2, 6-phenyl), 7.02 (dd, 1, CH), 5.49 (dd, J = 10.7, 0.7 Hz, 1, one of C=CH_2), 4.85 (dd, J = 17.3, 0.7 Hz, 1, one in C=CH_2) 2.15 (s, 3, CH_3); IR (neat) 1742, 1240, 1220, 1018, 1010 cm^{-1}.

3e: yield 80%; NMR ($CDCl_3$) δ 8.7–8.4 (m, 2, 2- and 6-pyridyl), 7.56 (dt, 1, 4-pyridyl), 7.4–6.7 (m, 6, aromatic and CH), 5.39 (dd, J = 11.0, 1.4 Hz), 1, one in C=CH_2), 4.78 (dd, J = 17.4, 1.4 Hz, 1, one in C=CH_2), 3.78 (s, 3, CH_3O), 2.10 (s, 3, CH_3).

3f: yield 80%; NMR ($CDCl_3$) δ 8.6–8.4 (m, 2, 2- and 6-pyridyl), 7.8–7.1 (m, 6, aromatic), 7.08 (dd (partly concealed), 1, CH), 5.43 (br d, J = 11.0 Hz, 1, one of C=CH_2), 4.72 (br d, J = 17.4 Hz, 1, one of C=CH_2), 2.16 (s, 3, CH_3).

3g: yield 86%; NMR ($CDCl_3$) δ 8.8–8.3 (m, 2, 2- and 6-pyridyl), 7.9–7.1 (m, 7, aromatic), 6.96 (dd (partly concealed), 1, CH), 5.39 (br d, J = 11.4 Hz, 1, one of C=CH_2), 4.80 (br d, J = 17.4 Hz, 1, one of C=CH_2), 2.11 (s, 3, CH_3); IR (neat) 1742, 1593, 1408, 1230, 1210, 700 cm^{-1}.

3h: yield 47% (after chromatography); NMR ($CDCl_3$) δ 8.6–8.4 (m, 1, 6-pyridyl), 7.7–6.8 (m, 8, aromatic), 6.49 (dd, 1, CH), 5.36 (dd, J = 11.0, 1.6 Hz, 1, one of C=CH_2), 4.90 (dd, J = 17.6, 1.6 Hz, 1, one of C=CH_2), 2.16 (s, 3, CH_3); IR(KBr) 1730, 1250, 1240, 762, 706 cm^{-1}.

(Z)-3-Acetoxy-1-(4-bromophenyl)-1-(3-pyridyl)propene (6) was prepared from (Z)-3-(4-bromophenyl)-3-(3-pyridyl)-2-propen-1-ol by using the same procedure: yield 80%; NMR ($CDCl_3$) 8.8–8.3 (br s, 2, 2- and 6-pyridyl), 7.6–7.1 (m, 6, aromatic), 6.29 (t, 1, CH), 4.60 (d, J = 7.3 Hz, 2, CH_2O), 2.08 (s, 3, CH_3).

Palladium-Catalyzed Amination of Acetates 3 to 4. Compound 4c. Palladium acetylacetonate (9.3 mg, 0.03 mmol), 1,2-bis(diphenylphosphino)ethane (17.5 mg, 0.04 mmol), and acetate **3c** (211 mg, 0.78 mmol) were dissolved in THF (2.2 mL) at room temperature under nitrogen. A solution of dimethylamine in THF (3.2 mL of a 2.5 M solution) was added, and the resulting mixture was warmed to 55 °C and allowed to react for 1 h and 40 min. Evaporation of the solvent and workup by preparative TLC (silica gel; EtOAc–hexane–Et_3N, 48:48:4) gave 158 mg (79%) of **4c** as a mixture of E and Z isomers (Z/E ratio of 1.2). Anal. Calcd for $C_{16}H_{17}ClN_2$: C, 70.45; H, 6.28; N, 10.27. Found: C, 70.07; H, 6.31; N, 9.94.

The same procedure was used for the amination of the other acetates **3**. Results are given in Table I.

NMR Data for Amines 4 ($CDCl_3$). The 2- and 6-pyridyl protons appear in the region δ 8.6–8.4 and the other aromatic protons in the region δ 7.6–6.9. The detailed spectra of the remaining protons are given in Table III and physical and spectral data in Table IV: mass spectrum of **4d**, m/z (relative intensity) 318 (M^+, 26), 317 (24), 316 (M^+, 27), 315 (21), 240 (21), 238 (25), 193 (99), 192 (44), 161 (37), 70 (67), 58 (100).

Acknowledgment. We are grateful to the Swedish Natural Science Research Council and "Stiftelsen Bengt Lundqvists minne" for financial support. We thank Dr. Brian Pring for linguistic advice.

Registry No. **1a**, 5424-19-1; **1b**, 52779-56-3; **1c**, 14548-44-8; **1d**, 14548-45-9; **1e**, 23826-71-3; **1f**, 77744-06-0; **1f**·HCl, 77744-07-1; **1g**, 14548-46-0; **1h**, 91-02-1; **2a**, 77744-08-2; **2b**, 77744-09-3; **2c**, 77744-10-6; **2d**, 70263-43-3; **2e**, 77744-11-7; **2f**, 77744-12-8; **2g**, 77744-13-9; **2h**, 77744-14-0; **3a**, 77744-15-1; **3b**, 77744-16-2; **3c**, 77744-17-3; **3d**, 77744-18-4; **3e**, 77744-19-5; **3f**, 77744-20-8; **3g**, 77744-21-9; **3h**, 77744-22-0; (E)-**4a**, 58325-71-6; (Z)-**4a**, 58574-55-3; (Z)-**4a** sesquioxalate, 77744-23-1; (E)-**4b**, 77744-24-2; (Z)-**4b**, 77744-25-3; (Z)-**4b** oxalate, 77744-26-4; (E)-**4c**, 77744-27-5; (Z)-**4c**, 77744-28-6; (Z)-**4c** oxalate, 77744-29-7; (E)-**4d**, 56775-89-4; (Z)-**4d**, 56775-88-3; (Z)-**4d**·2HCl, 60525-15-7; (E)-**4e**, 77744-30-0; (Z)-**4e**, 77744-31-1; (Z)-**4e** oxalate, 77744-32-2; (E)-**4f**, 77744-33-3; (Z)-**4f**, 77744-34-4; (Z)-**4f** oxalate, 77744-35-5; (E)-**4g**, 58325-72-7; (Z)-**4g**, 58574-58-6; (E)-**4h**, 35344-68-4; (Z)-**4h**, 35344-69-5; **6**, 77744-36-6; (Z)-3-(4-bromophenyl)-3-(3-pyridyl)-2-propen-1-ol, 77470-73-6; palladium acetylacetonate, 14024-61-4.

A General Synthesis of N-Substituted 2-Azaadamantanes and Their 4,8-Disubstituted Derivatives[1]

James G. Henkel,* William C. Faith, and Jeffrey T. Hane

Section of Medicinal Chemistry and Pharmacognosy, School of Pharmacy U-92, The University of Connecticut, Storrs, Connecticut 06268

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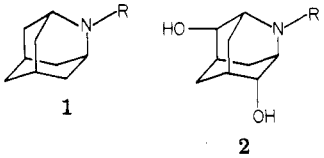
A general synthesis of N-substituted 2-azaadamantanes (1) is reported, along with the corresponding 4,8-dihydroxy derivatives (2). The synthesis offers the advantage of the use of inexpensive and readily available starting material. Dione **3**, obtained by decarboxylation of Meerwein's ester, is converted to diene **4** by Bamford–Stevens-type elimination of the corresponding ditosylhydrazone. Epoxidation of **4** affords diepoxide **12**, which reacts with primary amines to form the 2-azaadamantyl skeleton **2**. Removal of the hydroxyl groups to give **1** is accomplished by using $SOCl_2$ and then $LiAlH_4$.

There has been considerable interest in the chemistry and potential uses of the heteroadamantanes for a number of years.[2] While the 2-oxa- and 2-thiaadamantyl systems have been studied in some detail,[3] the corresponding 2-azaadamantyl system **1** is less familiar. One reason for this may be attendant greater synthetic difficulties for **1**. As part of another project, we had need for a number of N-substituted congeners of **1**, having stereochemically defined *anti,anti*-4,8-dihydroxy substituents, as in **2** (R = H, alkyl, aryl). Although syntheses of derivatives of **1** have



1 2

been reported,[4-9] the products either lack suitable func-

(1) An account of this work was presented at the 181st National Meeting of the American Chemical Society, Atlanta, GA, March 30, 1981.

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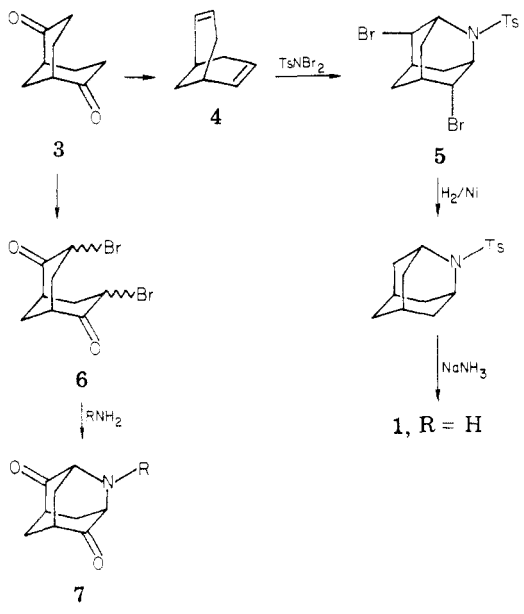
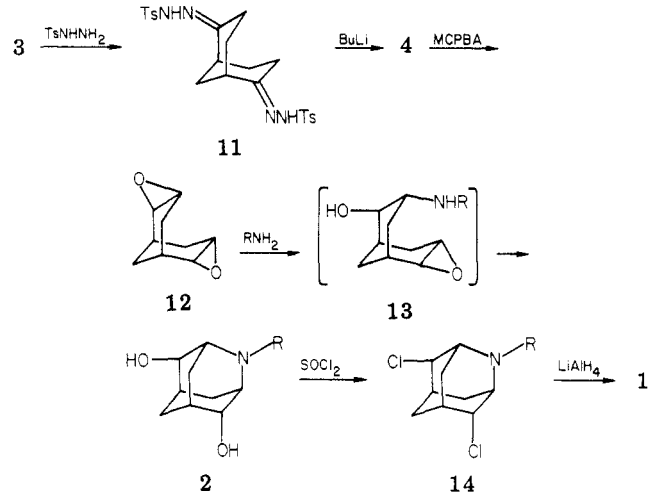
0022-3263/81/1946-3483$01.25/0

Scheme I



Scheme II

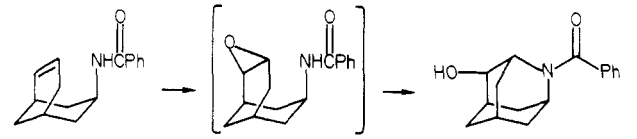


tionalization[4,5,8,9] or are subject to stereochemical ambiguity at the 4- and 8-positions.[6] We report here an improved synthesis of **2** from inexpensive and readily available starting materials. It appears to be general for N substituents (R = alkyl or aryl) and the hydroxyl groups can be easily removed to provide a general route to **1** (R = alkyl, aryl).

All of the reported syntheses of **1** and its derivatives involve transannular cyclization of a bicyclo[3.3.1]nonyl ring system in either a single step[6,7] or in a series of steps.[4,5,8] The most direct approach to both **1** and a precursor with appropriate stereochemistry is by addition of an electrophilic species to bicyclo[3.3.1]nona-2,6-diene **4** as reported by Stetter and Heckel[7] (Scheme I). Diene **4** may be obtained from dione **3**, which may in turn be synthesized by decarboxylation of Meerwein's ester.[9] However, this route contains one or more unfavorable steps and is not applicable to the general case.

Addition of $TsNBr_2$ to **4** proceeds in poor yield (17% at best, in our hands), and the product **5** is isolable only after a lengthy chromatographic separation from polymeric material. Presumably the low yields of ring-closed product result in part from the highly reactive nature of the electrophile and in part from the necessity for initial endo addition of electrophile to **4**. The more favorable exo addition process may account for the presence of polymeric product. Further, the resulting substituent pattern of **5** is nearly unmodifiable, since conditions necessary for removal of the N-blocking function are not compatible with the retention of the 4,8-halides. An alternative pathway based upon a nucleophilic ring closure step[6] (**3** → **7**) also apparently is nonselective, giving complex bromination mixtures, although product yields and experimental details have not been published.

We report here the development of a synthesis of **2** based upon **3**, which we feel to be highly attractive from the standpoint of both convenience and cost. The basis for our efforts was the observation by Staas and Spurlock[8] that the presumed intermediate **9** resulting from epoxidation of benzamide **8** is not isolable but undergoes facile ring closure to **10** during workup. To overcome the



poor product yields of the reactions shown in Scheme I, we sought to reverse the electron flow in the ring-closure reaction. In this approach, a nucleophilic species (presumably an amine) would react with an electrophile derived from diene **4**. If the electrophile is less reactive than that in Scheme I, improved selectivity and consequent product yield may result.[10] The resulting synthesis (Scheme II) is based upon the reaction of the electrophilic diepoxide **12** with a primary amine to produce **2** directly. The synthesis of the parent unsubstituted compound is shown. Dione **3** was obtained from dimethyl malonate and formaldehyde by a modification of the method of Schaefer and Honig[9] in ~29% isolated yield. Treatment of **3** with *p*-toluenesulfonohydrazide produced ditosylhydrazone **11**, which was subsequently converted to diene **4** in 70% isolated yield by the action of *n*-butyllithium in THF in a Bamford–Stevens[11] type elimination.[12] This conversion of **3** to **4** is more convenient than the original method,[4] which involved reduction, bromination, and dehydrohalogenation. Epoxidation of **4** with *m*-chloroperbenzoic acid afforded exo diepoxide **12** in 71% isolated yield after purification by sublimation. The stereochemical assignment for **12** is based upon the well-known stereoselective exo addition of electrophiles to bridged bicyclic alkenes (i.e., to the least-hindered side). Examples of this behavior are commonplace. For example, Marvell et al.[13] noted that epoxidation of bicyclo[3.3.1]nonene with H_2O_2 in benzonitrile afforded exclusively *exo*-bicyclo[3.3.1]nonene 2,3-oxide. Treatment of **12** with ammonia-saturated methanol at 120 °C in a stainless steel reaction vessel afforded *anti,anti*-4,8-dihydroxy-2-azaadamantane **2** (R = H) in 70% isolated yield after recrystallization. Because of the defined stereochemistry of **12**, ring opening of the epoxide rings must occur by endo nucleophilic attack. Following

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Table I. Syntheses of N-Substituted Derivatives of 2

compd	R	% yield[a]	mp, °C[b]
2a	H	70	321 dec
2b	CH_3	90	198–201.5
2c	C_2H_5	69	178–179
2d	$CH_3CH(CH_3)$	63	169–172
2e	$CH_3CH(CH_3)CH_2CH_2$	67	113–116.5
2f	$C_6H_5CH_2$	68	121–123.5
2g	C_6H_5	37	173–174

[a] Expressed as isolated, recrystallized product. [b] Melting point of the free base, uncorrected.

initial reaction of **12** to form what is likely amino epoxide **13**, the extreme proximity of the endo nitrogen and carbon-7 (~1.5 Å) will cause spontaneous ring closure to **2** at a very rapid rate. Such a process is undoubtedly much faster than the spontaneous closure observed by Staas and Spurlock in the case of the corresponding benzamide.[8] Similar transannular ring closure processes have been utilized in other ring systems.[14,15] The anti,anti stereochemistry of the 4- and 8-hydroxyl substituents of **2** is precisely defined by the stereoselectivity of the previous two reactions.

We have found that **2** (R = H) may be easily converted to **1** (R = H) by treatment with $SOCl_2$ to give dichloride **14** (R = H) followed by reductive dehalogenation with $LiAlH_4$. The overall yield of 2-azaadamantane from **3** by this method is ~20%, and considering its convenience and the cost of the reagents, we believe that it is the current method of choice for the synthesis of **1** (R = H). Moreover, the present synthesis appears to be general for both aliphatic and aromatic amino substituents, although the limits of tolerance of *N*-alkyl bulk have not been fully explored. Of particular significance is the demonstrated formation of an *N*-aryl derivative, which to our knowledge is not obtainable by any other route. Table I contains some representative congeners that illustrate the scope of the synthesis investigated to date. All yields are based on isolated, recrystallized products. The product yield for the *N*-phenyl derivative **2g** is significantly lower than those of the aliphatic derivatives **2b–2f**. This is expected, based upon the greatly decreased nucleophilicity of the aromatic nitrogen. Presumably, other activated aromatic derivatives of **2** are also accessible by this method, although deactivated phenyl substituents may present difficulty.

In summary, we have presented what we believe to be the current method of choice for the general synthesis of N-substituted 2-azaadamantanes and their 4,8-dihydroxy derivatives from inexpensive starting materials. This approach should make derivatives of 2-azaadamantane more readily available for future studies.

Experimental Section

General Methods. Melting points were taken on a Thomas-Hoover Mel-Temp apparatus and are uncorrected. Infrared spectra were taken on a Beckman MX-620 spectrophotometer. Proton NMR spectra were obtained on a Hitachi Perkin-Elmer R24B instrument, and ^{13}C NMR spectra were taken on a Bruker WP-60 spectrometer. Tetramethylsilane was used as internal standard, except as noted. High-resolution mass spectra were obtained on an AEI MS-902 mass spectrometer. Commercial reagent grade chemicals were used throughout unless otherwise noted.

Bicyclo[3.3.1]nonane-2,6-dione (3). A mixture of 345 g (2.63 mol) dimethyl malonate, 65 g (2.16 mol) of paraformaldehyde, and 7.5 mL of diethylamine in 540 mL of dry C_6H_6 was heated to reflux for 24 h, with H_2O collected in a Dean–Stark trap. The solvent was removed under reduced pressure, and the resulting pale-yellow oil was taken up in 225 mL of anhydrous CH_3OH and added to a warmed solution of methanolic $NaOCH_3$, prepared from 550 mL of anhydrous CH_3OH and 43 g (1.8 mol) of Na metal. After 24 h at reflux, the solvent was removed, the pale-yellow residue was taken up in ice water and Et_2O, and the layers were separated. The aqueous layer was extracted with 100 mL of Et_2O and then acidified with 6 N HCl, extracted with $CHCl_3$ (3 × 100 mL), dried over Na_2SO_4, and evaporated. The resulting honey-colored product was mixed with 250 mL of glacial acetic acid, 75 mL of 12 N HCl, and 75 mL of H_2O and then heated to reflux for 24 h. The volume was reduced in vacuo to about 300 mL, and the residue taken up in $CHCl_3$ and extracted with saturated $NaHCO_3$ (5 × 100 mL), dried over Na_2SO_4 and evaporated to yield 29.2 g (29%) of **3** after recrystallization from acetone–petroleum ether; mp 142–143 °C (lit.[9] mp 119–135 °C). Spectra were identical to published values.[9,12]

Bicyclo[3.3.1]nona-2,6-diene (4). Conversion of 10.0 g (65.8 mmol) of **3** to the dihydrazone was carried out according to Moreland[12] in 96% yield: mp 185–189 °C (lit.[12] mp 179.5–183 °C); IR (Nujol) 3215, 1402 cm^{-1}; NMR (Me_2SO-d_6) δ 1.25–1.95 (12 H, m) 2.35 (6 H, s, CH_3), 3.37 (2 H, s, NH), 7.26–7.76 (8 H, m, C_6H_4). The product was treated with *n*-BuLi in THF again according to Moreland[12] to afford 5.30 g (70%) of **4** after purification by fractional distillation: bp 105–107 °C (110 mm) [lit[12] bp 158–162 °C (734 mm)]; ^{13}CMR ($CDCl_3$) δ 28.5, 28.7 (C1 + C5 and C4 + C8), 30.9 (C9), 125.0 (C2 + C6), 131.7 (C3 + C7). IR and ^1H NMR were identical with published values.[12]

2,3:6,7-Diepoxybicyclo[3.3.1]nonane (13). To a suspension of 3.47 g (17.1 mmol) of mCPBA in 35 mL of CH_2Cl_2 at 0 °C was added dropwise a solution of 0.854 g (7.12 mmol) of **4** in 35 mL of CH_2Cl_2. After being stirred at room temperature for 31 h, the solution was diluted with an additional 50 mL of CH_2Cl_2, washed with 10% aqueous $NaHSO_3$ (2 × 100 mL), 5% $NaHCO_3$ (3 × 100 mL), H_2O (2 × 100 mL), and then dried over Na_2SO_4 and evaporated to produce 1.30 g of a thick, colorless oil. The oil was subjected to sublimation in vacuo (125 °C, 0.5 mm) to produce 0.771 g (71%) of **13**: mp 148–151 °C; IR (Nujol) 1273, 830, 784 cm^{-1}; NMR ($CDCl_3$) δ 1.33–2.43 (8 H, m), 2.83–3.33 (4 H, m); M^+ found, *m/e* 152.0827 (calcd for $C_9H_{12}O_2$, *m/e* 152.0837).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 69.77; H, 8.08.

2-Azaadamantane-*anti*-4,8-diol (2a). To a solution of 1.0 g (6.6 mmol) of **13** in 7 mL of CH_3OH was added 7 mL of ammonia-saturated CH_3OH. The mixture was heated to 120 °C for 18 h in a steel bomb, which upon cooling yielded 0.966 g (86%) of a white crystalline precipitate, collected by filtration. Recrystallization from absolute EtOH produced 0.786 g (70%) of **2a**: mp 321 °C dec; IR (Nujol) 3283 and 3261 cm^{-1}; NMR (D_2O + DCl) δ (DSS) 1.50–2.60 (8 H, m), 3.50 (2 H, m, CHN), and 4.00 (2 H, m, CHOH); M^+ found, *m/e* 169.1103 (calcd for $C_9H_{15}NO_2$, *m/e* 169.1104).

***anti,anti*-4,8-Dichloro-2-azaadamantane Hydrochloride (14).** A 15.61-g (0.131 mol) quantity of freshly distilled $SOCl_2$ was added dropwise to 0.500 g (3.0 mmol) of **2a** with stirring at 0 °C. The solution was brought to reflux for 2.5 h and the excess $SOCl_2$ was then evaporated, leaving an oily residue, which was triturated with Et_2O to produce 0.543 g (76%) of **14**·HCl as a white solid; mp 272 °C dec. The product was used in the following step without further purification.

2-Azaadamantane (1). A suspension of 0.486 g (2.0 mmol) of **14** in 75 mL of dry THF was combined with a suspension of 0.479 g (12 mmol) of $LiAlH_4$ in 75 mL of THF and brought to reflux with stirring under a N_2 atmosphere for 24 h. After the mixture was cooled, an additional 0.429 g (11.3 mmol) of $LiAlH_4$ was added, and the mixture was brought to reflux for 3 more days. The solvent was evaporated under a stream of N_2 to produce a residue which was suspended in anhydrous Et_2O, to which was successively added 1.0 mL of H_2O, 3.3 mL of 15% aqueous NaOH, and 1.0 mL of H_2O to produce a precipitate, which was filtered with the aid of Celite. The filter pad was washed with hot THF, and the combined organic layers were evaporated to produce a white solid, which was dissolved in 50 mL of CH_2Cl_2 and extracted with 2 N HCl (3 × 150 mL). Solid NaOH was added to the

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combined acidic layers until it was strongly basic. The basic mixture was extracted with CH_2Cl_2 (5 × 150 mL), and the combined extracts were dried over Na_2SO_4 and concentrated to produce 0.181 g (66%) of a gummy tan solid. Purification by sublimation (90 °C, 2 mm) gave **1** as a waxy white solid; mp 224–227 °C (sealed tube) (lit.[4] mp 265–268 °C). Resublimation produced no significant change in melting point. NMR ($CDCl_3$) δ 1.5–2.2 (12 H, m), 2.45–2.75 (1 H, br s, exch), 2.90–3.25 (2 H, br s, NCH); M+ found, *m/e* 137.1208 (calcd for $C_9H_{15}N$, *m/e* 137.1206).

***N*-Methyl-2-azaadamantane-*anti*-4,8-diol (2b).** Treatment of 0.980 g (6.4 mmol) of **12** with CH_3NH_2 using the reaction conditions for **2a** produced 1.06 g (90%) of **2b** after recrystallization from acetonitrile: mp 198–201.5 °C; IR (Nujol) 3362 cm^{-1}; NMR (D_2O + DCl) δ (DSS) 4.30 (1 H, m, CHOH), 4.10 (1 H, m, CHOH), 3.43 (2 H, m, CHN), 3.02 (3 H, s, CH_3), 1.56–2.40 (8 H, m); M^+ found, *m/e* 183.1258 (calcd for $C_{10}H_{17}NO_2$, *m/e* 183.1260).

***N*-Ethyl-2-azaadamantane-*anti*-4,8-diol (2c).** Treatment of 0.50 g (3.29 mmol) of **12** with $EtNH_2$ using the reaction conditions for **2a** produced 0.446 g (69%) of **2c** after recrystallization from acetonitrile: mp 178–179 °C; IR (Nujol) 3338 cm^{-1}; NMR (D_2O) δ (DSS) 1.01 (3 H, t, CH_3), 1.5–2.6 (8 H, m), 2.75 (4 H, m, NCH), 3.95 (2 H, s, CHOH); M^+ found, *m/e* 197.1414 (calcd for $C_{11}H_{19}NO_2$, *m/e* 197.1417).

***N*-Isopropyl-2-azaadamantane-*anti*-4,8-diol (2d).** A solution of 1.00 g (6.58 mmol) of **12** and 1.94 (2.39 mmol) of isopropylamine in 14 mL MeOH was heated at 130 °C in a steel bomb for 24 h. After the solution was cooled, the solvent was evaporated and the residue recrystallized from acetonitrile to produce 0.869 g (63%) of **2d**: mp 169–172 °C; IR (Nujol) 3284 cm^{-1}; NMR (D_2O + DCl) δ (DSS) 1.38 (6 H, dd, CH_3) 1.6–2.6 (8 H, m), 3.55–4.35 (5 H, m, CHNH, CHOH); M^+ found, *m/e* 211.1567 (calcd for $C_{12}H_{21}NO_2$, *m/e* 211.1573).

***N*-Isoamyl-2-azaadamantane-*anti*-4,8-diol (2e).** Treatment of 1.00 g (6.58 mmol) of **12** with 2.87 g (32.9 mmol) of isoamylamine using the reaction conditions for **2d** produced 1.058 g (67%) of **2e** after recrystallization from acetonitrile: mp 113–116.5 °C; IR (Nujol) 3320 cm^{-1}; NMR (D_2O + DCl) δ (DSS) 0.92 (6 H, d, CH_3), 1.4–2.4 (11 H, m), 3.20–3.67 (4 H, m, CHN), 4.12 (1 H, m, CHOH), 4.28 (1 H, m, CHOH); M^+ found, *m/e* 239.1874 (calcd for $C_{14}H_{25}NO_2$, *m/e* 239.1886).

***N*-Benzyl-2-azaadamantane-*anti*-4,8-diol (2f).** Treatment of 1.00 g (6.58 mmol) of **12** with 3.52 g (33.0 mmol) freshly distilled benzylamine using the reaction conditions for **2d** produced 1.157 g (68%) of **2f** after recrystallization from benzene: mp 121–123.5 °C; IR (Nujol) 3440 cm^{-1}; NMR (D_2O + DCl) δ (DSS) 1.75–2.42 (8 H, m, ring CH_2, CH), 3.43, 3.49 (2 H, br d, CHN), 4.15 (1 H, m, C*H*OH), 4.54–4.70 (3 H, m, C*H*OH, CH_2Ph), 7.54 (5 H, s, Ph); M^+ found *m/e* 259.1566 (calcd for $C_{16}H_{21}NO_2$, *m/e* 259.1573).

***N*-Phenyl-2-azaadamantane-*anti*-4,8-diol (2g).** To a stirred solution of 0.400 g (2.63 mmmol) of **12** dissolved in 5 mL of trifluoroethanol under N_2 was added 0.270 g (2.89 mmol) of freshly distilled aniline. The mixture was brought to reflux for 2 days and then stirred at room temperature for 5 days. Column chromatography on silica gel eluting with CH_2Cl_2/acetone (85:15) produced 0.237 g (37%) of **2g**: mp 173–174 °C; IR (Nujol) 3320, 1595, and 1497 cm^{-1}; NMR (D_2O + DCl) δ (DSS) 1.98–2.11 (6 H, m, ring CH_2's), 2.49 and 2.54 (2 H, br d, ring CH's), 4.25 and 4.34 (4 H, br d, NCH and C*H*OH), 7.59–7.71 (5 H, m, Ph); M^+ found, *m/e* 245.1413 (calcd for $C_{15}H_{19}NO_2$, *m/e* 245.1417.

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Registry No. **1**, 768-41-2; **2a**, 78127-55-6; **2b**, 78127-56-7; **2c**, 78127-57-8; **2d**, 78127-58-9; **2e**, 78127-59-0; **2f**, 78127-60-3; **2g**, 78127-61-4; **3**, 16473-11-3; **4**, 13534-07-1; **11**, 13534-08-2; **12**, 78127-62-5; **14**·HCl, 78127-63-6; ammonia, 7664-41-7; methylamine, 74-89-5; ethylamine, 75-04-7; isopropylamine, 75-31-0; isoamylamine, 107-85-7; benzylamine, 100-46-9; aniline, 62-53-3.

Synthesis of Novel Phosphorus Heterocycles: 2-Aryl-1-methyl-2,3-dihydro-1*H*-2,1-benzazaphosphole 1-Oxides

J. A. Miles, R. C. Grabiak,* and M. T. Beeny

Research Department, Monsanto Agricultural Products Company, St. Louis, Missouri 63166

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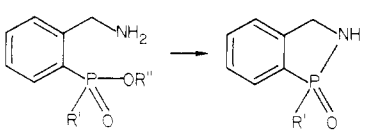
A class of novel phosphorus heterocycles, 2-aryl-1-methyl-2,3-dihydro-1*H*-2,1-benzazaphosphole 1-oxides (**1**), has been prepared, beginning with the nickel-catalyzed Arbuzov reaction of diethyl methylphosphonite and *o*-iodotoluene and ending with an intramolecular alkylation of the suitably substituted phosphinanilide **18**. Overall yields for the five-step synthesis are generally in the 30–50% range. The crystalline 2,3-dihydro-1*H*-2,1-benzazaphosphole 1-oxides are stable, easily handled compounds with interesting chemical and spectral properties. In particular, the carbon-13 chemical shifts of the aromatic carbons in the benzazaphosphole nucleus were assigned according to the magnitude of the carbon–phosphorus coupling constants as well as by consideration of the mesomeric effects of the phosphorus substituent. Also, the phosphorus-31 chemical shifts of the monosubstituted *N*-aryl derivatives correlated with Hammet values (r = 0.9951), suggesting that π_{p-d} back-donation by the nitrogen lone pair was significant.

In the past decade there has been continuing interest in phosphorus heterocyclic chemistry, prompted to a large extent by developments in the concepts of pseudorotation[1] and pentacoordinate phosphorus chemistry.[2] Interest in our laboratories has focused on a variety of benzo-fused ring systems featuring the C–P–X–C linkage (X = O, N). Several syntheses of five- and six-membered C–N–P heterocycles **2**–**6** (Chart I) have appeared in the literature.[3-8]

Scheme I



7 **1**

(1) *Organophosphorus Chem.*, 1–8 (1963–1979), and references therein.

(2) For a comprehensive reference of current organophosphorus chemistry, see L. Maier and G. M. Kosalopoff, Eds., "Organic Phosphorus Compounds", Vol I–VII, Wiley Interscience, New York, 1976.

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