# Photochemistry and Photocyclization of Aryl Halides

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## 1 Introduction

The vast range of photochemical reactions that haloarenes undergo with other species can broadly be divided into a few classes. Photochemically induced homolysis reactions of the carbon–halogen bond have been known since around 1960, and bond reactivity follows the order expected from carbon–halogen bond energy considerations. Iodobenzene[1] was investigated first, and then later bromobenzene[2] was shown to undergo equivalent reactions, and chlorobenzene to react with a low quantum yield. Thus, whereas iodo- and bromo-arenes have received attention as potential sources of aryl radicals, chloro-compounds have received little attention. Here we consider the broad range of photohomolysis reactions, some of which are of value in synthesis, while others are important as possible routes by which polutant chloro- and bromo-arenes can be degraded[3] under environmental conditions. Inevitably, to give a coherent account of photochemistry and photocyclization, the discussion must include reactions which cover a broader range of mechanisms than simple homolysis.

Fluoroarenes undergo a variety of photoinduced electrocyclic reactions where the carbon–fluorene bond remains intact.[4] Such reactions are not relevant to this review.

Nucleophilic photosubstitution reactions occur on haloarenes; some activating substituent such as nitro is usually necessary. A variety of nucleophiles including alkoxy, hydroxy, amino, and thiocyanate can be used and fluoride or chloride are the most satisfactory leaving groups, although other leaving groups as well as halides are possible. Such reactions have been known since around 1956. The bromo- and iodo-arenes show competition between nucleophilic substitution and

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[1] J. McD. Blair, D. Bryce-Smith, and B. W. Pengilly, *J. Chem. Soc.*, 1959, 3174; J. McD. Blair and D. Bryce-Smith, *J. Chem. Soc.*, 1965, 1788; W. Wolf and N. Kharasch, *J. Org. Chem.*, 1961, **26**, 283; *ibid.*, 1960, **30**, 2493.

[2] T. Matsuura and K. Omura, *Bull. Chem. Soc. Jpn.*, 1966, 39, 944; G. R. Lappin and J. S. Zanucci, *Tetrahedron Lett.*, 1969, 5085.

[3] N. J. Bunce, Y. Kumar, and B. G. Brownlee, *Chemosphere*, 1978, 7, 155.

[4] R. D. Chambers, J. R. Maslakiewicz, and K. C. Srivastava, *J. Chem. Soc., Perkin Trans.* 1, 1975, 1130; M. G. Barlow, D. E. Brown, and R. N. Haszeldine, *ibid.*, 1978, 363; B. Sket and M. Zupan, *J. Am. Chem. Soc.*, 1977, 99, 3504; J. Libman, Z. Ludner, B. Louris, and V. Yakhot, *J. Chem. Res.* (*S*), 1978, 472; (*M*), 1978, 5557.

bond homolysis. Nucleophilic photosubstitution reactions have received adequate discussion elsewhere[5] and have largely been excluded from this review.

A class of reactions that proceed according to the example in Scheme 1 was discovered in 1970. The reaction is initiated by photochemically induced electron-transfer to give the substrate radical-anion in catalytic amounts. The reaction can also be promoted electrochemically. These radical-anion substitution reactions have been reviewed by Bunnett.[6]

$$\mathrm{PhBr} + \text{electron source} \xrightarrow[\text{liq. NH}_3]{h\nu} [\mathrm{PhBr}]^{\cdot -} + \text{residue}$$

$$[\mathrm{PhBr}]^{\cdot -} \longrightarrow \mathrm{Ph}^{\cdot} + \mathrm{Br}^{-}$$

$$\mathrm{Ph}^{\cdot} + \mathrm{MeCO\bar{C}H_2} \longrightarrow [\mathrm{PhCH_2COMe}]^{\cdot -}$$

$$[\mathrm{PhCH_2COMe}]^{\cdot -} + \mathrm{PhBr} \longrightarrow \mathrm{PhCH_2COMe} + [\mathrm{PhBr}]^{\cdot -}$$

Overall:

$$\mathrm{PhBr} + \mathrm{MeCO\bar{C}H_2} \xrightarrow[\text{liq. NH}_3]{h\nu} \mathrm{PhCH_2COMe} + \mathrm{Br}^{-}$$

**Scheme 1**

Bryce-Smith and his colleagues showed that the photolysis of iodobenzene gives rise to phenyl radicals as reactive intermediates by comparing the relative yields of products from reaction in isopropylbenzene and in neat iodobenzene with the relative yields from decomposition of dibenzoyl peroxide, a known phenyl radical source, in these solvents.[1] Kharasch and his school showed that a reaction of preparative value results when conditions are arranged under which aryl radicals, generated by photohomolysis from an iodoarene, can interact with a second arene ring. The photolysis of iodobenzene in benzene solution to yield diphenyl is one example of a general intermolecular reaction.[1] The equivalent intramolecular process has been used to effect a large number of ring-closure reactions, in yields which vary from small to acceptable, and constitutes an important step in the synthesis of many alkaloids. A selection of syntheses is given in Scheme 2 to serve as an introduction to the mechanistic discussion in the following section. Aryl radicals intermediate in some of these reactions can be formed by other routes, for example by reductive decomposition of diazonium salts in the Pschorr reaction, and the relative merits of the various related processes have been discussed recently.[7]

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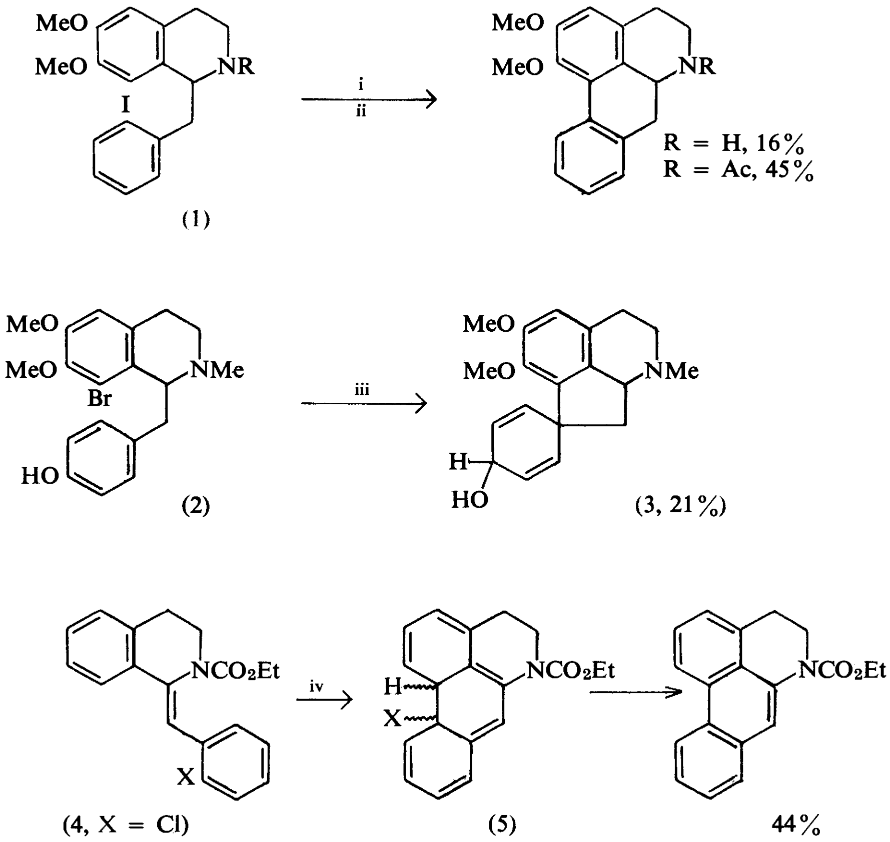
[5] J. Cornelisse, G. P. de Gunst, and E. Havinga, *Adv. Phys. Org. Chem.*, 1975, **11**, 225; J. Cornelisse and E. Havinga, *Chem. Rev.*, 1975, **75**, 353; E. Havinga and J. Cornelisse, *Pure Appl. Chem.*, 1976, **47**, 1; J. Cornelisse, G. Lodder, and E. Havinga, *Rev. Chem. Intermed.*, 1979, **2**, 231.

[6] J. F. Bunnett, *Acc. Chem. Res.*, 1978, **11**, 413.

[7] M. Sainsbury, *Tetrahedron*, 1980, **36**, 3327.



Reagents: i, Aq. MeOH, HCl, $NaHSO_3$ if R = Me or H, $h\nu$; ii, $C_6H_6$, $Na_2S_2O_3$ if R = Ac, $h\nu$ iii, $H_2O$, NaOH, $NaBH_4$, $h\nu$; iv, $h\nu$, $C_6H_6$, $Bu^tOH$, $KOBu^t$

**Scheme 2**

It has been suggested that some photocyclization reactions of haloarenes which possess a stilbene system [*e.g.* (4)] proceed by an electrocyclic intermediate, followed by elimination to reform an aromatic system.[8] In the other reactions shown in Scheme 2, photohomolysis of the aryl–halogen bond was considered to be the first step, and so either iodo- or bromo-substrates were used. The benzene ring upon which substitution occurs can be either without phenolic substituents,[9]

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[8] M. P. Cava, M. J. Mitchell, S. C. Havlicek, A. Lindert, and R. J. Spangler, *J. Org. Chem.*, 1970, **35**, 175. See also M. P. Cava, P. Stern, and K. Wakisaka, *Tetrahedron*, 1973, **29**, 2245; M. P. Cava and S. S. Libsch, *J. Org. Chem.*, 1974, **39**, 577; L. Cleaver, S. Nimgirawath, E. Ritchie, and W. C. Taylor, *Aust. J. Chem.*, 1976, **29**, 2003.

[9] S. M. Kupchan, J. L. Moniot, R. M. Kanojia, and J. B. O'Brien, *J. Org. Chem.*, 1971, **36**, 2413; J. L. Neumeyer, K. H. Oh, K. K. Weinhardt, and B. R. Neustadt, *ibid.*, 1969, **34**, 3786.

as in (1), or can carry a phenoxide substituent,[10] as in (2) when this substituent exerts a pronounced *ortho*, *para* directing effect, allowing the formation of spiro-compounds. Spirodieneones formed in this way are themselves subject to photodegradation, so that better yields are obtained by *in situ* reduction of the first formed carbonyl compound to an alcohol, (3), with sodium borohydride. Cyclization of substrates with a tertiary amino-function (1, R = alkyl) is best carried out in acidic solution where the amino-function is protonated, while secondary amines are best acylated to give (1, R = acyl) and photolysed in benzene. Where aryl radicals are intermediate in a ring-closure reaction, they can be diverted by hydrogen abstraction from the solvent, or some other source, to give overall replacement of halogen by hydrogen. Often the yield of cyclized product is low. The early work in this field of haloarene photochemistry has been reviewed.[11-13]

## 2 Reaction Mechanisms

There have been a number of mechanistic studies on the photochemical reactions which lead to replacement of halogen by hydrogen and the results are relevant to the more useful preparative aspects of aryl halide photochemistry. Only a few such studies have been made of the preparatively useful ring-closure reaction.

**A. Energy Transfer and Homolytic Bond Cleavage.**—The u.v. spectrum of iodobenzene shows evidence for a $n\sigma^*$ excited state, involving the iodine group, which is dissociative in nature. This transition is of low intensity and partly overlapped by an intense $\pi \rightarrow \pi^*$ transition. Simple homolytic fission in iodoarenes may arise from population of $n\sigma^*$ or $\sigma\sigma^*$ states. This mechanism is not available in the ordinary solution photochemistry of bromo- and chloro-compounds, which do not possess a low energy $\sigma^*$ orbital, however, homolysis of cholorobenzene *via* a triplet $\sigma\sigma^*$ state is suggested for the short wavelength vapour phase photolysis.[14] Radiationless decay of the $\pi\pi^*$ state to a vibrationally excited ground-state can also lead to homolysis of the weakest bond in the system before the vibrational energy is dispersed as heat.[15] For chloro-, bromo-, and iodo-arenes the weakest bond is usually, but not necessarily, the carbon–halogen bond. These two processes for energy transfer to the $\sigma$-bond lead ultimately to radical species which may recombine before one radical is able to break from the solvent cage (see Scheme 3). Further reactions of the solvent-separated aryl radical lead to the final products.

In the chemistry of thermally-generated free radicals, cage recombination can be demonstrated because the rate of the forward reaction is diminished in

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[10] Z. Horii, Y. Nakashita, and C. Iwata, *Tetrahedron Lett.*, 1971, 1167.

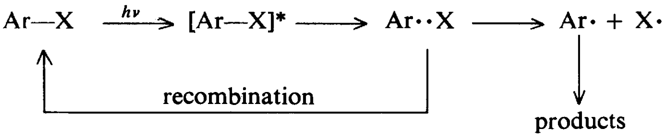
[11] R. K. Sharma and N. Kharasch, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 36.

[12] P. G. Sammes in 'The Chemistry of the Carbon–Halogen Bond', ed. S. Patai, Wiley, New York, 1972, p. 747.

[13] T. Kametani and K. Fukumoto, *Acc. Chem. Res.*, 1972, **5**, 212.

[14] G. Porter, 'Reactivity of the Photoexcited Molecule', Interscience, London, 1967, p. 104.

[15] G. Porter and B. Ward, *Proc. R. Soc. London, Ser. A*, 1965, **287**, 457.



**Scheme 3**

solvents of high viscosity.[16] In the context of a photodissociative process, cage recombination shows itself by the influence of solvent viscosity on the quantum yield for decomposition of the starting material. The quantum yield for the photoreduction of bromobenzene has been measured in mixtures of ethanol and ethane-1,2-diol and shows a decrease with increasing solvent viscosity.[17] For the photocyclization of (6) and the related bromo- and iodo-compounds, the quantum yield showed a smooth variation with solvent viscosity in a range of solvents including cyclohexane, methanol, and ethane-1,2-diol.[18] For preparative work with reactions which follow this mechanism, less viscous solvents will allow shorter reaction times because of this greater quantum yield for bond homolysis.

Simple energy considerations indicate which aryl halides can be expected to undergo the simple homolysis reaction, since the energy of the excited state must be greater than the bond energy. Substitution by the halogen changes the excited-state energies of the parent aromatic system very little, so we can compare the energy data given in Table 1 in order to justify the quantum yield data given in Table 2 for some reactions that have been studied in detail.

**Table 1** *Triplet energies compared to carbon–halogen bond energies in arene compounds*

| *Arene* | $E_T$/kJ mol$^{-1}$ | *Haloarene* | $D_{C-X}$/kJ mol$^{-1}$ |
|---|---|---|---|
| Benzene | 352 | PhCl | 397 |
| Biphenyl | 275 | PhBr | 334 |
| Naphthalene | 255 | PhI | 268 |

Data from: S. L. Murov, Handbook of Photochemistry, M. Dekker, New York, 1973; K. W. Egger and A. T. Cocks in 'Chemistry of the Carbon–Halogen Bond', Part 2 ed. S. Patai. Part 2, Wiley, 1973

Flash excitation of fluoro- and chloro-benzene in solution shows emission spectra from triplet states. Bromo- and iodo-benzene show rapid flash photolysis and a triplet intermediate cannot be detected.[19] Chloro- and bromo-substituted naphthalenes and biphenyls show slow photolysis *via* the triplet state even though from bond energy considerations cleavage of the carbon–

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[16] D. Gegiou, K. A. Muszkat, and E. Fischer, *J. Am. Chem. Soc.*, 1968, **90**, 12; D. Booth and R. M. Noyes, *ibid.*, 1960, **82**, 1868; W. A. Pryor and K. Smith, *ibid.*, 1970, **92**, 5403.

[17] J. Szychlinski and L. Litwin, *Rocznik Chem.*, 1963, **37**, 671.

[18] J. Grimshaw and A. P. de Silva, *Can. J. Chem.*, 1980, **58**, 1880.

[19] I. Loeff, H. Lutz, and L. Lindquist, *Isr. J. Chem.*, 1970, **8**, 141.

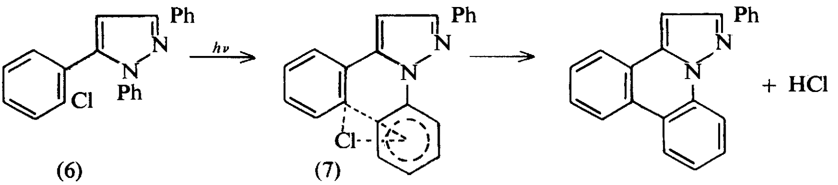
**Table 2** *Quantum yields ($\Phi$) for the decomposition of haloarenes*

| *Haloarene* | *Solvent* | $\Phi$ | *Haloarene* | *Solvent* | $\Phi$ |
|---|---|---|---|---|---|
| 1-Chloronaphthalene[a] | MeOH | 0·005 | 4-Chlorobiphenyl[b] | iso-octane | 0·0006 |
| 1-Bromonaphthalene[a] | MeOH | 0·170 | 2-Bromobiphenyl[c] | cylohexane | 0·046 |
| 2-Chlorobiphenyl[b] | iso-octane | 0·39 | 2-Bromobiphenyl[c] | cyclohexane | 0·004 |
| 3-Chlorobiphenyl[b] | iso-octane | 0·001 | 4-Bromobiphenyl[c] | cyclohexane | 0·015 |

[a] L. O. Ruzo, N. J. Bunce, and S. Safe, *Can. J. Chem.*, 1975, **53**, 688; N. J. Bunce, P. Pilon, L. O. Ruzo, and O. J. Sturch, *J. Org. Chem.*, 1976, **41**, 3023. [b] N. J. Bunce, Y. Kumar, L. Ravanal, and S. Safe, *J. Chem. Soc., Perkin Trans.* 2, 1978, 880; [c] N. J. Bunce, S. Safe, and L. O. Ruzo, *J. Chem. Soc., Perkin Trans.* 1, 1975, 1607.

halogen bond is unlikely since the reaction would be so endothermic. A mechanism of photoinduced intermolecular electron-transfer (see section B) has been proposed to account for the observed reactivity. The triplet energy of biphenyl is raised by 2-substitution as a result of the benzene rings being forced out of plane, and this accounts for the higher reactivity of 2-halobiphenyls.

Cyclization of the chlorophenylpyrazole (6) is also not expected from simple energy considerations, since for 1, 3, 5-triphenylpyrazole, values of $E_S$ = 351 and $E_T$ = 272 kJ mol$^{-1}$ have been found. The reaction can be effected either directly through the singlet state or by triplet sensitization, and either way the quantum yield is of the same order for chloro-, bromo-, or iodo-analogues. Solvent effects indicate the direct singlet reaction to be a radical process and, surprisingly, the reaction leads in all cases to quantitative cyclization with no replacement of halogen by hydrogen, as a side reaction. A transition state (7) leading to an intermediate involving $\pi$-complexation by the adjacent benzene ring of radical species which develop during bond homolysis has been proposed to account for these observations.[18] Complexation can be expected to lower the energy requirement for bond homolysis. A related effect attributed to complexation of radicals by a $\pi$-cloud has been noted in general free radical chemistry.[20]



(6) (7)

**B. Electron Transfer and Radical-anion Decomposition.**—Photochemically induced electron transfer between dialkylanilines and aryl halides is well documented.[21] Irradiation by light ($\lambda$ = 313 nm) of a mixture of dimethylaniline and a halobenzene leads to exciplex formation between the excited state of the amine and the halobenzene followed by electron transfer from the amine. The fluorescence of dimethylaniline is quenched by this process and decomposition of the halobenzene radical-anion then yields a phenyl radical and halide ion according to Scheme 4.

Aliphatic amines also promote bond cleavage in aryl halides by a similar mechanism where an electron is transferred from the nitrogen lone pair to the excited state of the aryl halide.[22] Such photoinduced electron-transfer could

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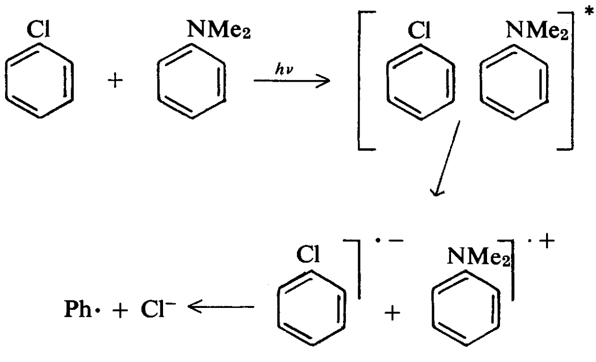
[20] T. W. Koenig and J. C. Martin, *J. Org. Chem.*, 1964, 29, 1520; D. B. Denney, R. L. Ellsworth, and D. Z. Denney, *J. Am. Chem. Soc.*, 1964, **86**, 1116.

[21] T. Latowski, *Z. Naturforsch.*, *Teil A*, 1968, 23, 1127; C. Pac, T. Tosa, and H. Sakuri, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 1169; M. Grodowski and T. Latowski, *Tetrahedron*, 1974, **30**, 767.

[22] J. Nasieliski and A. Kirsch-Demesmaeker, *Tetrahedron*, 1973, **29**, 3153; M. Ohashi, K. Tsujimoto, and K. Seki, *J. Chem. Soc., Chem. Commun.*, 1973, 384.



**Scheme 4**

clearly give rise to unwanted side-reactions in the photochemical ring-closure step for the synthesis of a number of alkaloids and the earlier workers discovered empirically that best yields for cyclization are obtained when a free amino-group is protected either by protonation or by conversion to an *N*-acyl derivative. Added triethylamine also promotes the photochemical decomposition of chlorinated biphenyls,[23] *para*-terphenyls,[24] and bromobiphenyls[25] by electron transfer to the excited state. Related reactions may be in part responsible for the photodegradation of chlorinated aromatic compounds in the environment.

A related photochemically induced electron-transfer process has been used to explain carbon–halogen bond cleavage in the triplet state of chloronaphthalenes[26] and chloro- and bromo-biphenyls[25] where the triplet energy is less than that required for bond cleavage (Table 1). Electron transfer is proposed between the excited state and some other aromatic species in solution, either the haloarene or photochemically produced arene, to give the haloarene radical-anion which undergoes rapid bond cleavage.

The rate of carbon–halogen bond cleavage in some radical-anions is known to be slow, which appears to be the case for a variation of the electron-transfer mechanism shown by the photolysis of 9,10-dichloroanthracene in the presence of 2,5-dimethylhexa-2,4-diene.[27] Irradiation in acetonitrile gives rise to a singlet exciplex which relaxes to a pair of radical-ions. That the radical-anion of 9,10-dichloroanthracene is protonated by traces of water and then loses a chlorine atom to give 9-chloroanthracene is demonstrable since, in the presence of 0·06 M deuterium oxide, deuterium is incorporated into the product. Deuterium is not incorporated into the product after photolysis in [$^2H_3$]acetonitrile

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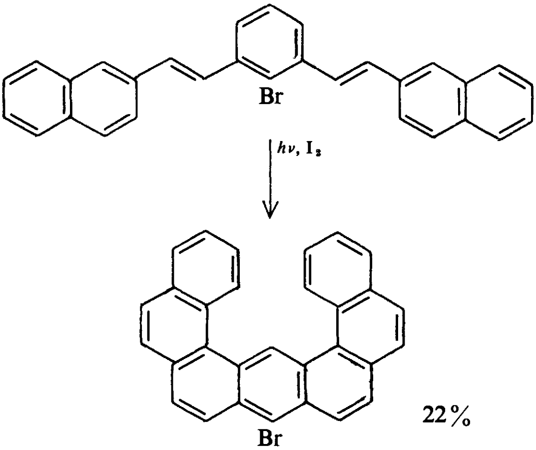
[23] N. J. Bunce, Y. Kumar, L. Ravanal, and S. Safe, *J. Chem. Soc., Perkin Trans.* 2, 1978, 880.
[24] B. Chittim, S. Safe, N. J. Bunce, L. O. Ruzo, K. Olie, and O. Hutzinger, *Can. J. Chem.*, 1978, **56**, 1253.
[25] N. J. Bunce, S. Safe, and L. O. Ruzo, *J. Chem. Soc., Perkin Trans.* 1, 1975, 1607.
[26] L. O. Ruzo, N. J. Bunce, and S. Safe, *Can. J. Chem.*, 1975, **53**, 688.
[27] W. K. Smothers, K. S. Schanze, and J. Saltiel, *J. Am. Chem. Soc.*, 1979, **101**, 1895.

indicating that, in this case, the radical-anion does undergo significant carbon–chlorine bond cleavage to give a $\sigma$-radical.

**C. Electron Reorganization to an Electrocyclic Intermediate and Subsequent HX Loss.**—Compounds such as (4) bear a formal resemblance to stilbene and so can be expected to show *cis*, *trans* photoconversion and to form the intermediate (5) on irradiation, subsequently losing hydrogen chloride. This cyclization elimination mechanism was proposed to account for the ready reaction of the chloroarene (4, X = Cl).[8] Cyclization onto carbon-6′ must also be expected but, if we assume that formation of the electrocyclic intermediate is reversible, then rapid irreversible loss of HCl will direct the overall process to cyclization onto the halogen-bearing carbon-2′. The value of halogen substituents in directing the electrocyclization step is, however, not clear and a number of examples can be cited where a halogen substituent has been used to block the oxidative photocyclization. Thus, 2-chlorostilbene undergoes oxidative photocyclization to 1-chlorophenanthrene in 57% yield[28] and the diolefin (8) undergoes a double cyclization without loss of bromine.[29] Bromine has been used as a blocking group in other helicene syntheses.[29]



(8)

Cyclization of (9) to 9-nitrophenanthrene is thought to proceed by carbon–iodine bond homolysis[30] and subsequent intramolecular arylation, rather than through an electrocyclic intermediate, because attempted oxidative ring-closure of unsubstituted $\alpha$-nitrostilbene fails. Some other examples of cyclization of

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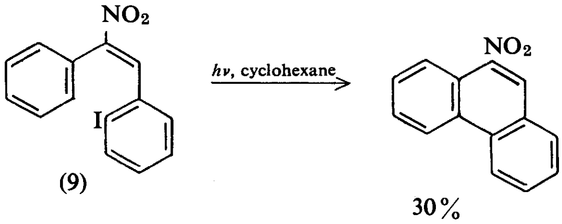
[28] C. S. Wood and F. B. Mallory, *J. Org. Chem.*, 1964, **29**, 3373.

[29] C. F. Wilcox, P. M. Lahti, J. R. Rocca, M. B. Halpen, and J. Meinwald, *Tetrahedron Lett.*, 1978, 1893; R. H. Martin, C. Eyndels, and N. Defay, *Tetrahedron Lett.*, 1972, 2731.

[30] S. M. Kupchan and H. C. Wormser, *J. Org. Chem.*, 1965, **30**, 3792.



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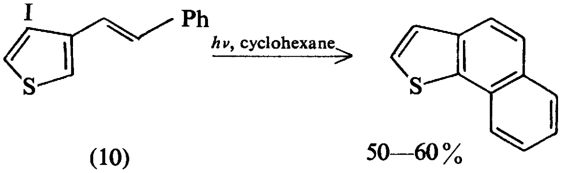

(10)

*ortho*-iodo compounds [e.g. (10)][31] have been shown to proceed by first photochemical reduction of the carbon–iodine bond (*via* bond homolysis) and then photo-oxidative ring closure of the stilbene in the presence of iodine formed from hydrogen iodide eliminated in the first step.

It appears, therefore, that in simple stilbenoid systems an *ortho*-halogen substituent tends to adopt a rotational conformation so as to avoid the other phenyl ring in the excited state of the *cis*-isomer, and this reduces the probability for cyclization at its root. In the case of iodo-substituents homolysis of the weak carbon–iodine bond is usually the preferred reaction to electrocyclization and oxidation. The successful dehydrohalogenative cyclization of (4) reflects the opposite conformational preferences of this crowded system and is not a typical example.

## 3 Reactions; a Survey

Most of the known photochemistry of aryl halides can be viewed formally as resulting from substitution processes occurring at the carbon–halogen bond, with displacement of the halogen by an incoming group. From this starting point we can classify these photoreactions according to the reactive atom of the incoming group.

**A. Reactions with Enolate-carbanionic Centres.**—An important photoreaction of enolates with aryl halides in liquid ammonia has been reviewed by Bunnett.[6] Analogous intramolecular reactions should have considerable potential in synthesis, and a few of these, such as the synthesis of (11),[32] have been described. The reaction proceeds by a chain mechanism, where the initiating step is

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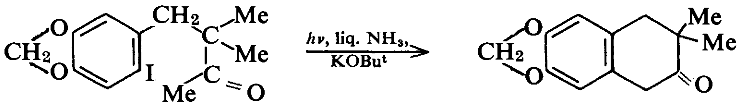
[31] G. Deluca, G. Martelli, P. Spagnolo, and M. Tiecco, *J. Chem. Soc. (C)*, 1970, 2504; R. M. Letcher and K. M. Wong, *J. Chem. Soc., Perkin Trans.* 1, 1977, 178.

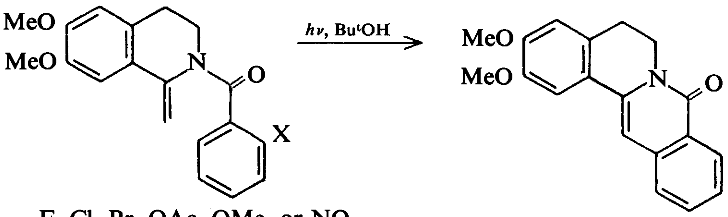
[32] M. F. Semmelhack, R. D. Stauffer, and T. D. Rogerson, *Tetrahedron Lett.*, 1973, 4519; M. F. Semmelhack and T. M. Barger, *J. Org. Chem.*, 1977, **42**, 1481.



(11, 99%)

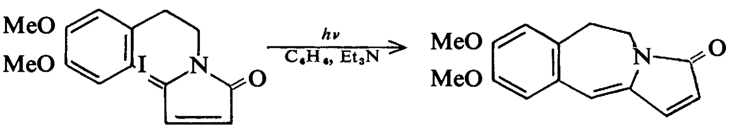
transfer of an electron from some source to the aryl halide. One of the two species involved is photoexcited and the energy required for electron transfer is offset by a return from the excited state to the ground state. The aryl halide anion-radical then undergoes anion exchange with the enolate. The product anion-radical transfers its electron to a second aryl halide group so that a chain of anion exchange reactions can occur from one initiating electron transfer.

**B. Reactions with Alkene Carbon Centres.**—The photocyclization of enamides has been a fruitful route for the synthesis of six- and seven-membered nitrogen heterocycles. Two distinct routes are followed. Cyclizations typified[33] by the reaction of (12, X = Cl or Br) proceed through an electrocyclic intermediate and then loss of HX to yield the product. In these reactions other leaving groups besides halogen can be used. Other examples,[34] such as the cyclization of (13), probably occur by a photochemically induced electron-transfer mechanism between the aryl halide, and triethylamine added as a scavenger for the hydrogen halide.



(12) X = F, Cl, Br, OAc, OMe, or $NO_2$

85% when X = F
50% when X = Cl



46%

(13)

An example of a reaction which may involve homolytic bond cleavage followed by intermolecular radical addition to an olefin is shown by the pyridine com-

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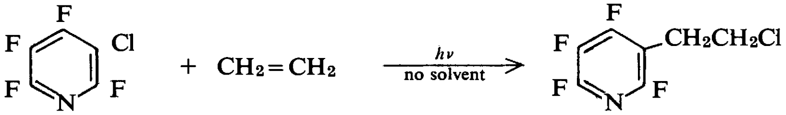
[33] G. R. Lenz, *J. Org. Chem.*, 1974, 39, 2839; T. Kametani, T. Sugai, Y. Shoji, T. Honda, F. Satoh and K. Fukumoto, *J. Chem. Soc., Perkin Trans.* 1, 1977, 1151.

[34] I. Tse and V. Snieckus, *J. Chem. Soc., Chem. Commun.*, 1976, 505; H. Iida, T. Takarai and C. Kibayashi, *J. Org. Chem.*, 1978, **43**, 975.

pound (14).[35] The reaction mixture, however, shows no products from the radical polymerization of ethylene. Similarly, irradiation of an equivolume mixture of chlorobenzene and cyclopentene gives a mixture of *cis*- and *trans*-1-chloro-2-phenylcyclopentane.[35]



77%

(14)

**C. Reactions with Aromatic Carbon Centres.**—The large number of reactions belonging to this class is divided into two categories.

*Intermolecular Reactions.* Reactions in this category mostly proceed by the homolysis mechanism and are typified by the conversion of 4-iodobiphenyl to *p*-terphenyl on irradiation in benzene solution. Kharasch's observations on the poor reactivity of 4-chloro- and 4-bromo-biphenyl promoted the generalization that photoreactivity decreased sharply on passing to the lower halides.[1] This observation is not, however, general because both bond-dissociation energy and excited-state energy are determining factors for reactivity. Simple halobenzenes with higher energy excited states relative to biphenyls can arylate benzene whether the halogen group is iodo,[1] bromo,[2] or chloro.[36] In cases where both chlorine and iodine are attached to an arene, *e.g.* (15), then the carbon–iodine bond is preferentially cleaved.[37] Interestingly, 2-chlorobiphenyl is able to take part in photo-arylation reactions,[36] whereas the 4-isomer is not, presumably because the excited-state energy levels in 2-substituted biphenyls are higher,[38,39] so that bond homolysis becomes possible.

The photolysis of halogenophenols (16) in aqueous alkaline medium provides another example where the reactivity is comparable for all three halides, though the product distribution differs in the three cases.[40] Formation of coupled products in this reaction seems to have inspired several alkaloid syntheses which are described below.

*Intramolecular Reactions.* Photocyclization reactions have been used extensively

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[35] M. G. Barlow, R. N. Haszeldine, and J. R. Langridge, *J. Chem. Soc., Chem. Commun.*, 1979, 608; D. Bryce-Smith, W. M. Dadson, and A. Gilbert, *J. Chem. Soc., Chem. Commun.*, 1980, 112.

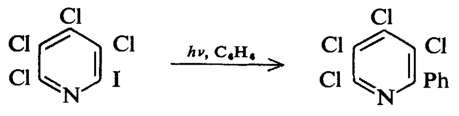
[36] G. E. Robinson and J. M. Vernon, *J. Chem. Soc.*, (*C*), 1971, 3363.

[37] J. Bratt, B. Iddon, A. G. Mack, H. Suschitsky, J. A. Taylor, and B. J. Wakefield, *J. Chem. Soc. Perkin Trans.* 1, 1980, 648.

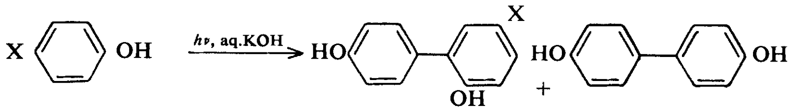
[38] C. M. O'Donnell, K. F. Harbaugh, R. P. Fisher, and J. D. Wine-Fordner, *Anal. Chem.*, 1973, **45**, 609.

[39] P. J. Wagner, *J. Am. Chem. Soc.*, 1967, **89**, 2820; P. J. Wagner and B. J. Scheve, *ibid.*, 1977, 99, 2888.

[40] K. Omura and T. Matsuura, *Tetrahedron*, 1971, **27**, 3101.



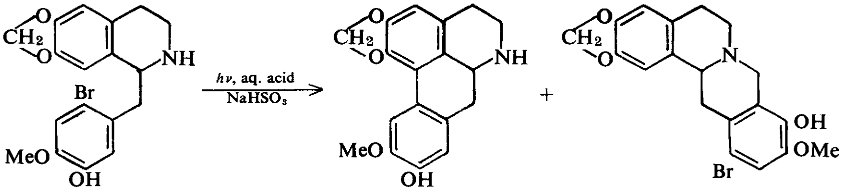
(15) 40%



(16) X = Cl, Br, or I (17)

+(17, X = H) + (16, X = H) + (16, X = OH)

in synthesis and a number of these reactions were used to illustrate the previous discussion of reaction mechanisms. The photosynthesis of isoquinoline alkaloids was reviewed in 1972.[13] The activating chromophore in these reactions is usually a benzene ring so that bromo-compounds such as (18), in addition to iodo-compounds, undergo satisfactory reaction by a bond homolysis process.[13, 41,42] A complication when using secondary amines is the parallel formation of berberines by addition of photo-liberated formaldehyde to the amino-function.[42] Thus (18) gives rise to (19) in addition to the expected product. Formaldehyde is liberated from substrates which contain methylenedioxy- or methoxy-groups and, in small amounts, from substrates which contain neither of these groups.[42]



(18) (19)

The influence of excited-state energy on the rate of bond cleavage can be seen in some examples of cyclization and in lack of reactivity reported in heterocyclic series. Thus, the pyridine compounds (20) cyclize satisfactorily[43] on irradiation, whereas the more conjugated quinoline (21) gives no cyclization owing to its

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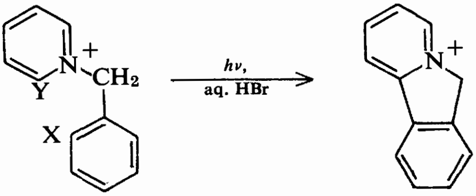
[41] S. Rajeswari, H. Suguna, and B. R. Pai, *Indian J. Chem., Sect. B*, 1977, **15**, 592; B. R. Pai, S. Natarajan, H. Suguna, and G. Manikumar, *ibid.*, 1977, **15**, 1042.

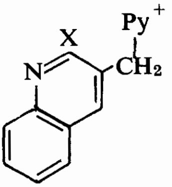
[42] T. R. Govindachari, K. Nagarajan, S. Rajeswari, H. Suguna, and B. P. Pai, *Helv. Chim. Acta*, 1977, **60**, 2138.

[43] A. Fozard and C. K. Bradsher, *J. Org. Chem.*, 1967, **32**, 2966; C. K. Bradsher and C. F. Voigt, *ibid.*, 1971, **36**, 1603.



(20) X = Cl or Br, Y = H
X = H, Y = Cl or Br

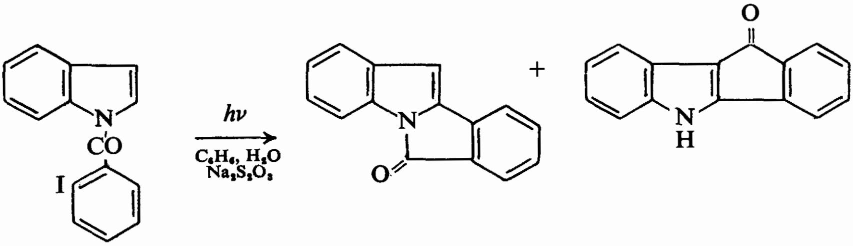
75% when
X = H, Y = Br



(21) X = Cl or Br

low excited-state energy and to the poor π-donor ability of the pyridinium ring, which reduces the possibility for assisted homolysis.[44]

Commonly encountered side reactions are of two types. Firstly, photoinduced homolytic bond cleavage occurs at the weakest bond in a structure so that unexpected reactions can be observed alongside the expected cyclization. Thus, reaction of (22) leads to a mixture of products where compound (23) is thought



(22) (23)

to result from a photo-Fries type migration of the *o*-iodobenzoyl group to the 3-position in competition with carbon–iodine bond homolysis.[45]

Secondly, ring photosyntheses involving aryl σ-radical intermediates are successful only if performed in a solvent of low hydrogen-donor ability, otherwise replacement of halogen by hydrogen occurs to a significant extent. Benzene or t-butanol are often used as solvent, and also aqueous acid for amine substrates or aqueous alkali for phenol substrates.

The majority of the reported photocyclization reactions involve formation of six-membered rings. There are a few examples of five-membered ring-forming reactions and some rings larger than six-membered have been successfully constructed by this photochemical route in spite of the inevitable competition with simple replacement of halogen by hydrogen. Examples are found of the

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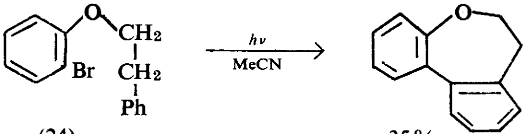
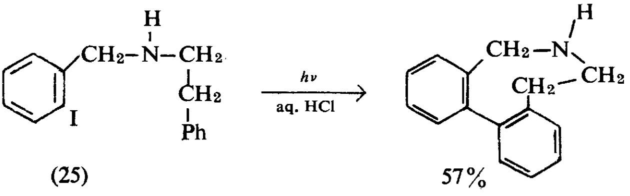
[44] D. E. Portlock, M. J. Kane, J. A. Bristol, and R. E. Lyle, *J. Org. Chem.*, 1973, **38**, 2351.
[45] W. Carruthers and N. Evans, *J. Chem. Soc., Perkin Trans.* 1, 1974, 1523.

formation of a seven-membered ring[46] from (24), an eight-membered ring[47] from (25) and a nine-membered ring[48] from (26).

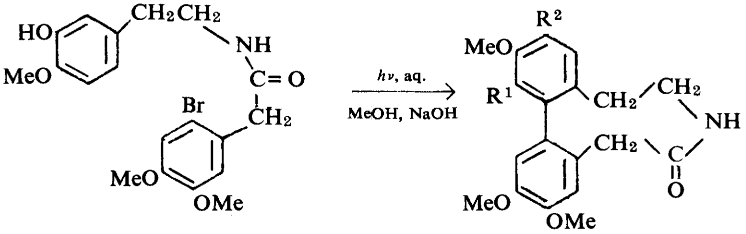


(24)

35%



(25)



(26)

$R^1$ = OH, $R^2$ = H
$R^1$ = H, $R^2$ = OH

A wide range of alkaloids have been synthesized by cyclization of substrates where the unhalogenated aryl moiety possesses a phenolic group and the reaction is carried out in aqueous alkaline solution. The first reports of this type appeared in 1971.[49] In these cases the substrates possess a basic nitrogen centre and so the phenoxide ion must effectively compete with the nitrogen lone pair for association with the excited aryl halide moiety in giving rise to cyclization by the electron-transfer mechanism. This cyclization shows a high degree of regiospecificity for arylation either *ortho-* or *para-* to the phenoxide group. The alternative view that

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[46] N. E. Brightwell and G. W. Griffin, *J. Chem. Soc., Chem. Commun.*, 1973, 37.

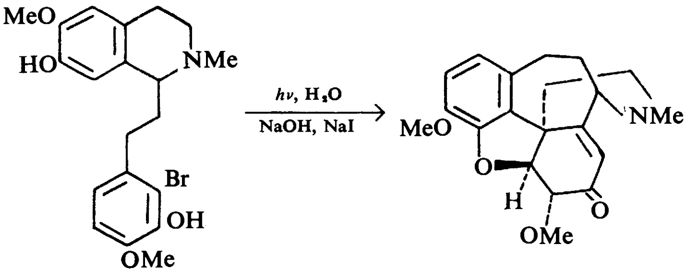
[47] P. W. Jeffs and J. F. Hansen, *J. Am. Chem. Soc.*, 1967, **89**, 2798; P. W. Jeffs, J. F. Hansen, and G. A. Brine, *J. Org. Chem.*, 1975, **40**, 2883.

[48] K. Ito and H. Tanaka, *Chem. Pharm. Bull. Jpn.*, 1974, **22**, 2108.

[49] T. Kametani, H. Nemoto, T. Nakano, S. Shibuya, and K. Fukumoto, *Chem. Ind. (London)*. 1971, 788; R. J. Spangler and D. C. Boop, *Tetrahedron Lett.*, 1971, 4851.

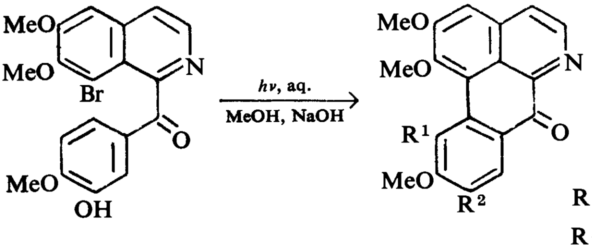
these reactions follow the energy transfer, homolytic bond cleavage mechanism dismisses the possibility of electron transfer from the amine lone pair which is known to occur in competition to simple homolysis.

The directing effect of the phenoxide group has been exploited for the synthesis of a large number of spiro-systems. Reducing conditions obtained by addition of sodium iodide have been used[50] to prevent the accumulation of bromine which would attack the substrate (27). Addition of sodium borohydride which reduces photosensitive cyclized products *in situ* has been made, for example in reaction of (2), so as to reduce the likelihood of photodegradation.[8] However, the known photoreduction of aryl halides by sodium borohydride merits caution in its use.



(27)

Even though the yields of cyclization products are rarely good, the simplicity of this reaction has been reason enough for its continued use. The yields improve when fully aromatic isoquinolines such as (28) are used as substrates.[51,52]



$R^1$ = H, $R^2$ = OH, 20%
$R^1$ = OH, $R^2$ = H, 21%

(28)

Phenanthridine systems are another class of heterocycles whose synthesis *via* aryl halide photochemistry has been examined in some detail. The reported photosynthesis of phenanthridone by irradiation of *o*-iodobenzanilide probably

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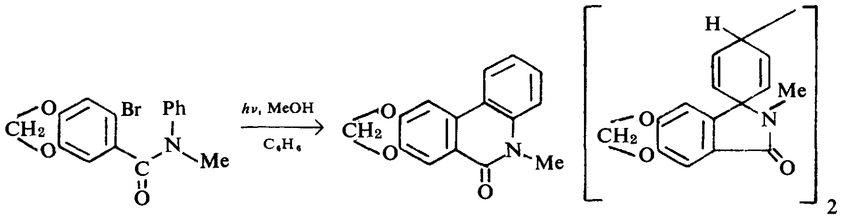
[50] T. Kametani, T. Kohno, R. Charubala, and K. Fukumoto, *Tetrahedron*, 1972, **28**, 3227.

[51] T. Kametani, R. Nitadori, H. Terasawa, K. Takahashi, M. Ihara, and K. Fukumoto, *Tetrahedron*, 1977, **33**, 1069.

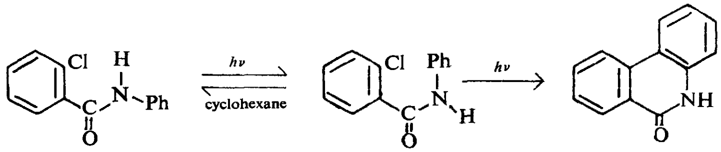
[52] S. M. Kupchan and P. F. O'Brien, *J. Chem. Soc., Chem. Commun.*, 1973, 915.

proceeds by formation of benzanilide which is known[53] to be further converted to phenanthridone in the presence of an oxidant. Since this early work, benzanilides have been demonstrated to show restricted rotation about the peptide bond and to adopt a configuration with *trans*-phenyl groups, so that cyclization cannot be expected for radicals formed by carbon–halogen bond homolysis of *o*-iodobenzanilides. Later work with *o*-iodo-*N*-methylbenzanilides, which adopt a *cis*-diaryl configuration, resulted in higher yields of the phenanthridone from bond homolysis followed by radical substitution, together with dimeric compounds resulting from cyclization to give a five membered ring.[54] This approach of cyclizing *N*-alkyl-*o*-halogenobenzanilides has led to several successful applications including the synthesis of substituted phenanthridones[55] such as (29) and the synthesis of benzophenanthridones[45,56] from *o*-bromo-*N*-methylbenznaphthamides.

*o*-Chlorobenzanilides can be made to undergo efficient photocyclization even though they adopt the *trans*-configuration in solution.[57] Because the excited state energy of benzanilide is less than the carbon–chlorine bond energy, the *trans*-form of (30) is photochemically stable and undergoes only the *trans*, *cis* inter-



(29) 22%



(30)

71%

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[53] B. S. Thyagarajan, N. Kharasch, H. B. Lewis, and W. Wolf, *J. Chem. Soc., Chem. Commun.*, 1967, 614.

[54] D. H. Hey, G. H. Jones, and M. J. Perkins, *J. Chem. Soc., Perkin Trans.* 1, 1972, 1150.

[55] A. Mondon and K. Krohn, *Chem. Ber.*, 1972, **105**, 3726; R. K.-Y. Zee-Cheng, S.-J. Yan, and C. C. Cheng, *J. Med. Chem.*, 1978, **21**, 199.

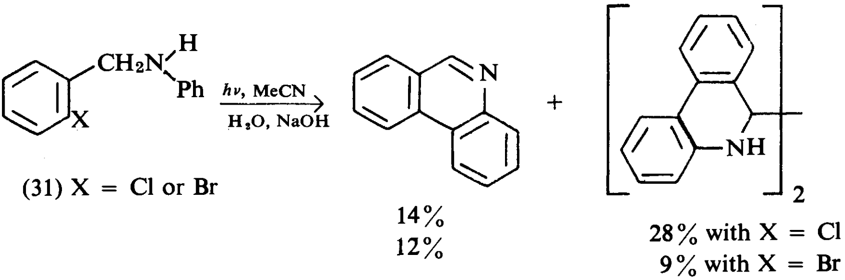
[56] W. J. Begley and J. Grimshaw, *J. Chem. Soc., Perkin Trans.* 1, 1977, 2324.

[57] J. Grimshaw and A. P. de Silva, *J. Chem. Soc., Chem. Commun.*, 1980, 302.

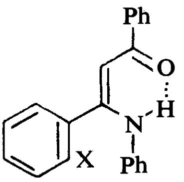
conversion. The *cis*-configuration has the assisted homolysis mechanism available to it and undergoes efficient cyclization. Thus, efficient photocyclization from these flexible molecules is possible for chloro-compounds but not for bromo- or iodo-compounds, since for these the *trans*-configuration undergoes carbon–halogen bond homolysis. *o*-Bromobenznaphthamides have also proved useful substrates for cyclization,[58] and a similar mechanism may operate here where the energy considerations make bromo-compounds the most satisfactory substrates.

The photoinduced electron-transfer between halobenzenes and aromatic amines has been applied to intramolecular examples. Reaction of (31) affords phenanthridine,[59] the expected dihydro-product dehydrogenates under the reaction conditions, and a dimer that may arise by photoalkylation[60] of phenanthridine by dihydro phenanthridine under the reaction conditions

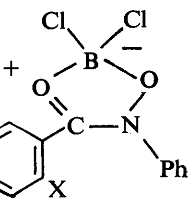
Compounds which have a fixed *cis*-diaryl configuration show an increased yield of cyclized product, often with the virtual exclusion of radical reactions with the solvent. For the synthesis of phenanthridine-type compounds this configuration has been achieved by incorporating the carbon–nitrogen bond into a heterocyclic system,[18] into a cyclic system (32) containing a hydrogen bond,[61] or into a co-ordination complex (33).[62] Compound (32) showed a



(31) X = Cl or Br



(32) X = Br or I



(33) X = Cl or Br

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[58] S. V. Kessar, O. Singh, and P. Balakrishnan, *Tetrahedron Lett.*, 1974, 2269; I. Ninomiya, J. Naito, and H. Ishii, *Heterocycles*, 1975, 307.

[59] K. Mizuno, C. Pac, and H. Sakurai, *Bull. Chem. Soc. Jpn.*, 1973, **46**, 3316.

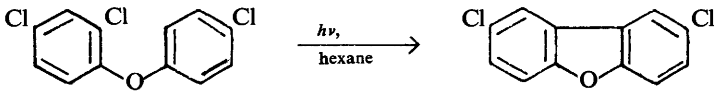
[60] F. R. Stermitz, R. Pua-Seiber, and D. E. Nicodem, *J. Org. Chem.*, 1968, **33**, 1136.

[61] J. Grimshaw and A. P. de Silva, *J. Chem. Soc., Chem. Commun.*, 1980, 301.

[62] S. Prabhakar, A. M. Lobo, and M. R. Tavares, *J. Chem. Soc., Chem. Commun.*, 1978, 884.

wavelength-dependent cyclization quantum yield demonstrating that, in this case, carbon–halogen bond fission occurs from an upper excited state and that it can compete with the normally fast internal conversion to a lower, and in this case inactive, excited state.

There are a number of examples of photocyclization of polychloro-compounds to indicate that, in general, in the benzene and pyridine series, *ortho*-halogeno-substituents are more photolabile than *meta*- or *para*-substituents. Thus, (34) is converted to a dichlorobenzofuran[63] and the chloropyridine (35) is cyclized[37] without loss of further chloro-substituents.



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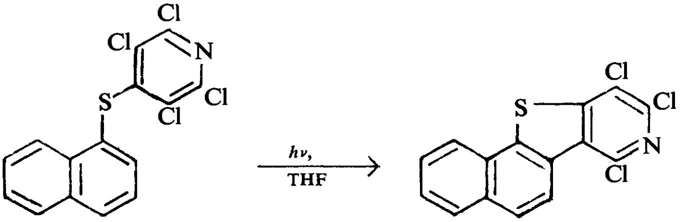
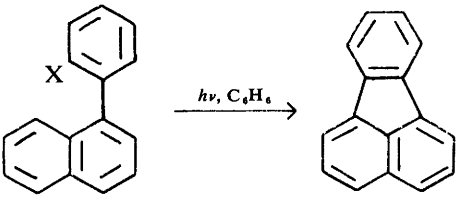


(35)

58%

This field of photocyclization is very large and some relevant mechanistic studies have already been discussed, yet in general the field suffers from a lack of any but the most rudimentary quantitative information. An exception is the photoreaction of (36) where the proportion of cyclized product, (37), is large



+ (36, X = H) + (36, X = Ph)

(36, X = Cl, Br, or I)

(37)

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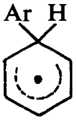
[63] A. Norstrom, K. Anderson, and C. Rappe, *Chemosphere*, 1976, **5**, 21.

from the chlorocompound but negligible from the iodocompound.[64] These facts were originally explained in terms of thermodynamic *versus* kinetic control determined by the oxidizing ability of the halogen atom. According to the assisted homolysis model, such halogen-atom dependent product distributions can arise by the higher electron affinity of chlorine causing a strongly complexed transition-state, which leads to cyclization. In the case of the iodo-compound the tendency will be to proceed by simple unassisted homolysis, especially where a high strain energy is associated with complexation.

**D. Reactions with Hydrogen Centres.**—Reductive dehalogenation is a ubiquitous phenomenon in aryl halide photochemistry and is the chief reason for the low yields attained in photocyclizations conducted in organic solvents. In extreme cases cyclization is totally inhibited[45,65] by the direct route, but secondary electrocyclic reactions of the dehalogenated product may allow oxidative ring-closure. Even during photoarylation reactions carried out in neat aromatic solvents, photoreduction takes place in varying degrees[2,11,36] because hydrogen atoms are transferred to aryl radicals from hydrogen iodide and species of the type (38). Traces of oxygen can assist the desired reaction by scavenging species (38), but excess oxygen also scavenges aryl radicals.[66]



(38)

Reductive dehalogenation has been turned to preparative advantage in a few cases. Irradiation of pentachloropyridine in dioxan gives 2, 3, 4, 6-tetrachloropyridine.[37] Positions on an aromatic ring can be blocked by halogenation and then unblocked by a photochemical reaction, as appropriate, during a synthetic sequence.[11] Irradiation of the aryl halide in [$^2H_6$]acetone leads to specific replacement of the halide by deuterium,[11] although nonphotochemical methods are usually more practical for purposes of specific deuterium labelling.

Environmental photochemists have studied photodehalogenation to assess the role of solar degradation in the detoxification of halogen-containing pollutants. Points of possible interest in general preparative work which arise are the following. *Ortho*-chloro- and *ortho*-bromo-substituents show enhanced photoreactivity, with respect to their positional isomers, in the biphenyl,[23,25,67]

[64] W. A. Henderson and A. Zweig, *J. Am. Chem. Soc.*, 1967, **89**, 6778; W. A. Henderson, R. Lopresti, and A. Zweig, *ibid.*, 1969, **91**, 6049.

[65] J. Stumpe, A. Mehlhorn, and K. Schwetlick, *J. Photochem.*, 1978, **8**, 1.

[66] N. Kharasch and R. K. Sharma, *J. Chem. Soc., Chem. Commun.*, 1966, 106.

[67] T. Nishiwaki, M. Usui, K. Anda, and M. Hida, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 821.

terphenyl,[24,68] and diphenyl ether[63,69] series. Some benzene derivatives show this effect, the most notable exceptions being substituted phenols and anilines where the *meta*-chloro-isomers are the most reactive.[70] The enhanced lability of *ortho*-substituents can be explained because, firstly in the biphenyl series *ortho*-substitution is known to raise the excited-state energy, and secondly elimination of a crowded substituent causes relief of strain.

Increased photodecomposition rates of aryl halides of low intrinsic reactivity have been attained by adding aliphatic amines[22,23,25] or aqueous alcoholic alkali,[67,71] and these effects could be important in pollution control. Exciplexes are demonstrable between aryl halides and aliphatic amines and the dehalogenation rate increases with solvent polarity, implying electron transfer as the key step. Quantum yields considerably larger than unity have been observed for dehalogenation in the presence of additives, and are attributed[22,67] to a chain reaction propagated by carbonyl radical-anions originating from the alchohol solvent. A chain propagation by borane radical-anions is reponsible for the high photoreactivity of halobenzenes in the presence of sodium borohydride.[72]

**E. Reactions with Halogen Centres.**—Halogen exchange is a little studied aspect of aryl halide photochemistry. Some of the early examples of iodine exchange do not involve photoexcitation of the aromatic system, but rather proceed by (visible) light-induced fission of molecular chlorine or bromine, followed by radical attack on the iodoarene.[73] Genuine cases of participation by the photoexcited states of aryl halides are found during the photolysis of the iodoarene in halogenated aliphatic solvents, such as carbon tetrachloride and bromoform[64,74] Arene radicals generated by homolysis of the carbon–iodine bond attack the halogenated solvent. In a reaction of some utility, molecular iodine containing a radioactive isotope can be exchanged with aryl iodides under the influence of ultraviolet, but not visible, radiation. This, and also the intramolecular reaction[75] of (39) are understandable in terms of simple homolysis of the carbon–iodine bond followed by further reaction of the aryl radical on iodine.

**F. Reactions with other Heteroatom Centres.**—Aryl halides form only a small part of the large number of aromatic substrates which undergo nucleophilic photosubstitution, and this reaction has been reviewed.[5] Thus alkoxy-, hydroxy-, amino-, and thiocyanato-groups undergo photosubstitution on a variety of

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[68] B. Chittim and S. Safe, *Chemosphere*, 1977, **6**, 269.

[69] A. Norstrom, K. Anderson, and C. Rappe, *Chemosphere*, 1977, **6**, 241.

[70] H. Parlar, P. G. W. Steven, R. Baumann, and F. Korte, *Z. Naturforsch.*, *Teil B*, 1979, **34**, 113.

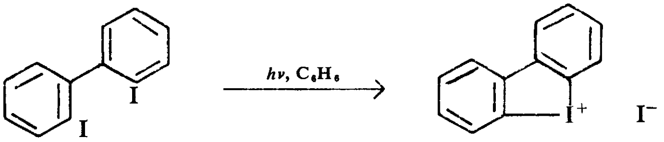
[71] C. Parkanyi and Y. J. Lee, *Tetrahedron Lett.*, 1974, 1115.

[72] J. A. Barltrop and D. Bradley, *J. Am. Chem. Soc.*, 1973, **95**, 5085.

[73] W. Voegtli, H. Muhr, and P. Lauger, *Helv. Chim. Acta*, 1957, **37**, 4170; B. Miller and C. Walling, *J. Am. Chem. Soc.*, 1957, **79**, 4187; J. T. Echols, V. T. C. Huang, C. S. Parrish, J. E. Rose, and B. Milligan, *ibid.*, 1967, **89**, 4081.

[74] F. Kienzle and E. C. Taylor, *J. Org. Chem.*, 1970, **35**, 528.

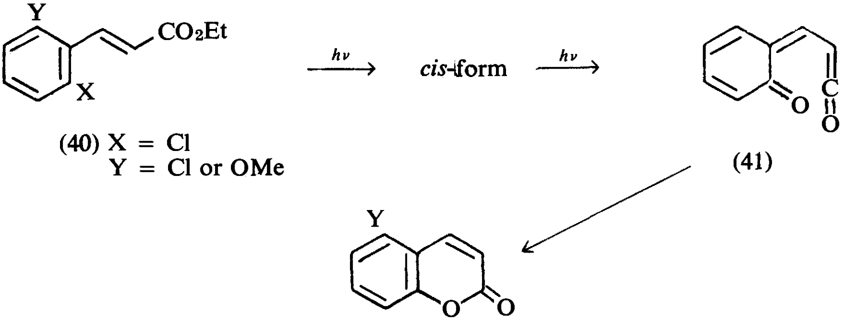
[75] T. Sato, S. Shimada, and K. Hata, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 2484.



(39) 21%

halogenated benzene, naphthalene, and other aromatic substrates. The halogen of choice for these reactions is either fluorine or chlorine, so as to avoid excessive competition from carbon–halogen bond homolysis, and subsequent radical processes.

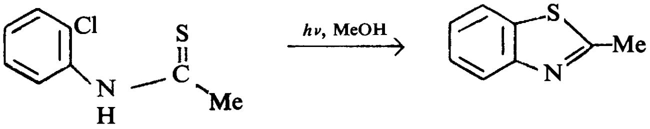
Radical-producing photochemical processes can also lead to heteroatom substitution, as in the formation of phenols during the photolysis of aryl iodides in the presence of oxygen.[66] The photoconversion of 2-iodo-2′-methylthiobiophenyl to dibenzothiophene[76] is probably a radical process. Similarly, aryl iodides and bromides can be sulphenylated with disulphides,[77] or converted to phenyl phosphonates with trialkylphosphites.[78]



(40) X = Cl
Y = Cl or OMe

(41)

Y = Cl or OMe



(42) 69%

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[77] T. Fujisawa and H. Ohta, *Bull. Chem. Soc. Jpn.*, 1976, 49, 2341.
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A few intramolecular heteroatom-centre reactions have been reported, and there appears to be considerable scope for further exploration. Photocyclization of (40) is interesting in that 2,6-disubstitution appears necessary for ring closure. This may be due to the 2-substituted compound adopting a conformation where the halogen atom and ethoxycarbonyl group are remote. Low-temperature studies support an electrocyclic reaction followed by elimination of RCl to yield (41), which can cyclize to give the product.[79] No information is available to decide if the cyclization[80] of (42) is a nucleophilic photosubstitution or a radical reaction.

## 4 Conclusions

Photohomolysis of haloarenes has proved to be a useful source of aryl radicals in synthesis and the intramolecular cyclization of the radicals so formed onto an adjacent arene group is a useful step for the synthesis of a large number of alkaloids. However, the yields of cyclized product have often been low and the route is, in many cases, considered attractive only because of its simplicity.

Quantitative information on these and related reactions has accumulated to indicate a range of mechanisms for carbon–halogen bond cleavage. It is now possible to select reaction conditions so as to achieve better yields, at least for some cyclizations. We hope that this review will assist in defining areas where photocyclization can be successfully used.

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