TABLE I

Amine N-oxide	Yield, %
Trimethylamine N-oxide	96
Tribenzylamine N-oxide	96
Dimethylaniline N-oxide	94
Nicotine N′-oxide	98
Nicotine N,N′-dioxide	98[a]
Codeine N-oxide	98
Morphine N-oxide	86[b]

[a] Using 2.0 molar equiv of *m*-chloroperbenzoic acid. [b] The solvent in this experiment was tetrahydrofuran. Methylation with diazomethane gave codeine N-oxide, identical by melting point, mixture melting point, and tlc.

cooled, stirred solution of 1.0 mol of the amine in chloroform. Stirring was continued for a total of 3 hr, during which the mixture was allowed to come to room temperature. The solution was passed through a column of alkaline alumina (100–200 mesh, *ca.* 20 times the weight of the combined starting materials), and traces of unreacted amine were removed by washing with chloroform. Elution with methanol–chloroform (1:3) then gave the amine N-oxide in the yield stated in Table I, after crystallization from alcohol–ether or acetone–hexane. All compounds had the melting points reported in the literature, and gave single spots on tlc.

Registry No.—*m*-Chloroperbenzoic acid, 937-14-4; trimethylamine N-oxide, 1184-78-7; tribenzylamine N-oxide, 6852-46-6; dimethylaniline N-oxide, 874-52-2; nicotine N,N′-dioxide, 2055-29-0; codeine N-oxide, 3688-65-1; morphine N-oxide, 639-46-3.

Acknowledgment.—Financial assistance from USPHS Research Grant HE-05881 is gratefully acknowledged.

Bridged Polycyclic Compounds. LX. *syn*-Bromine Activation in Free-Radical Bromination of Janusenes[1]

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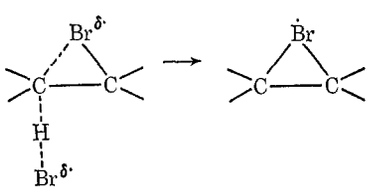
Recently, several workers have postulated neighboring-group participation by bromine in the radical bromination of a variety of alkyl bromides.[2-5] They suggest that the bromo substituents assist in the abstraction of a β hydrogen by bridging in the transition state. An *anti* orientation between the β hydrogen and the bromo substituent is presumably required



in the transition state for this mechanism to obtain. We wish now to report an example in which the β hydrogen of an alkyl bromide is activated in a compound where that hydrogen is *cis* to and eclipsed by the bromo substituent.

When janusene (5,5a,6,11,11a,12-hexahydro-5,12:6,11-di-*o*-benzenonaphthacene, **1**)[6] was treated with bromine in carbon tetrachloride, it was observed that replacement of the second hydrogen atom occurred more rapidly than that of the first. From the data in Table I, we calculate[7] that k_2/k_1 in eq 1 is 1.4 at 72°. As

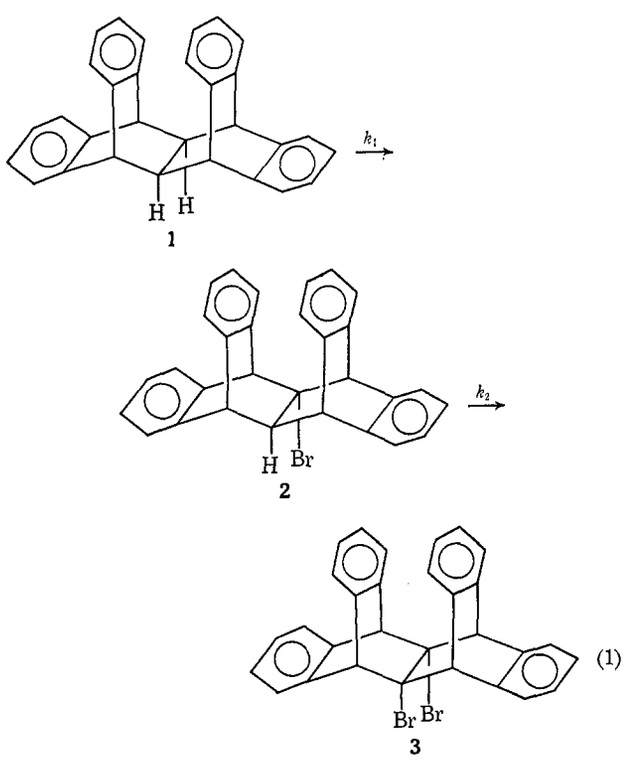
TABLE I

PRODUCT DISTRIBUTIONS FROM PHOTOBROMINATION OF JANUSENE (1) IN CARBON TETRACHLORIDE AT 72°

% 1	% 2	% 3
76	19	5
66	25	9
51	28	20
50	30	20
36	31	33
32	26	42
31	28	41[a]
8	14	78

[a] These data were from a reaction that was run until only 40% of the initial bromine added had been consumed.

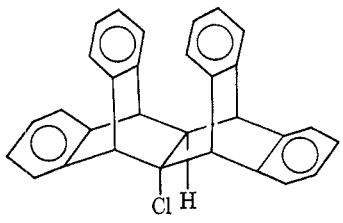
there are two reactive hydrogen atoms in **1** and only one in **2**, this means that, compared with hydrogen, bromine activates the β hydrogen by a factor of 2.8 Similar data at 12° gave a factor of 5.2.



Unlike bromine, chlorine decreased reactivity. A competitive photobromination experiment between 5a-chlorojanusene (**4**) and janusene (**1**) at 72° revealed

(1) Previous paper: S. J. Cristol, R. J. Bopp, and A. E. Johnson, *J. Org. Chem.*, **34**, 3574 (1969).
(2) W. Thaler, *J. Amer. Chem. Soc.*, **85**, 2607 (1963).
(3) P. S. Skell, D. L. Tuleen, and P. D. Readio, *ibid.*, **85**, 2849 (1963).
(4) P. S. Skell and P. D. Readio, *ibid.*, **86**, 3334 (1963).
(5) J. Traynham and W. Hines, *ibid.*, **90**, 5208 (1968).
(6) S. J. Cristol and D. C. Lewis, *ibid.*, **89**, 1476 (1967).
(7) S. Glasstone, "Textbook of Physical Chemistry," 2nd ed, Van Nostrand-Reinhold Co., New York, N. Y., 1946, p 1075.

that chlorine had a deactivating effect upon the β hydrogen compared with hydrogen ($k_4/0.5\ k_1 = 0.5$). From a competitive bromination experiment between 5a-bromojanusene (**2**) and 5a-chlorojanusene (**4**) k_2/k_4



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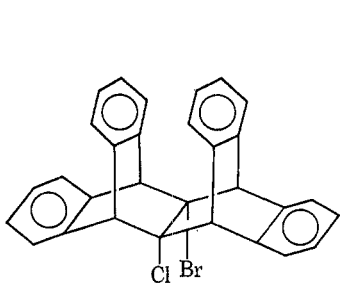

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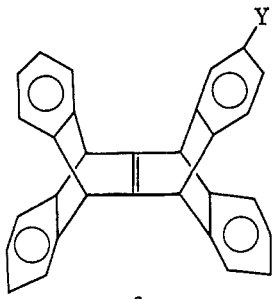

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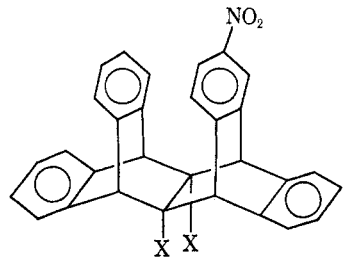
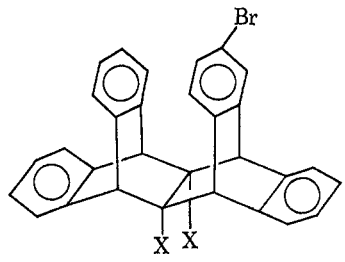
was 6.0 (calcd 5.6). These results are consistent with those in acyclic systems.[8] All of the products from these radical bromination experiments were prepared independently by additions to dehydrojanusene (**6H**).

It has been suggested[9,10] that the apparent enhanced reactivity of hydrogen atoms β to bromine atoms described earlier and ascribed to bridged bromine radicals is an artifact which disappears under appropriate experimental conditions. For example, Tanner and his coworkers[10] showed that the 2 position of 1-bromobutane was not significantly different in reactivity from other 1-substituted butanes toward bromine atoms. However, attack at this position led, *via* elimination of a bromine atom, to 1-butene which then added bromine to give 1,2-dibromobutane. On the other hand, radicals formed at carbon atoms other than C-2 suffered capture by hydrogen bromide formed during the course of the reaction. Put another way, a β-bromo radical led principally to dibromide product, while other radicals returned in large part to starting material. The conclusion[9,10] that at least a part, and perhaps all, of what has been ascribed to anchimeric assistance has this alternative explanation now seems inescapable, and presumably many or all such cases may have similar explanations.

For this reason, we needed to show that an elimination–addition mechanism involving olefin **6H** as an intermediate did not obtain. To this end, bromination of two face-ring-labeled janusenes, **7a** and **8a**, and one lateral ring-labeled compound, **9a**, was carried out. In each case, the corresponding dibromide, **7b**, **8b**, and **9b** was obtained without scrambling of the ring label. If the ring-labeled intermediate **6Y** had been produced, a mixture of face- and ring-labeled dibromojanusenes should have resulted. It has also been reported that 2-bromo-2,3-dimethylbutane is brominated in the dark.[11] This was ascribed to an ionic mechanism. **1** and **2** are inert to bromine in the dark in the absence of Lewis acids.



7a, X = H
b, X = Br



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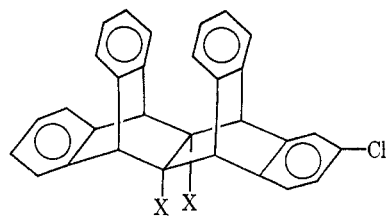

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Clearly the removal of a hydrogen atom from 5a-bromojanusene (**2**) cannot involve a transition state similar to that proposed[2–5] for the presumed anchimeric assistance, as an *anti* configuration from **2** would have prohibitively high strain. It would seem possible to explain the enhanced reactivity (note that the factor of 6 is not a large one) by the assumption of a *syn* hyperconjugative electron delocalization in the *syn*-bromo radical and in the transition state leading to it.

Experimental Section

All nmr spectra were taken on a Varian A-60A instrument as saturated solutions in chloroform-d_1, using tetramethylsilane as an internal standard. All chemical shifts are reported in τ units (τ = 10.00 for tetramethylsilane). Infrared spectra were taken on a Beckman IR-5 spectrophotometer in KBr. All elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Melting points were uncorrected.

Preparation of 5a-Bromojanusene (**2**).—Hydrogen bromide was bubbled through a solution of 405 mg (1.07 mmol) of dehydrojanusene (**6**),[12] mp 361°, in 100 ml of CH_2Cl_2 for 30 min. After 1.5 hr, the solvent was evaporated and the residue was dissolved in 100 ml of ether, treated with charcoal, and dried ($MgSO_4$). Evaporation of the solvent from the filtered mixture under reduced pressure gave 418 mg (85%) of 5a-bromojanusene (**2**): mp 262–263° dec, after recrystallization from benzene; pmr ($CDCl_3$) τ 6.79 (t, 1, J = 2 Hz), 5.74 (d, 2, J = 2 Hz), 5.23 (s, 2), and 2.80–3.40 (m, 16, aromatics).

Anal. Calcd for $C_{30}H_{21}Br$: C, 78.09; H, 4.56. Found: C, 78.06; H, 4.68.

(8) H. Singh and J. M. Tedder, *J. Chem. Soc.*, 4737 (1964).
(9) W. O. Haag and E. I. Heiba, *Tetrahedron Lett.*, 3683 (1965).
(10) D. D. Tanner, D. Darwish, M. W. Mosher, and N. J. Bunce, *J. Amer. Chem. Soc.*, **91**, 7398 (1969).
(11) G. A. Russell and H. C. Brown, *ibid.*, **77**, 4025 (1955).
(12) The preparation of dehydrojanusene *via* treatment of **3** with zinc will be reported later, as will its characterization.

Preparation of 5a,11a-Dibromojanusene (3).—To a solution of 850 mg (2.23 mmol) of dehydrojanusene (6) in 100 ml of CH_2Cl_2 was added 360 mg (2.23 mmol) of bromine. Work-up as described above gave 1.05 g (89%) of 5a,11a-dibromojanusene (3).[13] Crystallization was from acetone–95% EtOH: mp 268–270° dec; pmr ($CDCl_3$) τ 5.13 (s, 4) and 2.87–3.30 (m, 16, aromatics); ν_{max} 1450, 1165, 850, 753, and 685 cm^{-1} (KBr).

Preparation of 5a,11a,Dibromojanusene (3). Photobromination.—A solution of 10.3 g (27.1 mmol) of janusene (1) in 130 ml of CCl_4 was irradiated and heated to reflux with a 150-W tungsten bulb. To this solution was added, over a 30-hr period, 9.2 g (57.5 mmol) of bromine and 290 mg of benzoyl peroxide in 30 ml of CCl_4. The reaction was halted after 68 hr. During the course of the reaction dibromide 3 precipitated out of solution and, after the reaction was stopped, it was allowed to stand for 2 days so that more dibromide 3 could crystallize. The dibromide was filtered and the filtrate was diluted with 100 ml of CH_2Cl_2, washed four times with 300-ml portions of water, and then dried ($MgSO_4$). The mixture was filtered, the solvent was evaporated under reduced pressure, and the residue was crystallized from CH_2Cl_2–benzene to give about 2 g of dibromide 3. This was combined with the dibromide obtained from the initial filtration to give 13.7 g (94%) of 5a,11a-dibromojanusene. Recrystallization was from acetone–95% EtOH: mp 268–270° dec: pmr ($CDCl_3$) τ 5.13 (s, 4) and 2.87–3.30 (m, 16, aromatics); ν_{max} 1450, 1165, 850, 753, and 685 cm^{-1} (KBr).

Anal. Calcd for $C_{30}H_{20}Br_2$: C, 66.67; H, 3.70. Found: C, 66.55; H, 3.77.

Preparation of 5a-Chlorojanusene (4).—Hydrogen chloride was bubbled through a solution of 300 mg (0.79 mmol) of dehydrojanusene (6) in 60 ml of CH_2Cl_2 for 30 min at room temperature. The reaction mixture was allowed to stand for 3 hr and then worked up as described for 2. Crystallization from acetone–95% EtOH gave 232 mg (70%) of 5a-chlorojanusene (4): mp 260–262° (lit.[6] mp 260–262°); pmr ($CDCl_3$) τ 7.04 (t, 1, J = 2 Hz), 5.77 (d, 2, J = 2 Hz), 5.43 (s, 2), and 2.80–3.40 (m, 16, aromatics).

Preparation of 5a-Bromo-11a-chlorojanusene (5).—A solution of bromine chloride in CH_2Cl_2 was added dropwise to a solution of 150 mg (0.40 mmol) of dehydrojanusene (6) in 25 ml of CH_2Cl_2 until the brownish red color persisted. The solution was boiled to drive off the excess bromine chloride and then diluted with 50 ml of CH_2Cl_2. This solution was washed twice with 100-ml portions of 10% Na_2CO_3 solution and twice with 100-ml portions of water and dried ($MgSO_4$). Filtration and evaporation under reduced pressure gave a residue, weighing 172 mg (85%), of 5a-bromo-11a-chlorojanusene (5). Crystallization was from acetone–95% EtOH: mp 319–322° dec; pmr ($CDCl_3$) τ 5.35 (s, 2), 5.15 (s, 2), and 2.83–3.30 (m, 16, aromatics).

Anal. Calcd for $C_{30}H_{20}BrCl$: C, 72.65; H, 4.04. Found: C, 72.41; H, 4.08.

Photobromination of Janusene (1).—In a 50-ml, one-neck, round-bottom flask, a solution of 200 mg (0.52 mmol) of janusene (1) in 25 ml of CCl_4 was irradiated and heated to reflux with a 60-W tungsten bulb. To this solution was added 10 ml of 0.06 M Br_2–CCl_4 solution. After 10 hr the reaction mixture was colorless. It was washed with 100 ml of water, twice with 60-ml portions of 10% Na_2CO_3 solution, twice with 60-ml portions of water, and once with 100 ml of saturated NaCl solution. The CCl_4 solution was dried ($MgSO_4$) and filtered and the solvent was evaporated under reduced pressure, giving 230 mg of a yellow oil. The oil was identified by its pmr spectrum as 36% unreacted janusene (1), 31% 5a-bromojanusene (2), and 33% 5a,11a-dibromojanusene (3).

Photobromination of a Mixture of Janusene (1) and 5a-Chlorojanusene (4).—A mixture of 168 mg (0.44 mmol) of janusene (1), 184 mg (0.44 mmol) of 5a-chlorojanusene (4), and 15 mg (0.09 mmol) of *p*-dinitrobenzene was dissolved in 50 ml of CCl_4. This solution was irradiated and heated to reflux with a 60-W tungsten bulb. To this solution was added 6 ml of 0.15 M Br_2–CCl_4 solution, and the reaction was stopped after 1.5 days. The reaction mixture was worked up as described above and the product was identified by pmr as 14% janusene (1), 43% 5a-chlorojanusene (4), 14% 5a-bromojanusene (2), 21% 5a,11a-dibromojanusene (3), and 8% 5a-bromo-11a-chlorojanusene (5). The yield, based upon internal standard (*p*-dinitrobenzene), was 94%, which indicated that no preferential decomposition of any of the products had occurred.

Photobromination of a Mixture of 5a-Bromojanusene (2) and 5a-Chlorojanusene (4).—A mixture of 117 mg (0.25 mmol) of 5a-bromojanusene (2), 188 mg (0.45 mmol) of 5a-chlorojanusene (4), and 18 mg of *p*-dinitrobenzene, dissolved in 50 ml of CCl_4, was treated with 7 ml of 0.04 M Br_2–CCl_4. The reaction procedure was essentially the same as the previous experiment. The product mixture was identified by its pmr spectrum as 15% 5a-bromojanusene (2), 54% 5a-chlorojanusene (4), 22% 5a,11a-dibromojanusene (3), and 9% 5a-bromo-11a-chlorojanusene (5). The yield, based upon internal standard, was 98%.

Photobromination of Fβ-Nitrojanusene (7a).—In a procedure idential with those previously described, 2.16 g (5.06 mmol) of Fβ-nitrojanusene (7a) in 120 ml of CCl_4 was treated with 1.62 g (10.1 mmol) of bromine. The isolated oil was identified from its pmr spectrum as 5a,11a-dibromo-14-nitrojanusene (7b). Crystallization from acetone–95% EtOH gave 1.7 g (58%) of white crystals: mp 261–263° dec; pmr ($CDCl_3$) τ 5.07 (s, 2), 5.00 (s, 2) 3.29 (m, 5, aromatics), 2.77 (m, 8, aromatics), and 2.38 (s, 2, aromatics). The pmr spectrum indicated that the nitro substituent in the product is in the Fβ position.[6]

Anal. Calcd for $C_{30}H_{19}NO_2Br_2$: C, 61.54; H, 3.25. Found: C, 61.56; H, 3.41.

Photobromination of Fβ-Bromojanusene (8a).—In a manner identical with that previously described, 934 mg (2.02 mmol) of Fβ-bromojanusene (8a) in 50 ml of CCl_4 was treated with 650 mg (4.04 mmol) of bromine. The yield of 5a,11a,14-tribromojanusene (8b), which was identified by its pmr spectrum, was 800 mg (58%). The aromatic absorptions in the pmr spectrum showed that the bromine substituent was in the F ring.[6] Crystallization was from acetone–95% EtOH: mp 248–249° dec; pmr ($CDCl_3$) τ 5.24 (s, 1), 5.16 (s, 3), 3.26 (m, 7, aromatics), and 2.90 (m, 8, aromatics).

Anal. Calcd for $C_{30}H_{19}Br_3$: C, 58.16; H, 3.07. Found: C, 58.41; H, 3.02.

Photobromination of Lβ-Chlorojanusene (9a).—In a manner identical with that previously described, 925 mg (2.22 mmol) of Lβ-chlorojanusene (9a) in 50 ml of CCl_4 was treated with 710 mg (4.44 mmol) of bromine. The isolated oil, 730 mg, was identified by pmr as 85% 5a,11a-dibromo-2-chlorojanusene (9b). The aromatic absorptions in this spectrum indicated that the chlorine substituent was in the L ring, since the F-substituted compound would have given a spectrum similar to that of tribromide 8b. Crystallization was from acetone–95% EtOH: mp 265–267° dec; pmr ($CDCl_3$) τ 5.25 (s, 1), 5.18 (s, 3), 3.37 (m, 8, aromatics), and 2.90 (m, 7, aromatics).

Anal. Calcd for $C_{30}H_{19}Br_2Cl$: C, 62.66; H, 3.31. Found: C, 63.09; H, 3.38.

Registry No.—**1**, 23646-37-9; **2**, 23646-38-0; **3**, 23646-39-1; **4**, 23646-40-4; **5**, 23646-41-5; **7a**, 17344-73-9; **7b**, 23646-43-7; **8a**, 23646-46-0; **8b**, 23646-44-8; **9a**, 17604-06-7; **9b**, 23646-45-9.

Acknowledgments.—The authors are indebted to the National Science Foundation, to the Institute of General Medical Sciences (Public Health Service Grant GM-12139), and to the University of Colorado for support of this work.

(13) The structure of dibromide 3 has been determined from X-ray analysis by W. M. Macintyre and A. Tench.