $[D]_0$ for $[D]$ in equation (8), the given $[C]$ is represented as $[C]_1$. Then $[D]_0 - [C]_1$ becomes equal to $[D]_1$. This procedure is repeated until converging values of $[C]_n$ and $[D]_n$ are obtained which are determined as $[C]$ and $[D]$ (Table 1).

(c) *Stabilization of the singlet nitrene by CH_2Cl_2 .* After the determination of the values k_{TS}/k_C , k_{TT}/k_C , and K , and the concentration $[D]$, one obtains the $[T]:[S]$ ratio on various dilutions with CH_2Cl_2 by using equation (9). Then the ratio of the singlet nitrene to total nitrene species is obtained as shown in Table 1. The data show that the ratios are almost independent of CH_2Cl_2 concentration. Also, the absolute yield of urethane (1) (singlet nitrene product) or ethyl carbamate (triplet nitrene product) is nearly constant on dilution with CH_2Cl_2 for the photochemical reaction of ethyl azidoformate with cyclohexane (Table 3).

TABLE 3

Photochemical reaction of ethyl azidoformate with cyclohexane in the presence of CH_2Cl_2

CH_2Cl_2 (mol %)	Absolute yield (%)	
	Cyclohexylurethane (1)	Ethyl carbamate
0	50	19
29	52	16
53	52	17
72	51	18
87	52	16
94	47	15

These results suggest that singlet destabilization by heavy atom effects is counterbalanced by the singlet stabilizing ability due to an interaction between the nitrene and the lone pairs of electrons of CH_2Cl_2 . Gleiter and Hoffmann⁸ have proposed this type of singlet stabilization. Also such an effect was demonstrated experimentally.²⁻⁴

We have also carried out the photochemical experiments using CHCl_3 , CCl_4 , CH_2Br_2 , and *sym*-tetrachloroethane in place of CH_2Cl_2 as diluent, but these runs were not successful since the carbamate (2) decomposed in the acidic reaction mixture. The reaction mixture showed acidic pH, and the gradual decrease in carbamate (2) could be followed by g.l.c. analysis.

Effect of CH_2Cl_2 or CH_3I on the Insertion of Thermally Generated Ethoxycarbonylnitrene into THF and Cyclohexane.—Ethyl azidoformate was thermally decomposed in the THF–cyclohexane– CH_2Cl_2 or – CH_3I at 112° , and the k_{rel} value was obtained as described in the photochemical case. The data are summarized in Table 4. On higher dilution with CH_3I , the k_{rel} value increased remarkably. On the other hand, the effect of added CH_2Cl_2 was not so great as that of CH_3I . Since the k_{rel} value would be greater for higher concentrations of the triplet nitrene as expected from equation (9), these

results mean that the singlet destabilization caused by the promotion of intersystem crossing is greatly accelerated by the much heavier iodine atoms.

As seen in Table 4, the k_{rel} value decreased at first with the addition of CH_2Cl_2 , and then on further dilution with CH_2Cl_2 up to 92 mol %, the value 5.2 is obtained which is clearly higher than the value 4.2 obtained for

TABLE 4

Dilution effect of CH_2Cl_2 and CH_3I on the k_{rel} value for the insertion of thermally generated ethoxycarbonylnitrene into THF and cyclohexane

CH_2Cl_2 (mol %)	k_{rel}	CH_3I (mol %)	k_{rel}
0	4.2	0	4.2
39	3.2	38	10.2
61	3.1	86	∞
92	5.2		

no dilution. The decrease in k_{rel} caused by the THF– CH_2Cl_2 interaction in the thermal case would presumably be smaller than in the photochemical case because of temperature difference. Thus the k_{rel} value in the former case should be constant or tend to decrease on dilution with CH_2Cl_2 if the singlet stabilization and destabilization cancel each other as mentioned in the latter case. Therefore the above result can be explained by the fact that in the thermal reaction slightly more predominant singlet destabilization is observed compared with the photochemical case. Presumably a complex of the nitrene with the lone pairs of electrons of CH_2Cl_2 might bring about the singlet stabilization. Such complex formation seems to be suppressed at higher temperature, judging from the temperature dependence.

If such complex formation is more unfavourable than interaction of the nitrene with olefin, its formation would be prevented in the presence of an olefin. Then we might well explain that CH_2Cl_2 acts to destabilize the singlet nitrene state for the addition to olefins as pointed out by Lwowski *et al.*^{1,2}

EXPERIMENTAL

The general procedure for the analysis and characterization of the products, cyclohexylurethane (1), ethyl tetrahydrofuran-2-ylcarbamate (2), ethyl carbamate, and ethyl 1,4-dioxan-2-ylcarbamate have been previously described.⁷ Cyclohexane, THF, 1,4-dioxan, 1,3-dioxolan, CH_2Cl_2 , CH_3I , CHCl_3 , CCl_4 , CH_2Br_2 and *sym*-tetrachloroethane were purified by standard methods before use.

Preparation of Ethyl 1,3-Dioxolan-2-ylcarbamate.—A solution of ethyl azidoformate (2 mmol) and 1,3-dioxolan (45 mmol) was irradiated with an external 300 W high pressure Hg lamp (Eikosha PIH-300 model) at room temperature for 3 h, and the mixture was distilled under reduced pressure. The title compound was isolated by the preparative g.l.c. on aluminium column (1.5 m \times 3 mm) under the analytical conditions of ref. 7, m.p. 55.0° (lit.,⁹ 55.0 – 55.5°), ν_{max} (CCl_4) 3 450 (NH), 1 740 (C=O), 1 505 (NH), and 1 230 cm^{-1} (C–O), τ (CCl_4) 8.80 (3 H, t, CH_3), 6.30–5.90 (6 H, m, CH_2CH_3 and 4- and 5- H_2), 4.15 (1 H, m, NH), and 4.90 (1 H, d, 2-H).

Photochemical Decomposition of Ethyl Azidoformate in Cyclic Ether (THF, 1,4-Dioxan, or 1,3-Dioxolan)-Cyclohexane-CH₂Cl₂.—A fixed amount of solution which consisted of cyclic ether, cyclohexane, and ethyl azidoformate (20 : 20 : 1 molar ratio) was diluted with various amounts of CH₂Cl₂ to give a total volume of 10 ml. The mixture was placed in a quartz tube (25 cm × 1.8 cm). Dry nitrogen was bubbled through the liquid mixture for 1 h. Its quartz tube involving the solution was fixed at 2.5 cm distance from the above-mentioned lamp, and irradiated externally at 25° for 1 h. The experiment with 90% v/v CH₂Cl₂ in the presence of piperylene (0.25M) was also performed as before.⁷ But, in this case, degassing by nitrogen was not performed.

Photochemical Decomposition of Ethyl Azidoformate in the Cyclohexane-CH₂Cl₂ System.—A fixed amount of solution which consisted of cyclohexane and ethyl azidoformate (23 : 1 molar ratio) was diluted with various amounts of

CH₂Cl₂ to give a total volume of 5 ml. It was treated as above and irradiated externally at 20° for 2 h. The consumed ethyl azidoformate (ca. 90%) was determined by means of i.r. bands at 2 185 and 2 137 cm⁻¹. The absolute yields of urethane (1) and ethyl carbamate were calculated on the basis of the azide consumed.

Thermal Decomposition of Ethyl Azidoformate in the THF-Cyclohexane-CH₂Cl₂ or -CH₃I System.—A fixed amount of solution which contained THF, cyclohexane, and ethyl azidoformate as mentioned before was diluted with a given amount of CH₂Cl₂ or CH₃I to make the total volume 10.0 ml. It was heated in a Pyrex sealed tube (24 cm × 3 cm) at 112° for 4 h. The mixture was analysed as described in the photochemical case.

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