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EXPLORATORY PHOTOCHEMISTRY OF IODINATED AROMATIC AZIDES

by

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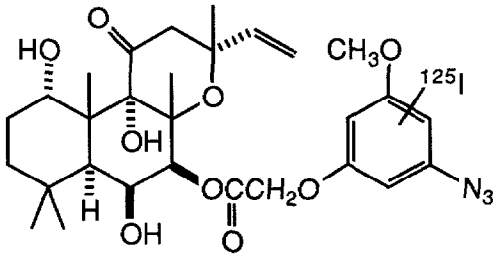
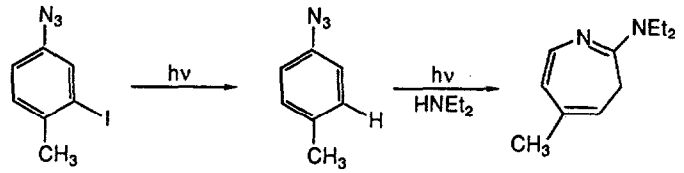
Abstract In contrast to the photolysis of p-toluyl azide, photolysis of ortho- or meta-iodo substituted p-toluyl azide in the presence of nucleophilic trapping agents produced the corresponding triplet nitrene which led to the simple aniline products and not to the dehydroazepine-nucleophile adducts.

Photoaffinity labelling (PAL) remains a widely used tool in biochemistry and aromatic azides are among the most popular of all PAL reagents. In these experiments it is often necessary to append a radioisotope tracer such as ^{125}I to the PAL reagent to monitor the incorporation of the label into the biomolecule. In this connection, we had occasion to prepare the radiolabeled forskolin photoaffinity probe shown below, but we noted relatively low levels of photo incorporation of the probe in biochemical cross-linking experiments. In order to determine if this observation was related to the juxtaposition of both the azide and the ^{125}I radiolabel in the same aryl ring, we prepared a series of simple iodinated p-toluyl azides **1a**, **1b**, and **1c**, and we report that the presence of iodine markedly alters the photochemistry of aryl azides and dramatically reduces their utility as PAL reagents.



The photochemistry of p-toluyl azide **1a** greatly resembles that of parent phenyl azide.[4] The results are reported in Table 1 and interpreted with the aid of Scheme 1. Photolysis of **1a** leads to loss of nitrogen and formation of a singlet nitrene (^{1}**2a**) which ring expands to a dehydroazepine (**3a**) and subsequently reacts with amines to form an adduct (**4a**)[5] in moderate yields. In the absence of amine, the major product is the aniline (**5a**) which is presumably derived from the triplet nitrene ^{3}**2a**. Although the mechanism of triplet nitrene formation is not completely established in this system, it is reasonable to expect equilibration between ^{1}**2a** and **3a**[6] followed by irreversible intersystem crossing (ISC) of ^{1}**2a** to ^{3}**2a**.

The product distribution is completely changed upon introduction of iodine. No trace of azepine **4b** or **4c**[7] is detected upon photolysis of **1b** or **1c** in the presence of diethylamine. The only products observed are anilines (**5b** and **5c**) which are totally useless from the point of view of PAL. Iodine has accelerated ISC by the heavy atom effect[8] in either the excited state of ^{1}**1b,c** or in the singlet state of the nitrene ^{1}**2b,c**, in order to furnish the triplet nitrene ^{3}**2b,c**. Some intersystem crossing from ^{1}**1a*** to ^{3}**1a*** in the non iodinated azide is deduced from an experiment involving the photolysis of **1a** in the presence of isoprene (a good triplet quencher)[9] which slightly reduces the yield of aniline and increases the yield of azepine. In any event, iodine suppresses the formation of dehydroazepines **3b** and **3c** which eliminates the possibility of their nucleophilic capture to form an iodinated azepine adduct **4b** and **4c**, respectively.[10] Photolysis of **1c** in diethylamine does produce azepine, but this azepine contained no iodine. In this case, the major pathway in the photochemistry of **1c** is loss of iodine to form **1a** which in turn leads to non-iodinated azepine adduct **4a**.



1c 1a 4a

This photodeiodination process raises the possibility that photolysis of an aryl azide tagged with ^{125}I in the same aryl ring, may produce radioactive iodine atoms which may subsequently label the biomolecule target.

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References

1. University of Kentucky
2. The Ohio State University
3. Bayley, H.; Photogenerated Reagents in Biochemistry and Molecular Biology, Elsevier, New York, N. Y. (1983).
4. (a) Schrock, A. K.; Schuster, G. B. J. Am. Chem. Soc. (1984) **106**, 5228.
   (b) Leyva, E.; Platz, M. S.; Persy, G.; Wirz, J. J. Am. Chem. Soc. (1986) **108**, 3783.

5. Doering, W. von B.; Odum, R. A. Tetrahedron (1966) **22**, 81.
6. Shields, C. J.; Chrisope, D. R.; Schuster, G. B.; Dixon, A. J.; Poliakoff, M.; Turner J. Am. Chem. Soc. (1987) **109**, 4723.
7. Ring expansion away from X and Y to form an isomer of **3** is plausible but not shown for the sake of clarity.
8. Turro, N. J. Modern Molecular Photochemistry, Benjamin/Cummings, Menlo Park, CA; (1978) pp. 125, 126, 192.
9. See reference 8, p. 422-425.
10. Personal communication from Professor G. B. Schuster, no trace of iodinated dehydroazepines are observed by time resolved IR.

Table 1. The distribution of products formed on photolysis of azides **1a-c**[a]

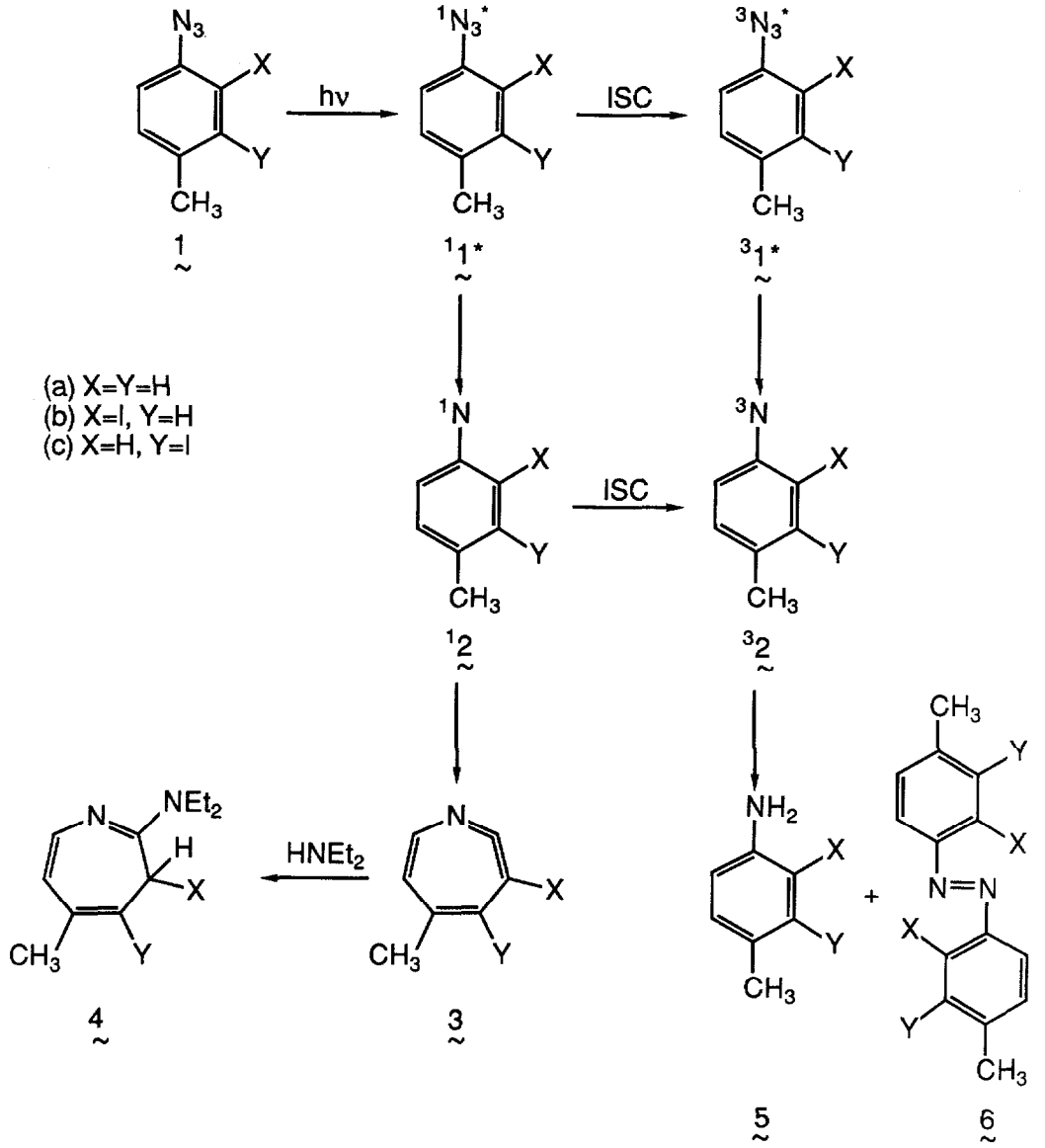
Azide	Amine (**5**)	Azo (**6**)	Azepine (**4**)	Conditions
1a	20	8	ND	2-MTHF[c]
1a	6	trace	38	DEA[d]
1a	3	trace	44	DEA-IP[e]
1b	39	ND[b]	ND	2-MTHF[c]
1b	37	ND	ND	DEA[d]
1b	29	ND	ND	DEA-IP[e]
1c (56%)[g]	10	ND	ND	2-MTHF[c]
1c (9%)[g]	16	ND	18[f]	DEA[d]
1c (12%)[g]	9	ND	14[f]	DEA-IP[e]

(a) Samples were photolyzed for 4 hours with 2 Rayonet RPR-3500 bulbs (principle radiation 365 nm) at ambient temperature. Samples were analyzed using a Perkin Elmer Model 8500 capillary gas chromatograph. Peaks were quantified relative to bibenzyl (0.01M) as internal standard GC peaks were identified by GC-MS and by comparison to authentic samples.
(b) ND, not detected
(c) 0.04 M azide in 2-methyltetrahydrofuran (2-MTHF)
(d) 0.04 M azide and 1.0 M diethylamine (DEA) in 2-MTHF
(e) 0.04 M azide, 1.0 M diethylamine and 10% isoprene (IP) (by volume) in 2 MTHF
(f) These azepines do not contain iodine, they are derived from loss of iodine in the starting azide to produce **1a**, followed by its photolysis to form **3a** and ultimately **4a**
(g) Yield of unreacted azide **1c**

4-azido-2-iodotoluene was prepared in 6 steps from para-toluic acid by a, I_2, H_5IO_6, H_2SO_4, HOAc, H_2O; b, $ClCO_2Et$, Et_3N, acetone, H_2O; c, NaN_3; d, reflux in toluene; e, HCl, H_2O; f, $NaNO_2$, HCl, H_2O, THF followed by NaN_3. IR(TF) 2100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40(s,3,CH_3) 6.91(dd, J=2 and 8Hz, 1, C-5CH), 7.19(d, J=8Hz, 1, C-6CH), 7.46(d, J=2Hz, 1, C-3CH); exact mass spectrum calcd. for $C_7H_6IN_3$ 258.9607, found 258.9607.

4-azido-3-iodotoluene was prepared in 2 steps from p-methylaniline by a, I_2, $NaHCO_3$, H_2O; b, $NaNO_2$, HCl, H_2O, THF followed by NaN_3. IR(TF) 2110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30(s,3,CH_3), 7.02(d, J=8Hz, 1,C-5CH), 7.20 (dd, J=2 and 8Hz, 1, C-6CH), 7.62(d, J=2Hz, 1, C-2CH); exact mass spectrum calcd for $C_7H_6IN_3$ 258.9607, found 258.9606.

Scheme 1



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