TABLE I
PRODUCTS OF THE COUPLING REACTION OF 1-BROMOADAMANTANES WITH GRIGNARD REAGENTS

Starting material	Grignard reagent, *M* (ethyl ether soln)	Molar ratio, RMgX/I	Coupling product, yield	Yield of adamantane[h]
Ia	CH_3MgBr, 3	3.2	IIa, 83%[a]	
Ia	CH_3MgI, 1.5	1.5	IIa, 70%[b]	
Ib	CH_3MgBr, 3	3.7	IIb, 92%[c]	
Ia	C_2H_5MgBr, 2	7.2	IIc, 39%[d]	36%[g]
Ia	*tert*-C_4H_9MgBr, 2	5.4	IId, 0%[e]	84%
Ia	$C_6H_5CH_2MgBr$, 2	2.0	IIe, 38%[f]	48%[g]
III[k]	CH_3MgBr, 3	3.5	IV, 87%[i]	
V[l]	CH_3MgBr, 3	3.5	VI, 90%[j]	

[a] Mp 102–103° (lit.[5a] mp 103°). [b] Mp 101–103°. 1-Iodoadamantane was formed in *ca.* 10% yield, mp 74–76° (lit.[12] mp 75.3–76.4°). [c] Bp 82° (13 mm) [lit.[5b] bp 88–89.5° (19 mm)]. [d] Separated by glc; nmr spectrum identical with literature.[3] [e] For a method of preparation of IId, see ref 13. [f] Mp 42–44° (lit.[14] mp 43–44°). [g] Yields by glc. [h] Reduction product; see text. [i] Mp 109–111°. [j] Mp 215–218°. See ref 8. [k] Reference 15. [l] Reference 16.

Experimental Section

General Procedure.—A high pressure aerosol glass bottle (Fischer and Porter Co.) was charged with 10 mm of the bromoadamantane (Ia or Ib[18]) and the quantities of the Grignard reagents are given in Table I. (It is important to use concentrated reagents. Lower yields are obtained with lower concentrations.) In the case of CH_3MgBr, commercial (Arapahoe Chemicals) reagent was used; otherwise the Grignard solutions in ethyl ether were prepared in the usual manner. The bottle was flushed with nitrogen and closed tightly. The reaction mixture was stirred magnetically while being heated in an oil bath at 90–100°. After about 10 min of heating, a white precipitate typically was observed; the total heating time was 20–30 min. After cooling, 20 ml of pentane was added and the excess Grignard reagent destroyed by cautious addition of 2% aqueous HCl at 0°. The layers were separated; the aqueous one was extracted with three 10-ml portions of pentane. The combined organic solutions were washed with 20 ml of 10% aqueous K_2CO_3, two 20-ml portions of water, and then dried over Na_2SO_4. After evaporation of the solvent through a Vigreux column, the product was isolated in an appropriate manner: sublimation *in vacuo* (IIa), distillation *in vacuo* (IIb), or preparative gas chromatography (20 ft × 0.25 in. 15% Carbowax 20M at 177°) (IIc and IIe). Table I provides further details. The identity of the products was confirmed by nmr and mass spectroscopy.[11,12]

Summary of Other Experiments. A. Refluxing Solvents.—Reaction of Ia with excess methylmagnesium bromide in refluxing ether solution gave only 13% IIa after 5 hr and 20% after 18 hr. If the ethyl ether was replaced by adding tetrahydrofuran and distilling off the lower boiling solvent, no IIa was observed after 50 min. A similar experiment employing dioxane in place of tetrahydrofuran led to the formation of a precipitate; refluxing this heterogenous mixture (after removal of ethyl ether) gave only 16% IIa in addition to unreacted starting material.

When 1-bromoadamantane (Ia) was refluxed with a 4 molar excess of methyllithium in ethyl ether, 1-methyladamantane (IIa) formed very slowly. The yields follow: after 2 days, 7%; 3 days, 14%; 5 days, 20%. The only other compound detected was starting material.

B. Use of $FeCl_3$ in Attempted Preparations of IId.—These reactions were carried out at *ca.* −65°.[19] Three attempts were made: anhydrous $FeCl_3$ (Fisher Scientific Co.) was dissolved in the ether solution of *tert*-C_4H_9MgBr and then Ia in ether added, $FeCl_3$ was added together with Ia to the Grignard solution, and $FeCl_3$ was added to the solution of Ia in the Grignard reagent. In no case did the nmr spectrum of the product show any significant formation of 1-*tert*-butyladamantane (IId).[13]

1-Methyladamantane-methyl-^{14}C.—1-Methyladamantane-methyl-^{14}C (specific activity 0.34 nCi/mg C) was obtained in 64% yield following the general procedure described above. Grignard reagent, prepared from 5.6 g (32 mmol) of $^{14}CH_3I$ (specific activity 3.80 nCi/mgC) and 730 mg (30 mg-atoms) of magnesium turnings in 20 ml of anhydrous ether, and 1-bromoadamantane (4.3 g, 20 mmol) were stirred at 100° for 30 min, followed by the usual isolation procedure.

The product was subjected to the Kuhn–Roth oxidation following the reported procedure.[9a] The acetic acid (isolated as thallous salt)[10] had a specific activity of 1.83 nCi/mg C. The Schmidt degradation[9b] of the TlOAc gave inactive CO_2 and methylamine which was assayed as *N*-phenyl-*N'*-methylthiourea (specific activity 0.46 nCi/mg C corresponding to 100.5% of the activity in the TlOAc).

1-Methyladamantane-methyl-^{13}C.—1-Methyladamantane-methyl-^{13}C was prepared as described for 1-methyladamantane-methyl-^{14}C using $^{13}CH_3I$ (70% ^{13}C). The (M + 1)/M ratio 151/150 (corresponding to 1-methyladamantane-^{13}C/1-methyladamantane) showed 71% of ^{13}C labeled molecules. The (M + 1)/M ratio 136/135 (corresponding to adamantyl-^{13}C/adamantyl) was found to be essentially the same as that of unlabeled 1-methyladamantane.

1-Benzyladamantane (IIe).—This compound had been prepared in the literature by a different route, but no spectral details were provided.[14] The mass spectrum shows a pattern characteristic of 1-alkyladamantane: the ring signal for the adamantyl cation (*m/e* 135) was the most intense. In addition, a strong molecular ion peak (*m/e* 226) and a strong peak from the benzyl group (*m/e* 91) were observed. Nmr spectrum in $CDCl_3$ showed C_6H_5 (m, δ 7.4–6.9, 5 H), $C_6H_5CH_2$ (s, 2.39, 2 H), adamantyl bridgehead protons (broad s, 1.9 3 H), adamantyl methylene protons (m, 1.4–1.7, 12 H).

3-Methylhomoadamantane (IV).—This compound was prepared from 3-bromohomoadamantane (III)[15] in 87% yield following the general procedure (above): mp 109–111°; nmr (15% in $CDCl_3$) CH_3 (s, δ 0.90, 3 H), the remainder of homoadamantane spectrum[20] appearing in the range δ 1.3–2.2 17 H; mass spectrum *m/e* 149 (base peak, $M^+ - CH_3$), 164 (M^+).

Anal. Calcd for $C_{21}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.46; H, 12.02.

1-Methyldiamantane (VI).[5]—1-Methyldiamantane[5] was prepared in 90% yield from 1-bromodiamantane[16] following the general procedure: mp 215–218°; nmr (~15% in $CDCl_3$) CH_3 (s, δ 0.93, 3 H), the remainder of the spectrum, δ 1.25–2.35, 19 H; mass spectrum *m/e* 187 (base peak, $M^+ - 15$), 202 (M^+).

Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96 Found: C, 89.32; H, 11.08.

Registry No.—IIe, 7131-11-5; IV, 26460-75-3; VI, 26460-76-4.

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(18) K. Gerzon, E. V. Krumkalns, R. L. Brindle, F. J. Marshall, and M. A. Root, *J. Med. Chem.*, **6**, 760 (1963).

(19) At higher temperatures $FeCl_3$ catalyzes a disproportionation of the adamantyl halides: F. N. Stepanov, G. I. Danilenko, V. M. Buzash, and K. Daisi, *Zh. Org. Khim.*, **5**, 2187 (1969); *Chem. Abstr.*, **72**, 66461u (1970).

(20) S. H. Liggero, P. von R. Schleyer, and K. C. Ramey, *Spectrosc. Lett.*, **2**, 197 (1969).

Anomalous Nitration in the 2,1,3-Benzothiadiazole Series

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Although examples of the replacement of nuclear bromine by a nitro group during nitration of aromatic bromo compounds have been known for several

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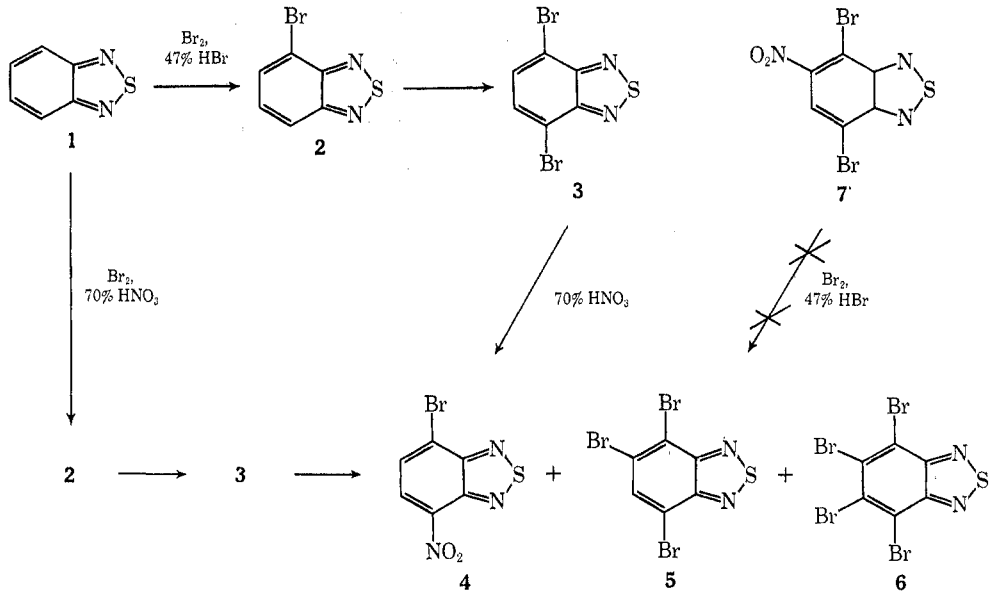
SCHEME I



years,[1-3] the mechanism of the displacement and the fate of the replaced bromine have not received much attention despite the synthetic usefulness of several of these reactions. Experimental data have now been obtained which give a clue to a probable reaction mechanism and which establish, in part, the fate of the displaced aromatic bromine.

We wish to report the direct observation of the formation and disappearance of 4,7-dibromo-2,1,3-benzothiadiazole (**3**) in the course of the bromination of 2,1,3-benzothiadiazole (**1**) in refluxing 70% nitric acid. In following the reaction by gas–liquid chromatography (glc) and thin layer chromatography (tlc), the formation of **3** *via* the monobromo analog **2** was shown to be very rapid (0.5–1 hr) until all of **1** is converted. Subsequently, **3** reacted more slowly (3–6 hr) to give a mixture of 4-bromo-7-nitro-2,1,3-benzothiadiazole **4**, 4,5,7-tribromo-2,1,3-benzothiadiazole (**5**), and 4,5,6,7-tetrabromo-2,1,3-benzothiadiozole (**6**) in the approximate molar proportion of 8:2:0.1 in 50–60% total yield.[4] Furthermore, it was demonstrated independently that treatment of **3** with refluxing 70% nitric acid over a period of 3–6 hr in the absence of bromine produces the same three compounds, **4**, **5**, and **6** in approximately the same ratio and yield. Fractional crystallization of the reaction mixture from acetone afforded **4**. Compounds **5** and **6** were separated by preparative tlc.[6] Compounds **4**[7a] and **5**[7b] were indistinguishable from authentic samples on the basis of comparisons of mixture melting points and thin layer and gas chromatograms.

It is important to note the failure to detect in the reaction mixture 4,7-dibromo-5-nitro-2,1,3-benzothiadiazole (**7**), which would result from electrophilic attack of nitrating species on the 5 position of **3**. Also striking is the observation that, when an authentic sample of **7** was treated with excess bromine in refluxing 70% nitric acid over a period of 5 hr, it was recovered unchanged.

The failure to observe **4** very early in the reaction of **1** with bromine in refluxing 73% nitric acid suggests that either the cationic bromine species is a much stronger acid and therefore a more powerful reagent in electrophilic substitution reactions than is the nitrating species or that by mass action the concentration of cationic bromine species is far in excess. The nitronium ion (NO_2^+) concentration in 100% nitric acid is about 4% and decreases with increasing water content.[8] It seems probable, therefore, that the nitrosonium ion (NO^+) which is a much less powerful reagent in electrophilic substitution reactions than the nitronium ion may be the substituting species, and one can see why cationic bromine species can compete with this weaker electrophile or any other than the nitronium ion. The resulting nitroso compound would be, in turn, very rapidly oxidized by nitric acid to the corresponding nitro compound **4**.

The formation of **5** can be characterized as nucleophilic displacement by the heterocycle **3** of the cationic bromine species formed in the above displacement step; the bromine atom, in its displacement by the nitrating species, may not assume a cationic charge but rather be accepted by **3** acting as a nucleophile to form **5**, a process which might be called an Se2 mechanism (Scheme I).

Experimental Section

Reaction of 4,7-Dibromo-2,1,3-benzothiadiazole (3) with Refluxing 70% Nitric Acid.—A mixture of 29.4 g (0.1 mol) of **3** in 150 ml of 70% nitric acid was heated under reflux with stirring. After 5 hr, the resulting clear solution was poured into 500 ml of ice water, and the product was filtered, washed well with water, and dried to give 14.2 g (50.8%) of light yellow crystalline solid. Gas–liquid chromatography indicated a mixture of two (major)

(1) D. V. Nightingale, *Chem. Rev.*, **40**, 117 (1947).
(2) D. J. Rabiger and M. M. Joullié, *J. Org. Chem.*, **26**, 16949 (1961).
(3) I. T. Barnish and M. S. Gibson, *J. Chem. Soc., C*, 8 (1968).
(4) When bromine was added dropwise at 126–130° to a mixture of **1** in 47% (constant boiling) hydrobromic acid, 4-bromo-2,1,3-benzothiadiazole (**2**) was formed exclusively at first. Toward the halfway point of the addition, glc indicated that the 4,7-dibromo analog, **3**, began to form. After completion of the bromination, **3** was isolated in almost quantitative yield.[5]
(5) K. Pilgram, M. Zupan, and R. D. Skiles, *J. Heterocycl. Chem.*, **7**, 629 (1970).
(6) Preparative tlc plates silica gel F_{254}, E. Merck A.G., Darmstadt, Germany. Solvent mixture (by volume): tetrahydrofuran (2), ethyl acetate (8), and *n*-hexane (40).
(7) (a) V. G. Pesin, A. M. Khaletskii, and V. A. Sergeev, *Gen. Chem. USSR*, **33** (2), 1714 (1963); (b) *ibid.*, **33** (2), 935 (1963).
(8) P. B. D. De la Mare and J. H. Ridd, "Aromatic Substitution–Nitration and Halogenation," Academic Press, New York, N. Y., 1959, pp 59–60. According to the referee, it is doubtful that any nitronium ion is present in 70% nitric acid.

components in the approximate ratio of 4:1 in addition to traces of **3** (starting material) and a third (minor) component. Fractional crystallization of the crude solid from acetone afforded 4.1 g of **4**: mp 214–218° (lit.[6a] mp 218–220°); ir spectrum (KBr pellet) intense bands at 1525 and 1350 cm^{-1} (NO_2).

Anal. Calcd for $C_6H_2BrN_3O_2S$: Br, 30.8; S, 12.3. Found: Br, 30.7; S, 12.6.

The combined mother liquors were concentrated to dryness. Fractional crystallization of the residual solid from ethanol gave 0.7 g of **5**, mp 155–157° (lit.[6b] mp 152–154°).

Anal. Calcd for $C_6HBr_3N_2S$: Br, 64.3; N, 7.5. Found: Br, 64.0; N, 7.7.

The combined mother liquors were concentrated to dryness. The residual solid (8.9 g) was resolved into its components by preparative tlc.[5] The first fraction, 120 mg (0.5%), consisted of **6**, a white crystalline solid melting at 144–145° (from methanol).

Anal. Calcd for $C_6Br_4N_2S$: C, 16.0; H, 0.0; Br, 70.8; N, 6.2; S, 7.1. Found: C, 16.0; H, 0.2; Br, 71.0; N, 6.2; S, 7.4.

The second fraction consisted of **3** (starting material) and was discarded. Fraction no. 3 consisted of 1.2 g of **5**; fraction 4 consisted of 5.1 g of **4**. The total yield of **4** was 35.3%; the total yield of **5** was 7.6%.

Reaction of 2,1,3-Benzothiadiazole (1) with Bromine in Refluxing 70% Nitric Acid.—A mixture of 27.2 g (0.2 mol) of **1** in 300 ml of 70% nitric acid was heated under reflux with stirring while 144 g (0.9 mol) of bromine was added within 30 min. After about 1 hr, a white crystalline solid precipitated from the refluxing solution; it was shown to be 4,7-dibromo-2,1,3-benzothiadiazole (**3**) (by glc), mp 188–189° (lit.[9] 184–185°). However, the precipitate redissolved gradually. After 6 hr, glc indicated that starting material **1** and intermediate **3** had disappeared. The cooled reaction mixture was poured into water and the product was filtered, washed well with water, and dried to yield 28.8 g (51.5%) of a light yellow crystalline solid consisting of a mixture of **4**, **5**, and **6** in the ratio of 84:14:2 (by glc).

Registry No.—**3**, 15155-41-6; **4**, 26460-78-6; **5**, 26460-79-7; **6**, 26460-80-0.

(9) V. G. Pesin, A. M. Khaletskii, and C. Chzhi-Chzhun, *J. Gen. Chem. (USSR)*, **27**, 1648 (1957).

Photolytic Studies on 4-Hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl, a Stable Nitroxide Free Radical

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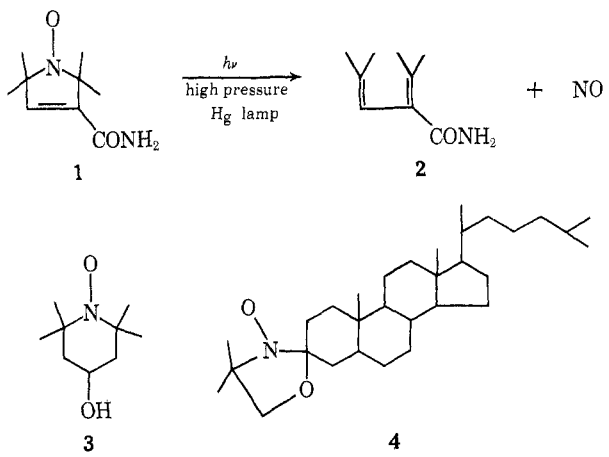
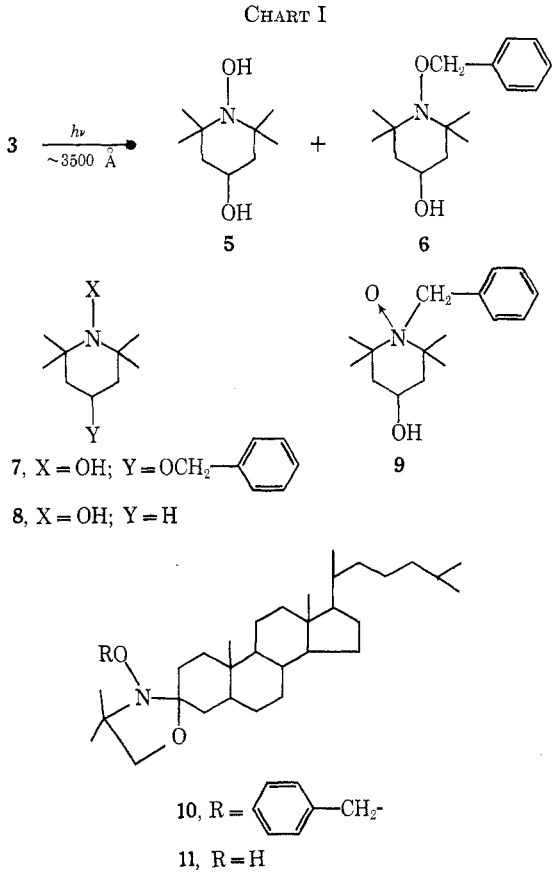
Recently,[3] we reported on the photolysis of the stable nitroxide, 3-carbamoyl-2,2,5,5-tetramethylpyrroline-1-oxyl (**1**), a process which afforded diene **2** in high yield. Under the same conditions the alcohol nitroxide **3** and the steroid nitroxide **4** underwent reaction at a much slower rate. We have now examined the photolysis of nitroxides **3** and **4** under somewhat different conditions. The products are in marked contrast to those derived from nitroxide **1** and are reported herewith.

Irradiation of a vacuum-degassed toluene solution



which was ~0.02 *M* in 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (**3**)[4] for 96 hr in sealed Pyrex tubes with ~3500 Å light resulted in almost complete (>98%) disappearance of starting material as estimated by esr spectroscopy. Removal of the solvent, followed by trituration of the resulting solid with benzene afforded a crystalline residue of 1,4-dihydroxy-2,2,6,6-tetramethylpiperidine (**5**)[5] (Chart I) (~50% crude yield).

CHART I



A recrystallized sample was shown to be identical with authentic **5**[5] by mixture melting point and spectral comparisons. Chromatography of the benzene-soluble

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(1) NDEA Graduate Fellow, 1966–1969; PRF Graduate Fellow, 1969–1970.

(2) Undergraduate Research Participant, 1966–1968.

(3) J. F. W. Keana and F. Baitis, *Tetrahedron Lett.*, 365 (1968).

(4) E. G. Rozantsev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **12**, 2187 (1964); *Chem. Abstr.*, **62**, 7721e (1965).

(5) E. G. Rosantsev and V. A. Golubev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **5**, 891 (1966); *Chem. Abstr.*, **65**, 10559e (1966).