Light-sensitive Amides. Photocleavage of *N*-Acyl-1,2,3,4-tetrahydro-8-nitroquinolines to give Free Carboxylic Acids

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The structural assignments of the 5- and 8-nitrotetrahydroquinolines have been reversed on the basis of their n.m.r. and mass spectra. U.v. irradiation cleaved the amide bonds of *N*-acyl-8-nitrotetrahydroquinolines to furnish free carboxylic acids in high yields, thus indicating the potential of 8-nitrotetrahydroquinolyl as a photosensitive protecting group for carboxylic acids. It has been shown that the release of the carboxylic acids involves a photocleavage and not a solvolysis. It has been experimentally demonstrated for the first time that oxygen transfer takes place from an excited nitro-group. This process precedes hydrogen abstraction and both processes are intramolecular.

PHOTOCLEAVAGE of derivatives of carboxylic acids to give the free acids has not been extensively reported. Irradiation of esters of carboxylic acids leads to complex mixtures, which in most cases contain only insignificant amounts of the free acids.[1] Consequently ester formation is in the main an inefficient means of providing a photosensitive protecting group for a carboxylic acid. Recently, however, several photosensitive protecting groups have been developed which can be removed from the corresponding esters by photolysis to furnish the free carboxylic acids in high yield, as a result of intramolecular reaction,[2] homolytic fission of a C–O bond,[3] or ionic cleavage.[4]

Of all the properties which efficient protecting groups should possess, two are apparently difficult to attain in the same group. Thus the bond between the protecting group and the protected function should be as stable as possible, but it should also undergo cleavage by a specific reaction under mild conditions. With respect to the first requirement, the amide group is superior to the ester function since it is much more resistant both to most chemical manipulations, as well as to the solvolytic conditions used to remove the most important protecting groups. This stability of the amide group, is, however, also its most serious shortcoming, since the vigorous solvolytic conditions demanded for its removal discourage its routine application as a protecting group. Its stability could, however, be used to advantage were a method for its specific and mild removal to be found. For this purpose we studied the development of amides susceptible to photocleavage.

Amides which undergo photocleavage to give free carboxylic acids in significant yields are almost unknown. Such a reaction has been observed in a single case only.[5] Aliphatic amides on irradiation undergo fragmentation to a mixture of carbon dioxide, hydrogen, amines, and saturated and unsaturated hydrocarbons, formed by homolytic fission of C–C, C–N, C–H, and N–H bonds.[6] The photochemistry of aromatic amides has been investigated in the anilide series in particular.[7] Anilides on u.v. irradiation undergo cleavage by a

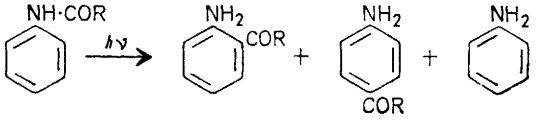

photo-Fries type of rearrangement,[7a,b] which has also been observed with other aromatic amides, such as *N*-acetyldiphenylamine,[8] *N*-acetylcarbazole,[8] and *N*-(3,4-methylenedioxybenzoyl)indoline.[9] *N*-Formyl has been suggested as a photosensitive protecting group for anilines, since on irradiation formanilides undergo quantitative decarbonylation.[10]

The mechanism of the photo-Fries rearrangement of anilides has been extensively investigated,[7] and it is now generally accepted that it involves homolytic fission of the amide bond to give an acyl and an anilino-radical which are trapped in a solvent cage, and which recombine before diffusion to yield rearrangement products. Formation of the free amine is visualized as escape of the anilino-radical from the solvent cage, followed by hydrogen abstraction. The fate of the acyl radical has hardly been studied. To a certain degree it probably undergoes decarbonylation [7b,d,11] and other secondary reactions.[11] In a few cases low yields of free carboxylic

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[7] (*a*) D. Belluš, *Adv. Photochem.*, 1971, **8**, 109; (*b*) V. I. Stenberg, in ' Organic Photochemistry,' ed. O. L. Chapman, Arnold, London, 1967, vol. 1, p. 127; (*c*) D. Elad, *Tetrahedron Letters*, 1963, 873; (*d*) D. Elad, D. V. Rao, and V. I. Stenberg, *J. Org. Chem.*, 1965, **30**, 3252; (*e*) H. Shizuka and I. Tanaka, *Bull. Chem. Soc. Japan*, 1968, **41**, 2343; (*f*) H. Shizuka, *ibid.*, 1969, **42**, 52; (*g*) H. Shizuka, *ibid.*, p. 57; (*h*) J. S. Bradshaw, R. D. Knudsen, and E. L. Loveridge, *J. Org. Chem.*, 1970, **35**, 1219.

[8] H. Shizuka, M. Kato, T. Ochiai, K. Matsui, and T. Morita, *Bull. Chem. Soc. Japan*, 1970, **43**, 67.

[9] H. Hara, O. Hoshino, and B. Umezawa, *Tetrahedron Letters*, 1972, 5031.

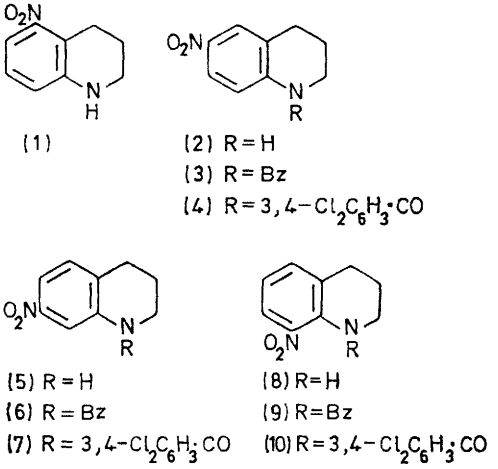
[10] B. K. Barnett and T. D. Roberts, *J.C.S. Chem. Comm.*, 1972, 758.

[11] M. G. Vinogradov and G. I. Nikishin, *Russ. Chem. Rev.*, 1971, **40**, 916.

acids have been obtained,[7b,d,9,12] but in no case has a convincing interpretation been advanced to explain their generation. The carboxylic acids formed cannot originate from the above-mentioned acyl radicals, because the latter have not been shown to abstract hydroxy-groups, but to undergo conversion into aldehydes in the presence of hydrogen donors.[13] Consequently direct photolytic cleavage of the amide bond in anilides cannot serve as a route to free carboxylic acids in high yield.

In contrast to the above, incorporation into the anilide system of an oxygen-containing substituent which absorbs light and which can, *via* electronic excitation, transfer oxygen to the acyl unit of the amide function, may lead to cleavage of the N–C bond to give a free acid. The nitro-function is just such a group. A nitro-group on a benzene ring does transfer oxygen [14] to the atom of an *ortho*-substituent directly bonded to the ring (α-atom).[2a,b,15] Oxygen transfer also takes place to the β-atom of the *ortho*-substituent.[16]

In order to check the feasibility of the above argument, we first studied the photolysis of *o*-nitroanilides: it turned out that they were photostable. However that *N*-alkyl- and *N*-aryl-*o*-nitroanilides were photolabile and afforded the free carboxylic acids.[17] This is apparently the first case of photocleavage of an amide bond to give a free carboxylic acid in high yield. In the above study we observed that hydrogen abstraction occurred exclusively from the carbon substituent on the amide nitrogen atom when hydrogen atoms were available on that carbon atom; when such hydrogen atoms were not available, photocleavage occurred only to a very minor extent unless a hydrogen-donor solvent was present. It was therefore of interest to inquire into the photolysis of *N*-substituted *o*-nitroanilides in which the hydrogen-donating carbon atom cannot approach the nitro-group by free rotation about the N–C amide bond. It was hoped that such a study would contribute to the understanding of the time sequence of hydrogen abstraction and oxygen transfer. In addition it was important to study the general scope of the photolysis by inclusion of cyclic systems, because of the novelty of the reaction and its potential applicability for protection of carboxylic acids. As a first in a series, we have irradiated *N*-acyl-1,2,3,4-tetrahydro-8-nitroquinolines (*N*-acylnitro-THQs). There has been confusion in the literature for a long time with respect to the correct structural assignments of 8-nitro-THQ (8) and its 5-nitro-isomer (1). Therefore their synthesis and identification, as well as their spectroscopic properties and those of the other two nitro-isomers, will be described in some detail.



A compound melting around 82° has been reported in three papers [18] to be 8-nitro-THQ (8). Since nitration of amino-substituted benzenes in strongly acid solution is *meta*-directed, whereas nitration of their *N*-acyl-derivatives is *ortho–para*-directed,[19] nitration of *N*-acetyl-THQ as carried out by Richardson and Amstutz [18b] appeared to be the most promising route to 8-nitro-THQ (8). However, on applying this procedure only the 6-nitro-isomer (2) was isolated, as also reported by other workers [20] who used the same method. Closer examination of the reaction mixture, however, showed that it consisted of two compounds, which after acidic hydrolysis were separated by recrystallisation and chromatography to afford the 6-nitro-isomer (2) in 80% yield, and a second nitro-THQ, m.p. 71°, in 16% yield. The latter nitro-THQ, together with the isomer (2), was also obtained by Utley and Vaughan [18c] on nitrating *N*-acetyl-THQ in concentrated sulphuric acid; they assigned to it the 5-nitro-structure (1). These authors have also nitrated THQ in strongly acid solution and isolated the 7-nitro-isomer (5) as well as a second nitro-isomer, m.p. 81—82°, to which they assigned the 8-nitro-structure (8). In our hands the nitration of THQ in concentrated sulphuric acid also yielded the 7-nitro-isomer (5) in 51% yield, as well as the isomer melting at 83° in 7.5% yield. We shall show that the

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[13] U. Schmidt, *Angew. Chem. Internat. Edn.*, 1965, **4**, 146; H. G. Kuivila and E. J. Walsh, jun., *J. Amer. Chem. Soc.*, 1966, **88**, 571; D. L. Bunbury and C. T. Wang, *Canad. J. Chem.*, 1968, **46**, 1473.

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[16] (*a*) D. Döpp, *Chem. Comm.*, 1968, 1284; (*b*) J. Bakke, *Acta Chem. Scand.*, 1970, **24**, 2650; (*c*) Y. Kitaura and T. Matsuura, *Tetrahedron*, 1971, **27**, 1583; (*d*) D. Döpp, *Chem. Ber.*, 1971, **104**, 1035, 1043, 1058; (*e*) D. Döpp and K.-H. Sailer, *Tetrahedron Letters*, 1971, 2761; (*f*) L. R. C. Barclay and I. T. McMaster, *Canad. J. Chem.*, 1971, **49**, 676; (*g*) R. E. McMahon, *Tetrahedron Letters*, 1966, 2307; (*h*) D. J. Neadle and R. J. Politt, *J. Chem. Soc.* (*C*), 1969, 2127.

[17] B. Amit and A. Patchornik, *Tetrahedron Letters*, 1973, 2205.

[18] (*a*) R. Stoermer, *Ber.*, 1898, **31**, 2523; (*b*) A. Richardson, jun., and E. D. Amstutz, *J. Org. Chem.*, 1960, **25**, 1138; (*c*) J. H. P. Utley and T. A. Vaughan, *J.C.S. Perkin II*, 1972, 2343.

[19] P. B. D. de la Mare, in ' Rodd's Chemistry of Carbon Compounds,' ed. S. Coffey, 2nd edn., Elsevier, Amsterdam, 1971, vol. 111A, p. 45.

[20] A. L. Mndzhoyan and A. S. Azaryan, *Sintezy geterotsikl. Soedinenii, Akad. Nauk Armyan. S.S.R., Inst. Tonkoi org. Khim.*, 1964, No. 6, 55 (*Chem. Abs.*, 1967, **66**, 55,361).

structural assignments of the 5- and 8-nitro-THQs have to be reversed, *i.e.* the 5- and 8-nitro-structures should be assigned to the compounds melting around 82 and 70°, respectively.

The ^1H n.m.r. data of the four nitro-THQs are presented in Tables 1 and 2. The methylene signals were treated by first-order analysis. In the case of the aromatic protons, the 8-nitro-isomer (8) was analysed as an AMX system, whereas the signals of the three other isomers were regarded as ABX spin patterns, with the X proton treated as a first-order multiplet.

TABLE 1

^1H N.m.r. chemical shifts (δ values) of nitrotetrahydroquinolines [a]

Compound	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8
(1)	3.98br,s [b,c]	3.35t [e]	1.93qn	2.96t		6.92—7.26 [d,e]		6.67dd
(2)	4.85br,s [b]	3.27—3.60 [f]	1.95qn	2.82t	H-5 and H-7: 7.80—8.00 [g]			6.42d [h]
(5)	4.16br,s [b,i]	3.37t [i]	1.95qn	2.82t	7.03dd	H-6 and H-8: 7.25—7.50 [j]		
(8)	8.42br,s [k]	3.52sx [k]	1.92qn	2.83t	7.12dd [l]	6.47dd	7.95dd [l]	

TABLE 2

Coupling constants (Hz) of nitrotetrahydroquinolines

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{5,6}$	$J_{5,7}$	$J_{5,8}$	$J_{6,7}$	$J_{6,8}$	$J_{7,8}$
(1)	2.6 [e]	5.2	6.3				8.0 [e]	1.3 [e]	7.1
(2)	2.0 [m]	5.7 [f]	6.4						9.6
(5)	2.2 [i]	5.6	6.5	7.6 [j]		1.0		2.3 [j]	
(8)	2.9 [n]	5.6 [k]	6.0	7.1	1.2		8.6		

[a] Measured on a Bruker HFX-10 spectrometer, operating at 90 MHz, in $CDCl_3$, relative to Me_4Si as internal standard; qn = quintet, sx = sextet. [b] On addition of D_2O the signal disappeared at once. [c] In [$^2H_5$]pyridine, δ(H-1) 6.61br,s, and δ(H-2) 3.17sx, $J_{1,2}$ 2.6 Hz; irradiation at H-3 caused collapse of the H-2 sextet to a doublet with $J_{1,2}$ 2.6 Hz. [d] Complex multiplet. [e] With $Eu(fod)_3$ in CCl_4 solution and already at a molar ratio [$Eu(fod)_3$] : [(1)] = 0.07 : 1 these signals were shifted downfield and exhibited a first order pattern: δ(H-6) 7.17dd, δ(H-7) 6.99t, $J_{6,7}$ 8.0 Hz, $J_{6,8}$ 1.3 Hz; extrapolation to zero concentration of shift reagent yielded δ(H-6) 7.08 and δ(H-7) 6.92; *cf.* B. C. Mayo, *Chem. Soc. Rev.*, 1973, **2**, 49. [f] Unresolved m; on addition of D_2O collapsed to a triplet at δ 3.40, $J_{2,3}$ 5.7 Hz. [g] Unresolved m; with $Eu(fod)_3$ in $CDCl_3$ solution all three aromatic proton signals were shifted downfield but those of H-5 and H-7 could not be resolved even at a molar ratio [$Eu(fod)_3$] : [(2)] = 1.37 : 1. [h] *Cf.* A. M. Monro and M. J. Sewell, *J. Chem. Soc.* (*B*), 1971, 1227. [i] In [$^2H_5$]pyridine, δ(H-1) 6.61br,s, and δ(H-2) 3.28sx, $J_{1,2}$ 2.2 Hz; irradiation at H-3 caused collapse of the H-2 sextet to a doublet with $J_{1,2}$ 2.2 Hz. [j] Complex m; with $Eu(fod)_3$ in CCl_4 solution and at a molar ratio [$Eu(fod)_3$] : [(5)] = 0.44 : 1 these protons yielded a first-order pattern: δ(H-6) 7.74dd, δ(H-8) 7.84d, $J_{5,6}$ 7.6 Hz, $J_{6,8}$ 2.3 Hz. [k] On addition of D_2O the H-1 signal disappeared only after about 3 h; this disappearance was accompanied by the collapse of the H-2 sextet to a triplet at δ 3.53, $J_{2,3}$ 5.6 Hz; irradiation at H-1 also caused collapse of the H-2 sextet to a triplet. [l] In CCl_4 solution *G*(LSR) for H-5 is 1.0 and for H-7 3.6; for definition of *G*(LSR) see A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, 1973, **73**, 553. [m] On irradiation at H-3, the H-2 multiplet collapsed to a doublet with $J_{1,2}$ 2.0 Hz. [n] Irradiation at H-3 casued collapse of the H-2 signal to a doublet with $J_{1,2}$ 2.9 Hz.

The ^1H n.m.r. spectral behaviour of the isomers (1) and (5) resembles that of *N*-methyl-*m*-nitroaniline, whereas that of the isomers (2) and (8) resembles that of *N*-methyl-*p*- and -*o*-nitroaniline, respectively.[21] Thus in $CDCl_3$ solution H-2 of isomers (2) and (8) is coupled to H-1, whereas in isomers (1) and (5) no such coupling is observed. This lack of coupling is due to rapid proton exchange which is a result of greater basicity.[21] The isomers (1) and (5) do however display this coupling in [$^2H_5$]pyridine solution, as is also the case with *N*-methyl-*m*-nitroaniline.[21]

Only in one of the four nitro-THQs [8-nitro-THQ (8)] is intramolecular hydrogen bonding between the amino-group and nitro-group possible.[21] In fact, exchange of H-1 by D_2O is slow in (8), but instantaneous in the other three isomers. The hydrogen bonding is further evidenced by the low-field shift of H-1 of (8) as compared with the other isomers. Finally, H-1 chemical shifts of the *N*-methylnitroanilines and the corresponding nitro-THQs in $CDCl_3$ solution are very close, and therefore in agreement with our structural assignments (Table 3).

Final confirmation of the structural assignments of (1) and (8) is based on calculation of the chemical shifts of the aromatic protons of the four isomers from substituent contributions.[22] Generally the method works well for *para*-substituted benzenes, reasonably well for *meta*-substituted benzenes, and least for *ortho*-substituted benzenes.[22b] The Figure, however, indicates that for the four nitro-THQs, the trend of calculated values is reflected in the observed values.[23]

TABLE 3

^1H N.m.r. chemical shifts (δ values) of NH protons

$O_2N{\cdot}C_6H_4{\cdot}NHMe$ [21]	O_2N-THQ [a]
meta 4.13	(1) 3.98
	(5) 4.16
para 4.62	(2) 4.85
ortho 8.00	(8) 8.42

[a] Chemical shifts from Table 1.

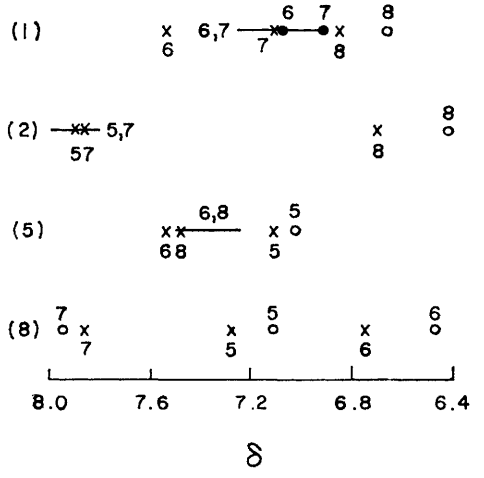
Use of $Eu(fod)_3$ simplified complex aromatic multiplets in the spectra of (1) and (5) (Tables 1 and 2), and made possible first-order treatment of their aromatic proton spectra. Whereas $Eu(fod)_3$ differentially shifted the aromatic protons of (1), (5), and (8), it failed to do so in the case of H-5 and H-7 of (2). In this molecule the co-ordination bond between the Eu atom and the lone-pair *p* orbital of the amino-nitrogen atom is taken

[21] I. D. Rae, *Austral. J. Chem.*, 1966, **19**, 409.

[22] (*a*) L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969, pp. 201—204; (*b*) M. Zanger, *Org. Magnetic Resonance*, 1972, **4**, 1; (*c*) D. A. Ben-Efraim, and B. S. Green, *Tetrahedron*, 1974, **30**, 2357.

[23] *Cf.* values for nitrotoluidines in J.-P. Morizur and R. Petit, *Bull. Soc. chim. France*, 1965, 346.

to be normal to the average plane of the molecule and also lying in a plane which is perpendicular to the aromatic ring and passing through N(1)–C(9)–C(6)–N(O_2). With respect to this plane, H-5 and H-7 are symmetrically located and therefore their distances from the paramagnetic ion as well as the angles N(1)–Eu–H(5) and N(1)–Eu–H(7) will be equal, resulting in equal pseudocontact shifts. Contact shifts also will be almost equal at the two protons because all the bonds leading from Eu to them are symmetrically disposed with respect to the amino-group and the nitro-group (ignoring methylene groups), thus yielding equal overall shifts. By contrast, in (8) we have found the shift gradients of H-5 and H-7 to differ, in spite of equal distances and



Calculated and observed chemical shifts of aromatic protons of nitro-THQs. Observed values (○); extrapolated values from lanthanide induced shifts (●); calculated values (×); width of unresolved multiplets (—); numerals refer to aromatic protons *

* Substituent contributions are from ref. 22*a* and observed and extrapolated values are from Table 1 and its footnotes. The contributions of $NHCH_2$ are taken as the mean of the contributions of NH_2 and NMe_2; for the C-4 contribution the value of Et is used.

angles as in (2). Here however the bonds leading from Eu to these protons are not symmetrically disposed with respect to the amino-group and the nitro-group, thus leading to different contact contributions and to overall different shifts.

N-Alkylnitroanilines show J_{HNCH} values in the range 5—6 Hz,[21,24] indicating that these observed coupling constants are average values of three possible low-energy conformations, resulting from free rotation about the N–C bond. On the other hand, the nitro-THQs discussed here have small coupling constants (*ca.* 2—3 Hz), and thus join the groups of cyclic compounds, such as cyclic dipeptides,[25a] dihydrouracils,[25b] dihydrothymines,[25b,c] and dioxopiperazines,[25c] in which the N–H bond is largely, if not wholly, equatorially oriented, as may be calculated from theoretical J_{HNCH}–dihedral angle relationships.[25a,26] This finding is also in accord with our results with lanthanide-induced shifts, discussed above, where the Eu–N bond was assumed to be normal to the plane of the ring. Recently Katritzky and his co-workers have also reached the conclusion, by another method, that in piperidines the N–H bond prefers the equatorial position.[27]

The mass spectra of compounds (1) and (8) display peaks which support their structures (Table 4). Thus the $M^+ - OH$ peak in the spectrum of (1) is strong whereas that in the spectrum of (8) is very weak; this behaviour parallels that of *o*-nitrotoluene and *o*-nitroaniline, respectively.[28] To corroborate this observation, the two nitro-THQs were deuteriated within the inlet system of the mass spectrometer [29] and their spectra recorded (Table 4). In the deuteriated mixture from (1) the *m/e* 162 peak [$M(C_9H_9DN_2O_2)^+ - OH$] becomes strong, whereas in the deuteriated mixture from (8) the *m/e* 161 and 162 peaks are almost unchanged in intensity. Thus in the case of (1) both the labelled and unlabelled molecules eliminate OH, whereas in that of (8) the unlabelled molecule eliminates OH, and the labelled one eliminates OD, as expected, since labelling occurs at the amino-nitrogen atom only.[29] Of the four nitro-THQs only (1) is photolabile, since it is the only isomer which has benzylic hydrogen atoms available *ortho* to the nitro-group.[14]

Conversion of the weakly nucleophilic (8) into its *N*-acyl derivatives required more vigorous conditions than the acylation of (2) and (5). The *N*-acyl derivatives of the latter two nitro-THQs were found to be photostable in methanolic or ethanolic solution and were unchanged even after long irradiation times (Table 5). None of the expected photoreactions, *i.e.* photo-Fries rearrangement, or abstraction of hydrogen by the nitro-group from the donor solvent, took place. Apparently the nitro-group is responsible for the deactivation of the photo-Fries rearrangement, as is also observed with other nitro-aromatic compounds.[7g,30]

In contrast to the above *N*-acyl derivatives of (2) and (5), the *N*-acyl derivatives of (8) proved extremely light-sensitive. Irradiation in either polar or non-polar solvents led to their disappearance within 2 h and to the liberation of the free carboxylic acids in high yields (Table 5). The fact that irradiation in alcohols afforded the free acids and not their esters indicates that the photocleavage is not a solvolysis. Further evidence

[24] B. Lamm and K. Nordfält, *Acta Chem. Scand.*, 1966, **20**, 1208; K. P. Shrestha and K. L. Henold, *J. Amer. Chem. Soc.*, 1973, **95**, 6699.

[25] (*a*) K. D. Kopple and M. Ohnishi, *J. Amer. Chem. Soc.*, 1969, **91**, 962; (*b*) P. Rouillier, J. Delmau, and C. Nofre, *Bull. Soc. chim. France*, 1966, 3515; (*c*) G. N. Ramachandran, R. Chandrasekaran, and K. D. Kopple, *Biopolymers*, 1971, **10**, 2113.

[26] M. Barfield and M. Karplus, *J. Amer. Chem. Soc.*, 1969, **91**, 1.

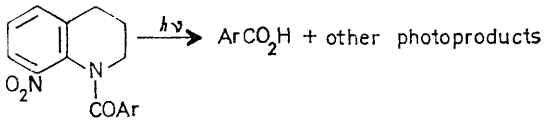
[27] R. A. Y. Jones, A. R. Katritzky, A. C. Richards, R. J. Wyatt, R. J. Bishop, and L. E. Sutton, *J. Chem. Soc.* (*B*), 1970, 127.

[28] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967, pp. 326—327 and 515—521.

[29] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Structure Elucidation of Natural Products by Mass Spectrometry,' Holden-Day, San Francisco, 1964, vol. I: Alkaloids, pp. 17—18.

[30] J. Hill, *Chem. Comm.*, 1966, 260; O. Hoshino, S. Sawaki, N. Miyazaki, and B. Umezawa, *ibid.*, 1971, 1572.

comes from irradiation of (10) in dioxan–$H_2{}^{18}O$. Treatment of the irradiation mixture with diazomethane gave the corresponding methyl 3,4-dichlorobenzoate,



which contained no ^{18}O (as verified from its mass spectrum). This result shows that the second oxygen atom of the formed acid is derived from the nitro-group. oxygen transfer is intramolecular.[31] The main argument in favour of this stemmed from earlier observations that oxygen transfer occurred only with compounds in which the nitro-group was *ortho* but not *meta* or *para* to the substituent in question. Thus photochemical rearrangement of *o*-nitrobenzaldehyde to *o*-nitrosobenzoic acid has been cited as involving intramolecular oxygen transfer.[31] Recently however it was shown that *p*-nitrobenzaldehyde yielded on irradiation *p*-nitrosobenzoic acid in high yield.[32] An unequivocal proof is thus needed to ascertain whether oxygen transfer in

TABLE 4

Mass spectra of nitro-THQs [a]

		(1)						(8)					
	m/e	161	162	177	178	179	180	161	162	177	178	179	180
		Relative intensities (%)											
Unlabelled	70 eV	57	9	4	100	15		6.4	2.5	50	100	14	
Labelled [b]	15 eV			0	100	133	13			0	100	78	8
Labelled [b]	70 eV	50	72	2	100	128		7.2	2.5	41	100	51	

[a] Recorded on an Atlas CH-4 spectrometer. [b] To obtain the isotopic composition of each isomer, spectra were also recorded at 15 eV in order to eliminate $M^+ - 1$ peaks; the isotopic compositions (including corrections for natural isotopic abundances) were for (1) 55% $^2H_1$, 45% $^2H_0$, and for (8) 40% $^2H_1$, 60% $^2H_0$.

TABLE 5

Irradiation of *N*-acylnitro-THQs [a]

Acid formed	Solvent	% Yield [b] (2) [c]	(5) [c]	(8)	Dehydrogenation products from solvent on irradiation of (8)
$PhCO_2H$	MeOH or EtOH	0	0	91	From EtOH: *ca.* 1% MeCHO; no AcOH formed [d]
$PhCO_2H$	Pr^iOH			85	*ca.* 7% Me_2CO [d]
$PhCO_2H$	PhH			80	
3,4-$Cl_2C_6H_3$·CO_2H	MeOH or EtOH	0	0	95	
3,4-$Cl_2C_6H_3$·CO_2H	PhH			80	

[a] Irradiation of solutions of the substrates (10^{-2}M; 20 ml) was conducted for 5 h in a Rayonet photochemical reactor with 3 500 Å lamps ($\lambda > 305$ nm) in Pyrex tubes. [b] % Yields of acids formed on irradiation of the corresponding *N*-acylnitro-THQs. Acids were converted into methyl esters by addition of an excess of diazomethane to the irradiation mixture, and the excess of reagent was decomposed with acetic acid. The mixtures were analysed by g.l.c. on a Packard gas chromatograph model 7421 (5% SE-30 column, $\frac{1}{4}$ in × 6 ft); the esters were identified by comparison of retention times with those of authentic samples, and their yields were determined by area comparison (by weighing) with traces from samples of known concentrations. [c] Irradiation time 15 h. [d] Mole % yield of dehydrogenated solvent per mole of (8). Acetaldehyde and acetic acid were analysed as described in footnote *b* on a Hewlett-Packard gas chromatograph model 5720 (Porapak Q column, $\frac{1}{8}$ in × 2 ft); acetone was analysed similarly on a Perkin-Elmer gas chromatograph model 800 (20% Carbowax column, $\frac{1}{8}$ in × 6 ft).

Direct evidence for oxygen transfer from the nitro-group to the *N*-acyl group has been obtained by performing the irradiation of (9) labelled with ^{18}O in the nitro-group. It was prepared in the usual fashion, but with ^{18}O-enriched nitric acid (see Experimental section). It was irradiated in ethanolic solution until its complete disappearance and the benzoic acid formed was analysed as its methyl ester; the isotopic composition clearly established that precisely one oxygen atom was transferred from the nitro-group to the benzoyl unit (see Experimental section). Oxygen transfer from the nitro-group has been invoked as a major step in the mechanisms of photoreactions of nitro-aromatic compounds.[14] The evidence presented here is apparently the first direct verification that such an oxygen transfer from a nitro-group does take place.

Another assumption which has been made is that *ortho*-substituted nitro-compounds is intramolecular or intermolecular. Irradiation of mixtures of ^{18}O-labelled (9) and unlabelled (10) (1 : 1 or 1 : 5) afforded mixtures of the corresponding acids, which were isolated as methyl esters by preparative g.l.c. Mass spectrometry showed that the methyl 3,4-dichlorobenzoate was unlabelled with ^{18}O, whereas the labelling in the methyl benzoate was as expected. Thus in our type of compound, oxygen transfer is experimentally shown to be intramolecular.

In addition to the above finding that oxygen is transferred intramolecularly from the nitro-group to the acyl unit, our experiments excluded the possibility of a solvolysis or hydrolysis, and thus pointed to a non-ionic mechanism. A further step in the elucidation of the mechanism of the photocleavage is the conclusion that the carboxylic hydrogen atom originates from the substrate itself. This is derived from the observation

[31] P. de Mayo, *Adv. Org. Chem.*, eds. R. A. Raphael, E. C. Taylor, and H. Wynberg, Interscience, New York, 1960, vol. II, pp. 412–414.

[32] G. W. Wubbels, R. R. Hautala, and R. L. Letsinger, *Tetrahedron Letters*, 1970, 1689.

that no dehydrogenation of hydrogen-donor solvents occurs during photolysis, nor does the photoreaction fail to take place in a poor hydrogen-donor solvent, namely benzene (Table 5). Since in the *N*-acyl-*o*-nitro-THQs the hydrogen-bearing C-2 cannot come close to the nitro-group by free rotation about the N–C amide bond, this means that oxygen transfer from the nitro-group to the acyl unit precedes hydrogen abstraction. This is at odds with postulated mechanisms of photoreactions of nitrobenzenes, according to which the electronically excited nitro-group first abstracts hydrogen from the solvent or intramolecularly from the substrate to give a free-radical intermediate which subsequently transfers a hydroxy-group to the site of attack.[14,16f,31,33] By contrast, the above observation is in line with a mechanism proposed for the photolysis of *N*-acyl-2-nitrodiphenylamines,[34] in which it is postulated that oxygen transfer precedes hydrogen abstraction as the reaction proceeds *via* addition of the excited nitro-group to the carbonyl group of the acyl moiety to give an intermediate which collapses with formation of a nitroso-radical and loss of an acyloxyl radical; the latter can then abstract hydrogen either from the nitroso-radical or from the solvent. In our case the acyloxyl radical apparently abstracts a hydrogen from C-2 before escaping from the solvent cage. In this context it is interesting that the photocleavage of 2,4-dinitrosulphenyl esters to free carboxylic acids proceeds by an ionic mechanism,[4] whereas the photocleavage of phenacyl esters involves a free-radical mechanism.[3]

As the *N*-acyl-*o*-nitro-THQs are stable under hydrolytic and solvolytic conditions, attention in this paper has been mainly directed to the fate of the acyl unit, since its mild photochemical release as a free carboxylic acid is of great significance in the protection of the latter. The photoproducts resulting from the nitro-THQ unit, as well as the photophysical processes and mechanism involved, are under investigation.

EXPERIMENTAL

M.p.s were determined with a Fisher-Johns apparatus. T.l.c. was performed on TLC cards Al F coated with alumina and fluorescent indicator (Riedel-de Haen AG, Seelze-Hannover), developed with benzene, and observed visually or by u.v. fluorescence. For column chromatography neutral alumina Woelm was used. Light petroleum refers to the fraction with b.p. 40—60 °C.

5-Nitro- (1) *and 7-Nitro-THQ* (5).—Tetrahydroquinoline (6 g) was dissolved below 20 °C in concentrated sulphuric acid (30 ml). The solution was cooled to 0 °C and concentrated nitric acid (*d* 1.5; 2.2 ml) was added dropwise between 0 and 5 °C. The mixture was stirred for 3 h, poured into ice–water (500 ml), made basic with solid sodium hydrogen carbonate, and extracted with ether (4 × 100 ml). The extracts were washed with aqueous 10% sodium hydrogen carbonate, water, N-hydrochloric acid, and water, dried (Na_2SO_4), and evaporated to furnish a red oil (6 g), which t.l.c. showed to be a mixture of the two isomers. The oil was chromatographed on an alumina dry column [35] (activity III; 400 g; 3.5 cm × 50 cm) and eluted with light petroleum–methylene chloride (2 : 1). A yellow band was first eluted and yielded a mixture of (1) and (5) (1.6 g). A second, orange band eluted with the same solvent furnished pure 7-nitro-THQ (5) (3.4 g), as orange prisms, m.p. 63—65° (lit.,[36] 62—63°). The first fraction (1.6 g) was rechromatographed on a column of the same type as above and eluted with the same solvent mixture. The first yellow band afforded *5-nitro-THQ* (1) (0.6 g, 7.5%) as orange crystals, m.p. 80—82°; 83° (from light petroleum) [lit.,[18b] 82—84°, but referred to there as 8-nitro-THQ (8)] (Found: C, 60.5; H, 5.9; N, 15.55. $C_9H_{10}N_2O_2$ requires C, 60.65; H, 5.65; N, 15.7%). Elution of the orange band furnished additional (5) (0.7 g; total 4.1 g, 51%).

6-Nitro- (2) *and 8-Nitro-THQ* (8).—A mixture of 70% nitric acid (4.6 g) and acetic anhydride (13 ml), cooled to 0 °C, was added dropwise to a solution of *N*-acetyl-THQ (8.6 g) in acetic anhydride (13 ml) between −10 and −5 °C. The mixture was stirred at 0 °C for 1 h and at room temperature for 10 h. It was then diluted with water (200 ml) and extracted with ether (2 × 100 ml). The extracts were washed with dilute aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated, and the residue was hydrolysed by refluxing for 4 h with concentrated hydrochloric acid (17 ml), water (13 ml), and ethanol (27 ml). After dilution of the mixture with water, a red solid precipitated and was collected. T.l.c. showed that it consisted of a mixture of (2) and (8). It was fractionally crystallised from 60% aqueous acetic acid to furnish crude 6-nitro-THQ (2) (7 g, 80%), which on recrystallisation from the same solvent yielded yellow crystals, m.p. 161—162° (lit.,[20] 161—162°). The filtrate from the original fractional crystallisation was evaporated *in vacuo* and then dissolved in benzene and chromatographed on alumina (activity I; 250 g) and eluted with benzene. The first eluted red fraction was recrystallised from hexane to furnish *8-nitro-THQ* (8) (1.4 g, 16%), as red crystals, m.p. 71° [lit.,[18c] 70—73°, but referred to there as 5-nitro-THQ (1)]; mixed m.p. with (1) 43—46° (Found: C, 60.45; H, 5.9; N, 15.5%).

N-Acylnitro-THQs.—The *N*-acyl derivatives of (2) and (5) were prepared by heating a mixture of the appropriate nitro-THQ (0.5 g) and an excess of acyl chloride in pyridine (5 ml) on a water-bath for 0.5 h. Dilution with water (50 ml) and collection of the precipitate afforded the *N*-acyl derivative, which was crystallised from ethanol: *N*-benzoyl-6-nitro-THQ (3) (70%), m.p. 135° (lit.,[36] 134—135°); N-3,4-*dichlorobenzoyl*-6-*nitro-THQ* (4) (70%), m.p. 172° (Found: C, 54.9; H, 3.3; Cl, 20.1; N, 7.95. $C_{16}H_{12}Cl_2N_2O_3$ requires C, 54.7; H, 3.45; Cl, 20.2; N, 8.0%); *N*-benzoyl-7-nitro-THQ (6) (80%), m.p. 154° (lit.,[36] 153—154°); N-3,4-*dichlorobenzoyl*-7-*nitro-THQ* (7) (80%), m.p. 161° (Found: C, 54.95; H, 3.55; Cl, 20.05; N, 8.15%).

The *N*-acyl derivatives of (8) were obtained by refluxing a mixture of the nitro-THQ (0.2 g) with an excess of acyl chloride in xylene (20 ml) for 15 h, evaporating the solution *in vacuo*, and adding ether, which caused solidification of

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[34] Y. Maki, M. Suzuki, T. Hosokami, and T. Furuta, *J.C.S. Perkin I*, 1974, 1354.
[35] B. Loev and M. M. Goodman, *Intra-Sci. Chem. Reports*, 1970, **4**, 283.
[36] M. Kulka and R. H. F. Manske, *Canad. J. Chem.*, 1952, **30**, 720.

the residue: N-*benzoyl*-8-*nitro-THQ* (9) (50%), m.p. 127° (from MeOH–H_2O, 1 : 1) (Found: C, 68.25; H, 5.0; N, 9.85. $C_{16}H_{14}N_2O_3$ requires C, 68.1; H, 5.0; N, 9.9%); N-3,4-*dichlorobenzoyl-THQ* (10) (50%), m.p. 165° (sinters at 160°) (from MeOH) (Found: C, 54.6; H, 3.6; Cl, 20.25; N, 8.0. $C_{16}H_{12}Cl_2N_2O_3$ requires C, 54.7; H, 3.45; Cl, 20.2; N, 8.0%).

8-[^{18}O]*Nitro-THQ* [*as* (8)].—A mixture of concentrated nitric acid (*d* 1.5; 4.5 ml) and [^{18}O]water (98 atom % ^{18}O; 20 ml) was kept sealed for 5 days. The mixture was concentrated by slow distillation in a Vigreux column at atmospheric pressure up to b.p. 118°. The remaining [^{18}O]nitric acid (3.6 ml) (*d* 1.42) had an ^{18}O content of *ca.* 70 atom %. It was used in the preparation of the [^{18}O]-(8) by the procedure used in the synthesis of the unlabelled (8). The isotopic composition of the [^{18}O]-(8), obtained from its mass spectrum, was $^{18}O_2$ 8.3%, $^{18}O_1$ 37.0%, $^{18}O_0$ 54.7% (corrected for natural isotopic abundance).

N-*Benzoyl*-8-[^{18}O]*nitro-THQ* [*as* (9)].—The [^{18}O]-(8) (0.3 g) and benzoyl chloride (1 g) in xylene (40 ml) were refluxed for 20 h. The solvent was evaporated off *in vacuo* to give a dark oil, from which the excess of reactants was removed by trituration with boiling hexane (3 × 50 ml). The residue on preparative layer chromatography (silica gel F_{254}; benzene) afforded N-*benzoyl*-8-[^{18}O]*nitro-THQ* (0.28 g, 45%), m.p. 127°. Its isotopic composition, obtained from the mass spectrum, was $^{18}O_2$ 8.2%, $^{18}O_1$ 36.7%, $^{18}O_0$ 55.1%. The small difference in the isotopic compositions of labelled (8) and (9) can be attributed to experimental errors.

Irradiation of N-*Benzoyl*-8-[^{18}O]*nitro-THQ* [*as* (9)].—The labelled (9) was irradiated in ethanolic solution under the usual conditions (see Table 5) until its complete disappearance. The benzoic acid formed was esterified with diazomethane and the methyl benzoate obtained was analysed on a Finnigan g.l.c.–mass spectrometer model 1015 (5% SE-30 column). The isotopic composition of the methyl benzoate was $^{18}O_1$ 25.0%, $^{18}O_0$ 75.0%. The $^{18}O_1$ value of 25.0% is in agreement with the value calculated from the starting labelled (9): (36.7/2 + 8.2)% = 26.6%.

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