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OXIDATIVE DEAMINATION OF AROMATIC 1,4-IMINES.
A NEW SYNTHESIS OF POLYNUCLEAR AROMATIC HYDROCARBONS

Gordon W. Gribble*,[1] and Robert W. Allen
Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755

Paul S. Anderson*, Marcia E. Christy and C. Dylion Colton
Merck Sharp & Dohme Research Laboratories, West Point, Pa. 19486

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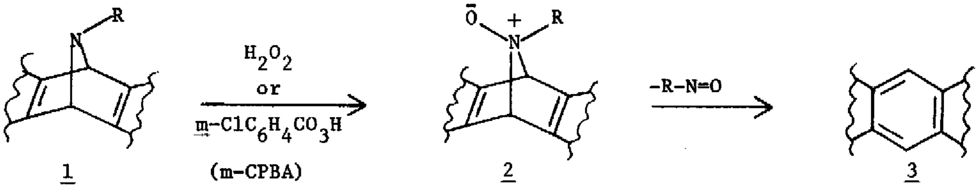
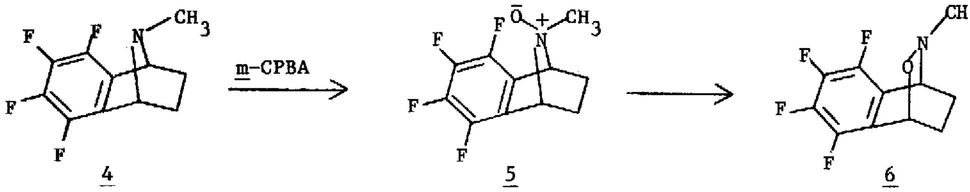
During the course of our studies on the synthesis of 1,4-dihydronaphthalen-1,4-imines[2a,b] and 9,10-dihydroanthracen-9,10-imines,[2c] the observation was made that peroxide or peracid oxidation of these aromatic 1,4-imines 1 rapidly resulted in loss of the nitrogen bridge and formation of the aromatic hydrocarbon 3, most probably via the amine oxide 2. Our results are summarized in the Table.



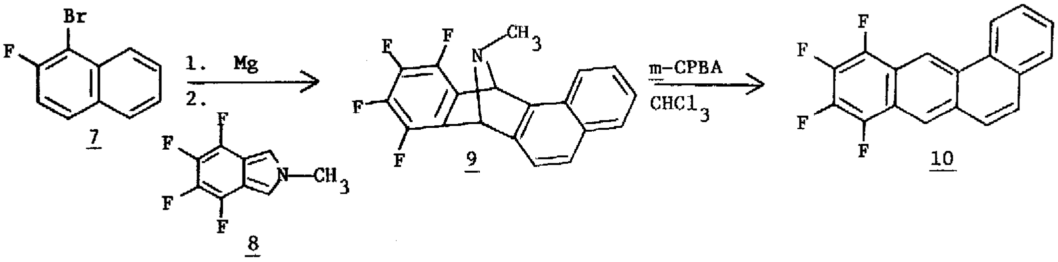
An appealing pathway for the decomposition of the presumed intermediate amine oxide 2 is cheletropic[3] loss of nitrosoalkane. Extrusion of nitrosoalkane is orbital symmetry-allowed to proceed in the *linear* cheletropic[3] sense (local C_s symmetry). This fragmentation has analogy in the decomposition of aziridine *N*-oxides[4] and we have isolated in 65% yield the known[5] dimer of nitrosocyclopropane (m.p. 93-94°; ir (nujol) 3100, 1260, and 1180 cm^{-1}; δ (C_6D_6) 0.5 (m, 2H), 1.2 (m, 2H), and 4.9 (m, 1H) ppm) from the oxidation of *N*-cyclopropyl-5,6,7,8-tetrafluoro-1,4-dihydronaphthalen-1,4-imine. The nitrosocyclopropane monomer can be detected in solution (deep blue) (ir (CCl_4) 1510 (N=O) cm^{-1}; δ (C_6D_6) 0.9 (m, 2H), 2.1 (m, 2H), and 4.0 (m, 1H) ppm), in equilibrium with the dimer. We have also isolated the known[6] dimer of α-nitrosotoluene in 69% yield from the oxidation of 11 (R=C_6H_5, R'=H, X=F) and have observed the formation and isomerization of the dimer of nitrosomethane from the oxidation of 11 (R=CH_3, R'=H, X=F).[7] A Meisenheimer rearrangement of 2 and a *retro* Diels-Alder loss of nitrosoalkane cannot be excluded at the present time. Baldwin,[4] however, has presented evidence excluding 1,2-oxazetidine as an intermediate in the fragmentation of aziridine oxide.

In contrast, the oxidation of saturated amine 4 gives the 1,2-oxazine 6 in 73% yield, the product of a Meisenheimer rearrangement[8] of amine oxide 5.[9]



As might be expected from the reduced nucleophilicity of the nitrogen, the urethane 11 ($R=CO_2C_2H_5$, R'=H, X=F)[10] on treatment with m-chloroperbenzoic acid gave only the corresponding epoxide in 76% yield.

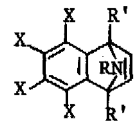
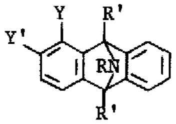
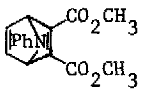
The availability of aromatic 1,4-imines,[2,11] notably from the Diels-Alder reaction of arynes and aza dienes (pyrroles, isoindoles), makes this method of deamination a particularly attractive one for the synthesis of highly substituted or complex polycyclic aromatic hydrocarbons as shown in the Table. For example, in connection with a chemical carcinogenesis study we have prepared 8,9,10,11-tetrafluorobenz[a]anthracene (10) in 64% overall yield from 1,2-naphthalyne (generated from 1-bromo-2-fluoronaphthalene (7)[12] and magnesium) and N-methyl-4,5,6,7-tetrafluoroisoindole (8).[13]



Furthermore, the method affords a very useful synthetic approach to pure monosubstituted anthracenes and, more particularly, to monosubstituted 9,10-dialkylanthracenes, which are difficult to prepare using other methods. For example, 1- and 2-fluoro-9,10-dimethylanthracene were easily synthesized by hydrogen peroxide oxidation of the Diels-Alder adduct 12 formed from 1,2,3-trimethylisoindole and 3- and 4-fluorobenzyne (generated from the appropriate difluorobromobenzene and n-butyllithium), respectively. The convenience of this method becomes apparent on comparison with alternative syntheses from anthraquinones[14] and 3-fluorophthalic anhydride.[15]

It is our view that this method of deamination is preparatively more convenient than two previous methods, involving loss of nitrous oxide from N-nitroso-1,4-dihydronaphthalen-1,4-imine[16] or dieneophile (benzyne, dimethyl acetylenedicarboxylate)-induced deamination of the N-alkyl nitrogen bridge.[11,17] Further applications of this new deamination method to synthetic problems are being investigated.

Table. Oxidation of N-Substituted Aromatic 1,4-Imines

Substrate	R	R'	X	Y	Y'	Method[18]	Product[19] (mp)	Yield,%[20]
 11	CH_3	H	F			A	1,2,3,4-tetrafluoronaphthalene (106°)	90
	$CH_2CH_2CH_3$	H	F			A	1,2,3,4-tetrafluoronaphthalene	89
	$CH_2C_6H_5$	H	F			A	1,2,3,4-tetrafluoronaphthalene	82
	cyclopropyl	H	F			A	1,2,3,4-tetrafluoronaphthalene	91
	C_6H_5	H	F			A	1,2,3,4-tetrafluoronaphthalene	87
	CH_3	CH_3	F			A	1,4-dimethyl-5,6,7,8-tetrafluoronaphthalene (105-107°)	90
	CH_3	H	Cl			A	1,2,3,4-tetrachloronaphthalene (193°)	94
 12	CH_3	H		H	H	B	anthracene	85
	CH_3	CH_3		H	H	B	9,10-dimethylanthracene	85
	CH_3	CH_3		H	H	A	9,10-dimethylanthracene	26
	$CH_2C_6H_5$	CH_3		H	H	A	9,10-dimethylanthracene	38
	cyclopropyl	CH_3		H	H	B	9,10-dimethylanthracene	52
	CH_3	CH_3		F	H	B	1-fluoro-9,10-dimethylanthracene (153-154°)	48
	CH_3	CH_3		H	F	B	2-fluoro-9,10-dimethylanthracene (141-143°)	68
9						A	8,9,10,11-tetrafluorobenz[a]anthracene 10 (258-259°)	92
						A	dimethyl phthalate	72

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References and Notes

1. Recipient of a Public Health Service Research Career Development Award (1 K04-23756) from the National Institute of General Medical Sciences, 1971-1976.
2. (a) P. S. Anderson, M. E. Christy, G. F. Lundell and G. S. Ponticello, Tetrahedron Letters, 2553 (1975); (b) G. W. Gribble, N. R. Easton, Jr., and J. T. Eaton, Tetrahedron Letters,

1075 (1970); (c) Merck & Co. German Patent 2,521,519. C.A., 84, 59189f (1976).

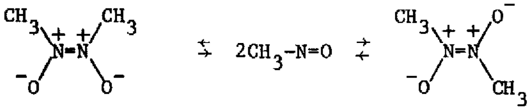
3. R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, GmbH, Weinheim/Berst, 1970, pp. 152-163.

4. J. E. Baldwin, A. K. Bhatnagar, S. C. Choi, and T. J. Shortridge, J. Amer. Chem. Soc., 93, 4082 (1971).

5. R. Stammer, J. B. F. N. Engberts and Th. J. DeBoer, Rec. Trav. Chim., 89, 169 (1970).

6. R. Behrend and E. Konig, Ann., 263, 212 (1891).

7. Thus, treating the amine in CDCl$_3$ with m-CPBA in an nmr tube and following the reaction by nmr showed after 2 min a mixture of the isomeric nitrosomethane dimers in the ratio: 32% trans (δ 4.0 ppm)[21] and 68% cis (δ 4.2 ppm).[21] This ratio gradually changed so that after 40 min only the trans dimer was present. A first-order rate constant could be easily calculated: $k_1 = 1.26 \times 10^{-3}$ sec^{-1} (37°); and from the Eyring equation: $\Delta G^{\neq} =$ 22 kcal/mol. This value agrees with that reported[22] for the energy difference between nitrosoparaffin monomers and dimers (~25 kcal/mol) and perhaps suggests that the monomer is the intermediate in the cis⇄trans dimer interconversion (as shown below).



8. A. C. Cope and P. H. Towle, J. Amer. Chem. Soc., 71, 3423 (1949).

9. For example, treatment of N-methyl-4,5,6,7-tetrachloro-1,2,3,4-tetrahydro-2,3-exo-dideuterionaphthalen-1,4-imine in CDCl$_3$ with an insufficient amount of m-CPBA in an nmr tube readily showed the presence of the starting material: δ 1.2 (s, 2), 2.1 (s, 3), and 4.5 ppm (s, 2); and the amine oxide: δ 1.5 (s, 2), 3.4 (s, 3), and 5.3 ppm (s, 2). After warming the mixture, the 1,2-oxazine could be detected: δ 1.4 (m, 2), 2.2 (s, 3), 4.6 (m, 1), and 5.4 ppm (m, 1).

10. P. S. Anderson, Tetrahedron Letters, 1141 (1976).

11. L. J. Kricka and J. M. Vernon, Adv. Heterocyclic Chem., 16, 87 (1974).

12. We prepared this in 36% overall yield from 2-naphthylamine by a sequence of acetylation, bromination, diazotization, and decomposition of the fluoroborate.

13. G. M. Priestley and R. N. Warrener, Tetrahedron Letters, 4295 (1972).

14. (a) G. Valkanas and H. Hopff, J. Org. Chem., 27, 3680 (1962); (b) S. J. Cristol and J. S. Perry, Jr., Tetrahedron Letters, 1921 (1974).

15. M. Bentov and E. D. Bergmann, Bull. Soc. Chim. France, 1316 (1961).

16. L. A. Carpino and D. E. Barr, J. Org. Chem., 31, 764 (1966).

17. L. J. Kricka and J. M. Vernon, J. Chem. Soc., Perkin I, 766 (1973).

18. Method A: room temperature addition of a slight excess of m-chloroperbenzoic acid to a chloroform or methylene chloride solution of the imine. Method B: addition of excess 30% hydrogen peroxide to a refluxing methanol solution of the imine. Method A was preferred for naphthalenimines while B worked best with anthracenimines.

19. Identified by comparison with commercial material or literature data and/or elemental analysis and mass spectrometry.

20. Yield refers to isolated material obtained after column chromatography, sublimation, or recrystallization.

21. J. P. Freeman, J. Org. Chem., 28, 2508 (1963).

22. J. H. Boyer, "The Chemistry of the Nitro and Nitroso Groups," Part 1, ed., S. Patai, John Wiley and Sons, New York, N.Y., 1969, pp. 253-255.