4-Methyl-1,3-cyclohexadiene-1-carboxaldehyde (35). Method A. A solution of 1.4 g (0.026 mol) of propiolaldehyde[34] and 1.8 g (0.026 mol) of isoprene was kept neat at room temperature for 70 h. Distillation of the reaction mixture yielded 2.0 g (63%) of **35**, bp 84–87 °C (10 Torr) [lit.[23] bp 95.5–96 °C (20 Torr)].

Method B. A solution of 2.8 g (0.052 mol) of **8** and 3.6 g (0.053 mol) of isoprene in 100 ml of Et_2O was kept at room temperature for 70 h. The volatiles were removed in vacuo and the residue weighing 0.34 g was distilled to give 0.14 g of **35**, bp 84–86 °C (11 Torr) [lit.[23] bp 95.5–96 °C (20 Torr)].

Registry No.—**5**, 58983-02-1; **6**, 58983-03-2; **7**, 762-42-5; **8**, 624-67-9; **9**, 58983-04-3; **10**, 58983-05-4; **11**, 58983-06-5; **12**, 58983-07-6; **13**, 58983-08-7; **14**, 557-31-3; **17**, 58983-09-8; **18**, 58983-10-1; **19**, 58983-11-2; **20**, 3054-95-3; **21**, 58983-12-3; **22**, 58983-13-4; **23**, 58983-14-5; **24**, 58983-15-6; **25**, 58983-16-7; **26**, 58983-17-8; **27**, 58983-18-9; **28**, 58983-19-0; **31**, 4214-28-2; **32**, 58983-20-3; **34**, 58983-21-4; PCl_5, 10026-13-8; triethyl phosphite, 122-52-1; isoprene, 78-79-5.

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Electron Impact Induced Fragmentations and Rearrangements of Aliphatic, Heterocyclic Phosphine Oxides[1]

George L. Kenyon,*[2a,3] Dolan H. Eargle, Jr.,[2a] and Charles W. Koch[2b]

Department of Pharmaceutical Chemistry, University of California, San Francisco, California 94143, and Department of Chemistry, University of California, Berkeley, California 94720

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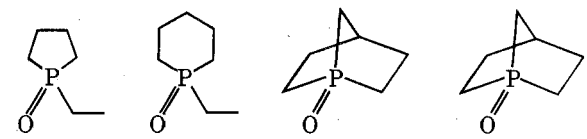
Common electron impact induced fragmentations and rearrangements of 1-ethylphospholane 1-oxide (**1**), 1-ethylphosphorinane 1-oxide (**2**), 1-phosphabicyclo[2.2.1]heptane 1-oxide (**3**), and 1-phosphabicyclo[2.2.2]octane 1-oxide (**4**) were investigated, and the nature of the fragments were compared with those resulting from similar decompositions of trimethylphosphine oxide (**5**), triethylphosphine oxide (**6**), quinuclidine (**7**), and quinuclidine *N*-oxide (**8**). Details of ethylene loss from and concomitant rearrangement of **1** were investigated using specifically deuterium-labeled derivatives. Possible structures for some of the major fragments and rearrangement products are proposed.

Reports of the consequences of electron impaction upon carbonyl-containing organic compounds abound in the chemical literature.[4] In contrast, only a few reports have appeared concerning analogous studies on phosphoryl-containing organic substances; mass spectral studies on the simplest class within this series, aliphatic phosphine oxides, have been even scarcer,[5–8] and these reports have dealt almost exclusively with acyclic phosphine oxides. No systematic studies of the mass spectral behavior of aliphatic, heterocyclic phosphine oxides have appeared up to this time.

We have recently synthesized monocyclic and bicyclic phosphine oxides containing five- and six-membered rings, namely compounds **1–4**.[9] In order to confirm these structural



1 **2** **3** **4**

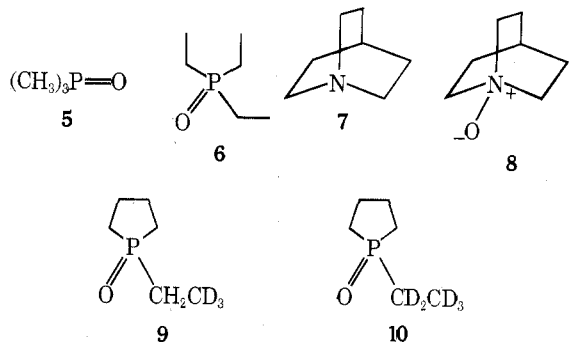
assignments, these compounds were subjected to electron impaction and the ions generated analyzed.[9] In this paper we present much more detailed observations on the fragmentations of **1–4**. Particular attention has been given to molecular rearrangements induced by electron impaction. The fragmentation patterns of trimethylphosphine oxide (**5**), trieth-

Table I. Major Mass Peaks in the Electron-Impact Spectra of 1–4[a]

Species	Fragment lost	Rel intensity, % 1 (132)[e]	2 (146)	3 (130)	4 (144)
M (parent ion)		25.6	51.0	100.0*[b]	100.0*
M − 1	H	15.9	17.8	24.9*	16.1*
M − 15	CH_3	2.0	*d*	6.2*	17.5*
M − 28	C_2H_4	100.0*	100.0*	91.6*	52.4*
M − 42	C_3H_6	*d*	24.7	*d*	1.6*
M − 56	C_4H_8	25.0*	88.9*[c]	2.6*[c]	14.4[c]
M − 68	C_5H_8	*d*	13.2*[c]	*d*	*d*

[a] Complete listings of fragments lost, their relative intensities and metastable transitions (where observed) for compounds examined in this study appear in the microfilm edition of this volume of the journal (see paragraph at end of paper regarding supplementary material). [b] Asterisk denotes confirmation by observation of metastable peak. [c] Metastables were found which indicated that these fragments were derived from other than $[M]\cdot^+$. [d] Less than 2% of the base peak. [e] Compound (mol wt).

ylphosphine oxide (**6**), quinuclidine (**7**), and quinuclidine *N*-oxide (**8**), and specifically deuterated compounds **9** and **10**



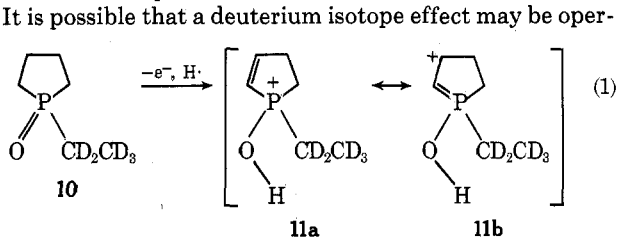
also have been examined in this study for purposes of comparison and mechanistic elucidation. Of the compounds **1–4**, **4** is of potential interest pharmacologically because of its close structural relationship to the quinuclidine moiety of the antimalarial quinine.

Results and Discussion

Complete listings of peaks found, their relative intensities and metastable transitions (where observed) for compounds **1–10** appear in the microfilm edition of this volume of the journal (see paragraph at end of paper regarding supplementary material). Table I summarizes the major peaks observed in the electron-impact mass spectra of heterocyclic phosphine oxides **1–4**. All four compounds gave relatively strong parent ions; indeed, parent ions are the base peaks for the bicyclic phosphine oxides **3** and **4**. Phosphine oxides of this type also exhibit great thermal stability; for example, bicyclic phosphine oxide **4** melts with no apparent decomposition between 291 and 293 °C and may be recovered in high yield after heating for 1 month at 152 °C in 2 N HCl in a sealed tube.[10]

Prominent peaks also appear at M − 1 in all four cases. In order to shed light on the nature of the M − 1 peak, using compound **1** as a specific example, the electron-impact spectrum of compound **10**, perdeuterated on the ethyl group, was examined. Once again a strong M − 1 peak appeared (35.0% of the base peak; see eq 1) whereas the M − 2 peak was only 6.4% of the base peak.

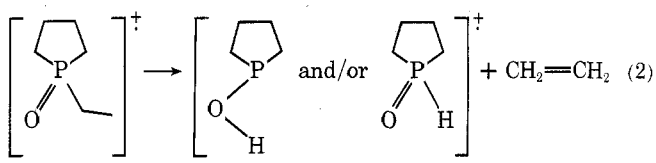
It is possible that a deuterium isotope effect may be operating to discriminate against the loss of a deuterium from the perdeuterated ethyl group of **10**. Owing to the relatively high energies involved in the electron impact process, however, such deuterium isotope effects are, when they have been determined in similar cases, generally rather small (~1–4%).[11,12]



This experiment, which is depicted in eq 1, establishes that the hydrogen which is lost in this specific case must come largely from the ring. Our conclusion is based in part on the assumption that major amounts of H/D scrambling between the ethyl side-chain group and the ring do not occur. This assumption will be examined more quantitatively later in the discussion. Also, that the M − 2 peak is relatively small suggests that deuterium loss from the side chain is minor.

Resonance structures **11a** and **11b** are reasonable representations of the M − 1 peak. Such phosphonium ions as **11a** are the well-known protonation products derived from phosphine oxides;[13] also, having the double bond conjugated in this way imparts some secondary carbonium ion character to the structure. The fact that trimethylphosphine oxide (**5**) has no β hydrogens and no detectable M − 1 peak is consistent with the proposed structure for the M − 1 fragment. Also, the idea leads correctly to the prediction that triethylphosphine oxide (**6**) should have a relatively weak M − 1 peak since, although it has β hydrogens available, the corresponding resonance hybrid representative of its M − 1 peak would have primary rather than secondary carbonium ion character.

Compounds **1**, **2**, and triethylphosphine oxide (**6**) all give base peaks corresponding to M − 28 (M − C_2H_4). In the case of compound **1**, for example, this corresponds for the most part to the rearrangement shown in eq 2. Although this type of



rearrangement has been noted before in the electron impact induced fragmentation of alkyl-substituted phosphine oxides,[7,8] the origin of the hydrogen which remains with the phosphorus-containing fragment has not been previously examined. In order to examine this question, specifically deuterated compounds **9** and **10** were synthesized. Table II shows comparisons among the relative intensities of the pertinent fragments of **1**, **9**, and **10**. Interpretation of the data in Table II is complicated by the fact that the large M − 1 peak (see above) in each case also fragments in an analogous fashion to that shown in eq 2, giving rise in the case of compound **1**, for example, to a strong peak at M − 29. The data of Table II are consistent with the conclusion that *either* an α or a β hydrogen (or deuterium) may migrate to the phosphorus-containing fragment in the course of the rearrangement. In the case of compound **9** at least, α-hydrogen migration dominates;

Table II. Comparison of M − Ethylene Peaks in the Electron-Impact Induced Fragmentations of 1, 9, and 10

Compd	Rel intensity, %[a] 103	104	105	106
1	32.8	(100.0)	5.1	0
9	52.9	(100.0)	33.8	10.5
10	50.7	22.8	(100.0)	10.5

[a] The relative intensities for these particular *m/e* values were normalized to make the largest peak for each compound 100%.

Table III. Evidence for Deuterium Migration into the Ring from the Side Chain in the Electron-Impact Induced Fragmentation of 10

Fragment	Rel intensity, %[a] 1	10
$[C_3H_5]^+$	5.3	20.6
$[C_3H_4D]^+$	0	6.1
$[C_4H_7]^+$	7.7	25.7
$[C_4H_6D]^+$	0	6.6

[a] Relative intensities are reported relative to the base peak in the spectrum of each compound.

this may be reflecting a slight discrimination against β-hydrogen migration owing to operation of a deuterium isotope effect.[11,12]

Another complicating factor in the interpretation of the spectra of **9** and **10** relative to that of **1** is the fact that some H/D scrambling is occurring upon electron impaction. To look at this possibility, fragments of **1** and **10** which have the highest probability of arising *only* from the carbons and hydrogens in the ring were chosen for examination (see Table III). It may be concluded from examination of this data that some deuteriums of **10** are migrating into the ring positions. This suggests that some of the β deuteriums on the ethyl group of **9** may also be migrating to the α positions of this ethyl group, accounting for some of the distribution of deuteriums in the fragments listed in Table II.

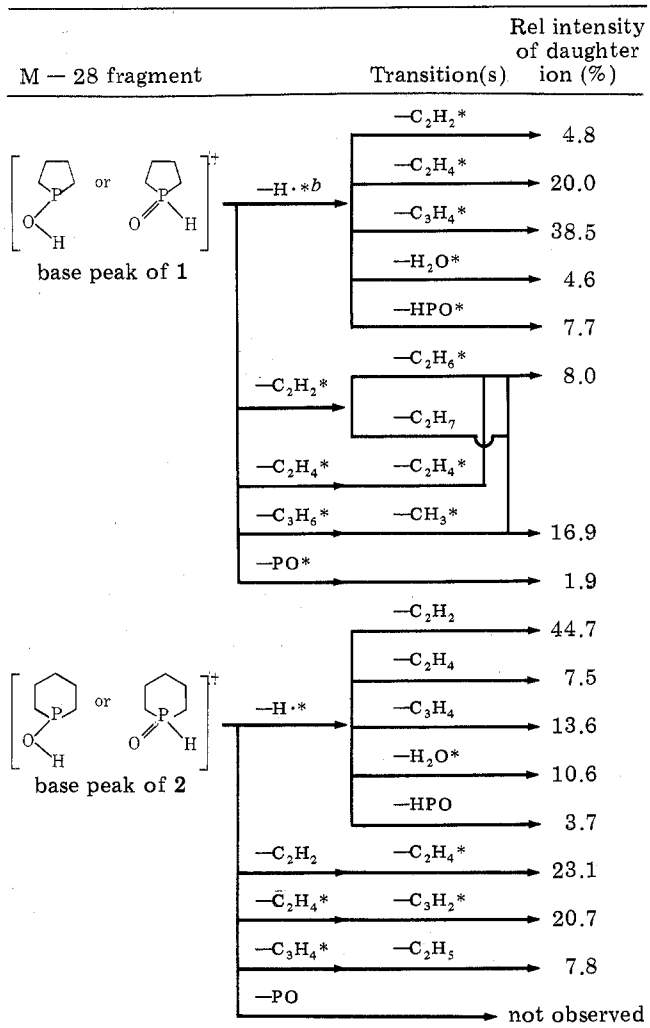
The complications which arise in interpreting the data in Table II are similar to those which were found by those investigating which hydrogen is preferentially abstracted by the carbonyl oxygen in the course of the McLafferty rearrangement.[4] That is, some hydrogens (or deuteriums) which remain with the carbonyl fragment in the McLafferty rearrangement of carboxylic acid esters may come from the α, β, γ, or δ positions.[14,15] Again, only small deuterium-isotope effects appear to be operating.[15] Also, some H/D scrambling reportedly occurs in the McLafferty rearrangement of partly deuterated aliphatic ketones.[16]

Some of the M − 28 peak for **1** is undoubtedly arising from cleavage of C_2H_4 from the ring, rather than from the ethyl group. The evidence for this is that although the base peak of **10** is at *m/e* 105 (corresponding to loss of C_2D_4), a strong peak at *m/e* 109 (51.6% relative intensity) also appears, which corresponds to loss of C_2H_4.

Table IV shows comparisons among the fragmentations of the base (M − 28) peaks in both **1** and **2**. It can be seen that, as in the parent ions themselves, loss of a single hydrogen from these M − 28 peaks is a common process, preceding the loss of many simple fragments. In the case of compounds **9** and **10** many of the fragments corresponding to those shown in Table IV are accompanied by corresponding peaks containing one or more deuteriums, whose relative intensities confirm the notion of H/D scrambling discussed above.

Bicyclic phosphine oxides **3** and **4** show large fragments corresponding to M − 28 (loss of C_2H_4), and each also shows

Table IV. Comparisons among Decompositions of M − 28 (Base) Peaks of 1 and 2[a]

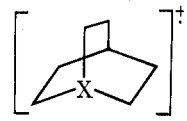


[a] See footnote *a*, Table I. [b] Asterisk denotes confirmation by observation of metastable peak.

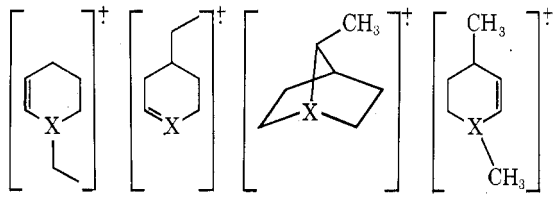
fragments corresponding to M − 15 (loss of CH_3). The relatively large peak (17.5% relative intensity of the base peak) for loss of CH_3 from **4** was quite unexpected. In order to examine the generality of loss of CH_3 from structures of this type, the electron-impact spectra of both quinuclidine (**7**) and quinuclidine *N*-oxide (**8**) were examined.

The electron-impact spectrum of **8**, isoelectronic with phosphine oxide **4**, was quite different in character from that of **4**. Loss of oxygen, a phenomenon observed previously in the electron-impact mass spectra of amine *N*-oxides,[17] is the predominant process. Consequently, a closer parallel to the character of the fragmentation of **4** was found in the fragmentation of quinuclidine (**7**) itself. Indeed many of the peaks observed in the electron-impact mass spectrum of **8** may be shown to be coming from the molecular ion of **7** which is formed from **8** by loss of oxygen. Significantly, the spectrum of **7** shows relatively large peaks corresponding to M − 15 (18.9% relative intensity), M − 28 (29.4%), and M − 29 (34.1%).

In order to account for these observations the following possibility is presented. The molecular ions of both **4** and **7** could be isomerizing via hydrogen shifts into one or more of the structures **4a–d** and **7a–d** shown below. By analogy to the electron-impact fragmentation of **1** [and the M − 1 peaks of **1** (see Table IV)], **4**, for example, would be expected to show relatively large peaks corresponding to the loss of C_2H_4 from **4a** or **4b**, and to the loss of CH_3 from **4c** or **4d**. In an analogous

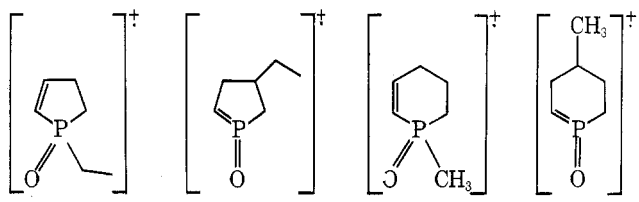


4, X = P=O
7, X = N



4a 4b 4c 4d
7a 7b 7c 7d

fashion, bicyclic phosphine oxide **3** might rearrange into one or more of the following structures (**3a–d**). Again these isomeric rearrangment products may be the parents of at least portions of the M − 15 and M − 28 fragmentation peaks.



3a 3b 3c 3d

The possibility that the hypothetical rearrangements shown above are thermal processes, not induced by electron impaction, was examined as follows. Electron-impact mass spectra for both **4** and **7** were examined as a function of inlet temperature. The relative ratios of peaks (e.g., M vs. M − 15) did not change appreciably over a wide temperature range. Thus, these processes are electron-impact induced. In contrast, the ratio of [M]/[M − 16] for quinuclidine *N*-oxide (**8**) decreased continuously as the inlet temperature was raised; this confirms the idea that loss of oxygen from such amine *N*-oxides is a thermal process.[17]

Experimental Section

Methods. Electron-impact mass spectra of **1–6** were obtained using either a Consolidated Model 21-103C or a Consolidated Model 21-110B double-focusing, high-resolution spectrometer at the University of California, Berkeley, and the corresponding spectra of **9** and **10** were observed at the University of California, San Francisco, using an Associated Electrical Industries MS-12 mass spectrometer coupled to an Infotronics Model 2400 gas–liquid chromatograph (GLC). Electron-impact spectra for **7** and **8** were measured using this same spectrometer with direct injection. Chemical ionization mass spectra were measured at the University of California, San Francisco, using an Associated Electrical Industries MS-902 mass spectrometer with isobutane as reagent gas. ^{1}H NMR spectra were taken using a Varian A-60 spectrometer using Me_4Si as an external standard. Melting points are uncorrected.

Materials. 1-Ethylphospholane 1-oxide (**1**), 1-ethylphosphorinane 1-oxide (**2**), 1-phosphabicyclo[2.2.1]heptane 1-oxide (**3**), and 1-phosphabicyclo[2.2.2]octane 1-oxide (**4**) were all prepared as described previously.[9] Both trimethylphosphine oxide (**5**) and triethylphosphine oxide (**6**) were obtained from K and K Laboratories Inc., Hollywood, Calif.

1-(Ethyl-*2,2,2-d*$_3$) phospholane 1-oxide (9) and 1-(ethyl-*d*$_5$)-phospholane 1-oxide (10) were prepared as follows. The appropriately deuterium-labeled sample of ethanol (BioRad Laboratories, Richmond, Calif.) (1.42 ml, 0.024 mol) was added over 15 min to an ice-cold, stirred solution of 5.0 g (0.026 mol) of freshly distilled *p*-toluenesulfonyl chloride in 10 ml of dry pyridine. The mixture was stirred at 0 °C for 3 h, diluted with 100 ml of ice-cold 6 N HCl, and then extracted with ligroin (bp 30–60 °C). The ligroin extract was washed with 5% NaOH solution and dried over Na_2CO_3. After removal of solvent, 2.20 g (0.011 mol, 46% yield) of appropriately deuterated ethyl *p*-toluenesulfonate remained. Ethyl-*2,2,2-d*$_3$ *p*-toluenesulfonate gave the following NMR spectrum (neat): δ 2.02 (s, 3 H), 3.7 (s, 2 H), 7.02 (d, 2 H, J = 8 Hz), 7.47 (d, 2 H, J = 8 Hz). The NMR spectrum of ethyl-*d*$_5$ *p*-toluenesulfonate measured under identical conditions was the same except that the singlet at δ 3.7 was missing. All peaks were matched with those of ethyl *p*-toluenesulfonate itself.

The appropriately deuterated samples of diethyl ethylphosphonate were prepared by adapting the previously reported procedure of Harvey et al.[18] To a very dry, 100-ml, three-necked flask fitted with a drying tube and two pressure-equalized dropping funnels was added 0.30 g (0.012 mol, 10% molar excess) of NaH (as a 57% mineral oil suspension, Alfa Inorganics) in 30 ml of dry tetrahydrofuran (THF). This and all other solutions used in this portion of the synthesis were flushed with dry N_2 at all stages. In one funnel was placed 5 ml of dry THF and freshly distilled diethyl phosphonate (Aldrich, 1.54 g, 0.011 mol) added by syringe to the solvent. Into the other funnel was placed 5 ml of THF and appropriately deuterated ethyl tosylate (2.29 g, 0.011 mol). The diethyl phosphonate solution was slowly added to the dry ice–methanol-cooled, stirred solution in the flask, and stirring was continued for 0.5 h. Very little foaming occurred. The tosylate solution was then slowly added to the solution at room temperature and allowed to stir for an additional 72 h. At this time 20 ml of H_2O and 30–40 ml of ligroin were added to the solution. This mixture was filtered and the ligroin extracts separated. The aqueous extract was itself extracted with $CHCl_3$ (50 ml), and, after drying over Na_2SO_4 and evaporation of the $CHCl_3$ by a stream of N_2, yielded 0.472 g of deuterated diethyl ethylphosphonate. Diethyl ethyl-*2,2,2-d*$_3$-phosphonate showed the following NMR spectrum ($CDCl_3$): δ 1.0 (t, 6 H, J = 7 Hz), 1.5 (d, 2 H, J = 20 Hz), 3.8 (m, 4 H). Diethyl ethyl-*d*$_5$-phosphonate had the same NMR spectrum ($CDCl_3$) except that the doublet at δ 1.5 was missing.

The deuterated final products, **9** and **10**, were prepared according to the procedure of Wetzel and Kenyon,[9] but miniaturized as follows. To a 100-ml flask, purged with N_2 and containing a solution of freshly distilled 1,4-dibromobutane (Eastman, 0.35 g, 1.62 mmol) in 25 ml of THF, was added 0.77 g of $NaAlH_2(C_2H_5)_2$ (0.15 mmol, a 25% solution in toluene, Ethyl Corp., Baton Rouge, La.) in 5 ml of THF and the appropriately deuterated diethyl ethylphosphonate (0.27 g, 1.63 mmol) also in 5 ml of THF. Transfer of the $NaAlH_2(C_2H_5)_2$ solution was carried out using an N_2-filled syringe. Stirring was continued for 3 days. The final $CHCl_3$ extract was evaporated leaving 88 mg of a mixture of products. This mixture was separated only by use of the GLC–MS system described above, and the appropriate GLC peak (identified by comparison with the retention time for authentic, nonlabeled **1**) was chosen for mass spectral display.

1-Azabicyclo[2.2.2]octane 1-oxide (quinuclidine *N*-oxide, 8) was prepared by the procedure below which was adapted from that reported by Craig and Purushothaman.[19] An attempt to synthesize this compound by the previously reported method[20] was unsuccessful in our hands.

To an ice-cold, stirred solution of 0.198 g (1.34 mmol) of quinuclidine hydrochloride (Aldrich) in 5 ml of $CHCl_3$ was added over a 5-min period 0.278 g (1.34 mmol) of 85% *m*-chloroperbenzoic acid (Aldrich). A precipitate formed soon after the addition which in turn redissolved in about 1 h. The solution was stirred for 12 h at 25 °C. The resulting product mixture was applied to a column of basic alumina (50 × 1.7 cm) which had been prepared with ligroin, and a primary elution was made with $CHCl_3$ to expel unreacted quinuclidine. The quinuclidine *N*-oxide was then eluted with 5% MeOH–$CHCl_3$ (v/v). The benzoic acid remained on the column. After removal of solvent 0.116 g (68% yield) of quinuclidine *N*-oxide remained as a very hygroscopic solid, mp 120 °C dec. Accurate mass measurement of its mass spectral parent ion (M + 1) confirmed its composition: calcd for $C_7H_{14}NO^+$, 128.1075; found, 128.1094. NMR ($CDCl_3$) peaks appeared at δ 2.03 (m, 7 H, β and γ hydrogens), 3.45 (m, 6 H, α hydrogens). Quinuclidine *N*-oxide hydrochloride was prepared by passing excess, dry HCl gas through a $CHCl_3$ solution of quinuclidine *N*-oxide; NMR ($CDCl_3$) peaks appeared at δ 2.25 (m, 7 H, β and γ hydrogens), 3.95 (m, 6 H, α hydrogens), 4.75 (s, 1 H, OH). For comparison, NMR spectra of both quinuclidine (**7**) and quinuclidine hydrochloride were measured under the same conditions. Quinuclidine (**7**) had NMR ($CDCl_3$) peaks at δ 1.56 (m, 7 H, β and γ hydrogens), 2.95 (m, 6 H, α hydrogens). Quinuclidine hydrochloride had NMR ($CDCl_3$) peaks at δ 2.00 (m, 7 H, β and γ hydrogens), 3.41 (m, 6 H, α hydrogens), 5.12 (s, 1 H, NH).

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Registry No.—**1**, 35434-90-3; **2**, 39763-54-7; **3**, 40614-39-9; **4**, 41809-52-3; **5**, 676-96-0; **6**, 597-50-2; **7**, 100-76-5; **8**, 25289-67-2; **9**, 59034-21-8; **10**, 59034-22-9; ethanol-2,2,2-d_3, 1759-87-1; ethyl-2,2,2-d_3 *p*-toluenesulfonate, 24344-87-4; ethyl-d_5 *p*-toluenesulfonate, 59034-23-0; *p*-toluenesulfonyl chloride, 98-59-9; ethanol-d_5, 1859-08-1; diethyl ethyl-2,2,2-d_3-phosphonate, 59034-24-1; diethyl ethyl-d_5-phosphonate, 59034-25-2.

Supplementary Material Available. Two tables, one giving comprehensive listings of relative intensities of peaks observed (and, in some cases, accurately mass-measured) and another listing metastable transitions which have been observed in these studies (23 pages). Ordering information is given on any current masthead page.

References and Notes

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(3) Recipient of a Career Development Award, AM 00014, from the National Institute of Arthritis, Metabolism and Digestive Diseases.
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Meta Bridging Reactions of Electron-Deficient Aromatics. 3. Isomeric Bridging of Di-, Tri-, and Tetranitronaphthalenes to 2- and 3-Benzazocines

Raymond R. Bard and Michael J. Strauss*

Chemistry Department, University of Vermont, Burlington, Vermont 05401

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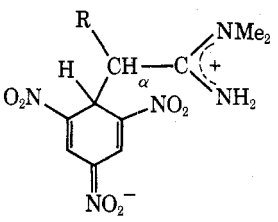
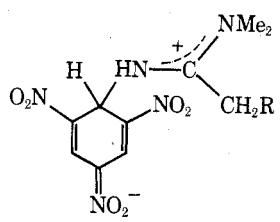
The preparation of a series of 2- and 3-benzazocines is described which utilizes a one-step meta-bridging reaction of polynitronaphthalenes. The mode of bridging depends on the number of nitro groups in the aromatic substrate. A detailed chemical shift analysis is used to assign product structure. Evidence is presented which shows that the precursor of meta-bridged products in benzenoid systems is not a carbon bonded anionic σ complex as previously reported.

We recently reported the novel meta-bridging reactions[1] of electron-deficient benzenes and naphthalenes with amidines.[2] The initial products of such reactions are σ complexes[3-5] which in certain instances undergo intramolecular cyclization to give meta-bridged products.[6] The reaction is a useful synthesis of 1,5-methano-3-benzazocines (6,7-benzomorphans), potentially useful narcotic antagonists.[7,8] Several of the 3-benzazocine amidinium nitronates which we have prepared (vide infra) are long-acting narcotic antagonists in mice.[9] We present here a detailed product study involving reactions of deuterium labeled napthalenes which provides evidence for isomeric modes of bridging. This work allows a more definitive assignment of product structures and provides additional evidence to substantiate the way in which meta bridging occurs.

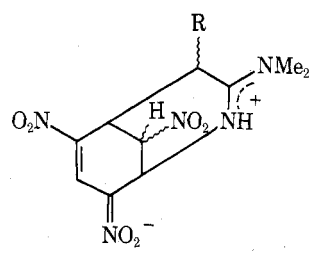
Our previous work[2] resulted in the isolation of only two types of adducts, **1** and **3**, from the reaction of amidines with *sym*-trinitrobenzene (TNB), 1,3-di- and 1,3,6,8-tetranitronaphthalene (DNN and TETNN). When R in the starting amidine was alkyl only adducts like **1** were obtained, with *no evidence for cyclized products like* **3**. The adducts **1** could not be induced to cyclize under a variety of conditions in which the amidine:aromatic ratio was varied. Interestingly, when R



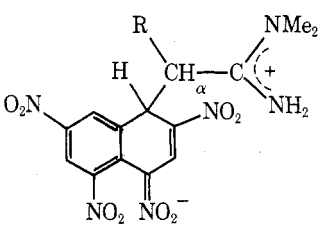
1a



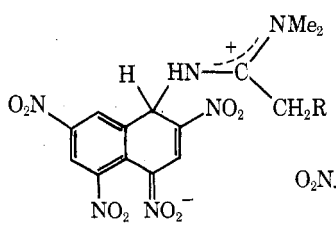
2a



3a (as zwitterion or salt)



1b



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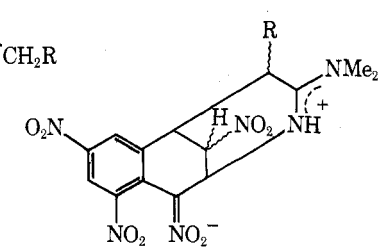

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