[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

# Unsaturated Amines. XII. Steric Requirements of Mercuric Acetate Oxidation of Tertiary Amines[1]

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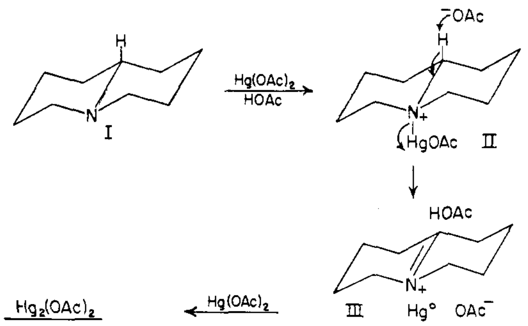
11-Methyl-11-azabicyclo[5.3.1]hendecane, a model tertiary amine in which the hydrogens on the equivalent $\alpha$-tert.-carbons are sterically prevented from attaining *trans* coplanarity with the N–Hg bond in the mercurated complex and in which epimerization at these $\alpha$-carbons is impossible, has been found to undergo demethylation in the mercuric acetate reaction. The importance of the steric requirements in determining the site of the mercuric acetate oxidation is demonstrated thereby. 10-Methyl-10-azabicyclo[4.3.1]decane also underwent oxidative attack at the N-methyl group, yielding 10-azabicyclo-[4.3.1]decane (in aqueous and glacial acetic acid) and 10-formyl-10-azabicyclo[4.3.1]decane (in glacial acetic acid).

In order to test further the mechanism proposed[3] for the mercuric acetate oxidation of tertiary amines (illustrated with quinolizidine I → II → III), involving a four-center elimination from the N-mercurated complex, we have investigated the action of this reagent on some atom-bridged bicyclic tertiary amines in which the hydrogen on the $\alpha$-tert.-carbon is sterically prevented from attaining *trans* coplanarity with the *p*-electrons on nitrogen (*i.e.*, with the nitrogen–mercury bond).



We have shown previously that cleavage of the $C_\alpha$–H bond is occurring in the rate-limiting step[1] and that the normal order of hydrogen removal from the $\alpha_N$-carbon is tert.-C–H > sec.-C–H > prim.-C–H.[4] Partial information is available concerning the preferred stereochemistry of the hydrogen on the $\alpha$-*tert*.-carbon for effective removal in the mercuric acetate reaction. Thus, sparteine, which has an axial–axial hydrogen (indicating the relation to two rings and assuming all four rings to be in the chair form) and an axial–equatorial hydrogen at otherwise equivalent bridgehead $\alpha$-tert.-carbons (C-6 and C-11, respectively), is known to lose the axial–axial hydrogen more readily than the axial–equatorial hydrogen.[5] The *cis* or *trans* relation of the leaving hydrogen with respect to the N-mercurated complex is not defined uniquely, since the ring juncture (A/B or C/D) is not rigid about the nitrogen. Nevertheless, the most logical assumption is that the C-6 axial–axial hydrogen and the N-1 bond to mercury are in the *trans* relation.

In the yohimbine–reserpine alkaloid series, studies in other laboratories[6–9] have shown that compounds with the "normal" (*e.g.*, yohimbine) and "allo" (allo- or $\alpha$-yohimbine, isoreserpine) configurations are more readily oxidized at C-3 by mercuric acetate than those with the "pseudo" (pseudoyohimbine) and "epiallo" (epialloyohimbine, reserpine, deserpidine) configurations. Caution must be attached to steric differentiation on this basis, however, since the precipitation of mercurous acetate alone is not a sufficient measure of the rate of oxidation[4] and since the optimum conditions for comparison must be selected to avoid the possibility of epimerization at C-3.[10] In compounds of the normal and allo series, the preferred configuration of the N-mercurated complex is that in which the axial hydrogen at C-3 (rings C and D in chair form) is *trans* to the N–Hg bond, and thus the stereochemistry is favorable for a four-center elimination.[6] In compounds of the pseudo (more examples of this type are needed) and epiallo series, the reason for their lower activity in mercuric acetate oxidation (assuring the prevention of epimerization) at C-3 may be found in the N-mercuration equilibrium strongly favoring the C/D-*cis* configuration of the N-mercurated complex.[11] If this steric situation obtains, with the C-3 hydrogen *cis* to the N–Hg bond, it would be unfavorable for the normal course of elimination.

We have constructed as our first model a tertiary amine in which the hydrogens on the equivalent $\alpha$-tert.-carbons are sterically prevented from attaining *trans* coplanarity with the N–Hg bond in the mercurated complex and in which epimerization at these $\alpha$-carbons is impossible. It has been

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[1] For previous paper in this series, see N. J. Leonard and R. R. Sauers, THIS JOURNAL, **79**, 6210 (1957).

[2] Eli Lilly and Co. Fellow, 1956–1957.

[3] N. J. Leonard, A. S. Hay, R. W. Fulmer and V. W. Gash, THIS JOURNAL, **77**, 439 (1955).

[4] N. J. Leonard and F. P. Hauck, Jr., *ibid.*, **79**, 5279 (1957).

[5] N. J. Leonard, P. D. Thomas and V. W. Gash, *ibid.*, **77**, 1552 1955).

[6] F. L. Weisenhorn and P. A. Diassi, *ibid.*, **78**, 2022 (1956).

[7] E. Wenkert and D. K. Roychaudhuri, *J. Org. Chem.*, **21**, 1315 (1956). We wish to thank the authors for the opportunity of reading this article in manuscript form.

[8] E. Farkas, E. R. Lavagnino and R. T. Rapala, *ibid.*, **22**, 1261 (1957). We wish to thank the authors for the opportunity of reading this article in manuscript form.

[9] F. L. Weisenhorn, private communication.

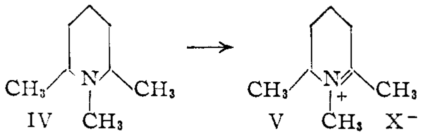
[10] Weisenhorn has indicated that reserpine with mercuric acetate in glacial acetic acid shows about 10% reaction in 1.5 hours at 60°, whereas isoreserpine reacts completely in a few minutes.[9] Using different conditions, Farkas, Lavagnino and Rapala[8] reported that reserpine, deserpidine, reserpic acid lactone and isoreserpic acid lactone all undergo oxidation at C-3 with mercuric acetate in 10% acetic acid held at reflux for 14 hours.

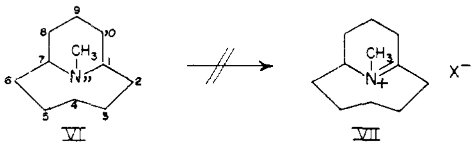
[11] The reason does *not* lie in an equilibrium unfavorable to N-mercuration (whether with C/D *trans* or *cis*), since a representative number of epiallo compounds are stronger bases than the corresponding allo compounds.[12,13]

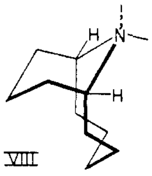
[12] E. Farkas and R. T. Rapala, private communication.

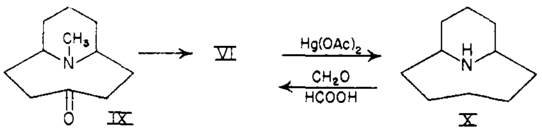
[13] E. Wenkert and L. H. Liu, *Experientia*, **11**, 302 (1955).

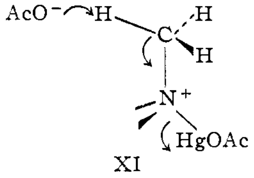
shown that 1,2,6-trimethylpiperidine (IV) is readily oxidized by mercuric acetate to the corresponding 1,2,6-trimethyl-$\Delta^1$-tetrahydropyridinium compound (V).[4] Thus, without any reference to the steric requirements of mercuric acetate oxidation and assuming that a carbon–nitrogen double bond can be incorporated at the bridgehead of a bicyclic system of the same size ($S = 9$) that will accommodate a carbon–carbon double bond,[14–20] 11-methyl-11-azabicyclo[5.3.1]hendecane (VI) might have been expected to undergo oxidation in a similar manner (→ VII). However, it will be seen from the conformational expression VIII that the hydrogens on C-1 and C-7 are necessarily equatorial to the six-membered ring and cannot be *trans* to either a *syn* or an *anti* N–Hg bond in the mercurated complex. 11-Methyl-11-azabicyclo[5.3.1]hendecane (VI) was obtained in 91% yield by the Wolff–Kishner reduction of 11-methyl-11-azabicyclo[5.3.1]hendecan-4-one (IX), recently described.[21] The tertiary amine VI in 5% aqueous acetic acid (95% water) was heated at 80° for 20 hours with four mole equivalents of mercuric acetate. The mercurous acetate which separated corresponded to 74% in excess of that required for a two-electron oxidation. Some of the original amine was found in the crude product, but the major component (*ca.* 60% yield) was the *des*-methyl compound, 11-azabicyclo[5.3.1]hendecane (X). Picrate, perchlorate, acetyl and benzenesulfonyl derivatives and infrared analysis were used for characterization, and the structure of X was confirmed by its remethylation, using formaldehyde–formic acid, to give 11-methyl-11-azabicyclo[5.3.1]hendecane (VI). Although the hydrogens at positions 1 and 7 in VI cannot become *trans* coplanar with the nitrogen–mercury complex, one of the hydrogens of the N-methyl group, which has virtually unrestricted rotation, can be aligned readily in the steric relationship favorable for oxidation (XI). The fact that here, for the first time, a methyl group is attacked before a methinyl group, in a reversal of the normal order,[4] is sufficient to indicate the importance of the steric requirements in determining the site of the mercuric acetate oxidation.





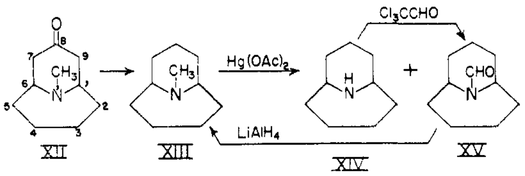






Desaturation of VI (see XI) followed by solvolysis will account for the formation of the secondary amine X, which should be relatively stable[4] toward oxidation with mercuric acetate in aqueous acetic acid. It has now been shown that mercuric acetate oxidations of formaldehyde and formic acid proceed at reasonable rates under the conditions employed. Thus, complete demethylation in aqueous acetic acid solution becomes a six-electron oxidation.[22]

The action of mercuric acetate on the lower ring homolog of VI, 10-methyl-10-azabicyclo[4.3.1]decane (XIII), was also studied. The immediate precursor of this amine was synthesized by the Robinson–Schöpf method from acetonedicarboxylic acid, methylamine and adipaldehyde. 10-Methyl-10-azabicyclo[4.3.1]decan-8-one (XII), obtained in 22% yield, has been made earlier by Blount and Robinson[23] but had been characterized only as the



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[14] V. Prelog, L. Ruzicka, P. Barman and L. Frenkiel, *Helv. Chim. Acta*, **31**, 92 (1948).

[15] V. Prelog, P. Barman and M. Zimmermann, *ibid.*, **32**, 1284 (1949).

[16] V. Prelog, M. M. Wirth and L. Ruzicka, *ibid.*, **29**, 1425 (1946).

[17] V. Prelog, P. Barman and M. Zimmermann, *ibid.*, **33**, 356 (1950).

[18] V. Prelog and K. Wiesner, *ibid.*, **30**, 1465 (1947).

[19] V. Prelog, *J. Chem. Soc.*, 420 (1950).

[20] A. C. Cope, R. J. Cotter and G. G. Roller, THIS JOURNAL, **77**, 3590 (1955).

[21] N. J. Leonard, D. F. Morrow and M. T. Rogers, *ibid.*, **79**, 5476 (1957).

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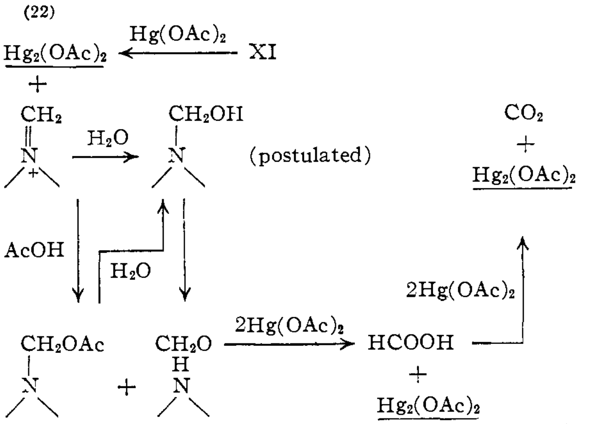
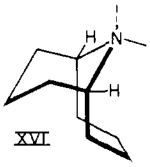
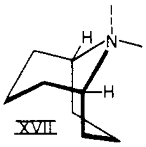


[23] B. K. Blount and R. Robinson, *J. Chem. Soc.*, 1429 (1932).

picrate and methiodide. Wolff–Kishner reduction of XII furnished 10-methyl-10-azabicyclo[4.3.1]-decane (XIII) in 88% yield. In this model again the hydrogens on the equivalent α-tert.-carbons are equatorial to the six-membered ring and are prevented from assuming *trans* coplanarity with either a *syn* or an *anti* N–Hg bond in the mercurated complex (XVI).[24] However, it is unlikely that a double bond could be generated at the bridgehead of this bicyclic system ($S$ = 8).[14–19] When XIII was oxidized by mercuric acetate in aqueous acetic acid under conditions similar to those applied to VI, demethylation occurred. The estimated yield of 10-azabicyclo[4.3.1]decane (XIV) was 40%, a figure consistent with the amount of mercurous acetate precipitated. When the oxidation of XIII was carried out in glacial acetic acid at the reflux temperature for 2 hours, the products were 10-azabicyclo[4.3.1]decane (XIV) (34%) and 10-formyl-10-azabicyclo[4.3,1]decane (XV) (18%). The structures were interrelated by the formylation of XIV by means of chloral to give XV, which was reduced with lithium aluminum hydride to yield the original amine XIII. The hydrogen of the methyl group in XIII represents the only α-H with the requisite steric relationship for removal in this oxidation process.[25] N-Methylgranatanine (XVII), the next lower homolog in this bicyclic series ($S$ = 7), was more resistant to mercuric acetate oxidation than XIII. The amount of demethylated compound, granatanine, produced could not have been greater than about 8%; recovery of the original material was 87%.



XVI



XVII

The steric requirements of the mercuric acetate oxidation of tertiary amines have been more clearly defined by means of the examples here studied. The added information may improve the value of the mercuric acetate oxidation reaction in its application to (stereochemical) structure problems. It may also aid in predictions as to the sites of oxidative attack.[26]

## Experimental[27]

**N-Methylgranatanine (9-Methyl-9-azabicyclo[3.3.1]nonane).**—The reduction of pseudopelletierine[28] by the Huang-Minlon modification of the Wolff–Kishner method produced N-methylgranatanine in 56% yield, purified through the **perchlorate**, colorless plates from absolute ethanol, which decomposed at 270° (immersed at 255°). The salt was transparent in the 6 μ infrared region (Nujol) and exhibited a peak at 3110 cm.$^{-1}$ ($\text{—}\overset{|+}{\underset{|}{\text{N}}}\text{—H}$).

*Anal.* Calcd. for $C_9H_{16}ClNO_4$: C, 45.09; H, 7.57; N, 5.84. Found: C, 45.00; H, 7.72; N, 5.77.

**The picrate** crystallized as short yellow needles from absolute ethanol and decomposed at 297–298° (reported[29] m.p. *ca.* 300°).

**10-Methyl-10-azabicyclo[4.3.1]decan-8-one.**—The procedure of Cope and co-workers[28] for the preparation of pseudopelletierine was followed, using adipaldehyde,[30] b.p. 76–80° (7 mm.), in place of glutaraldehyde; yield 22%, b.p. 106–107° (5 mm.). The infrared spectrum (5% in carbon tetrachloride) exhibited a carbonyl peak at 1713 cm.$^{-1}$ and was very similar to that of pseudopelletierine in the 3800–1300 cm.$^{-1}$ region.

*Anal.* Calcd. for $C_{10}H_{17}NO$: C, 71.81; H, 10.25. Found: C, 71.62; H, 10.34.

**The perchlorate** crystallized as colorless plates from absolute ethanol, m.p. 231.5–232° dec. The infrared spectrum (Nujol) exhibited peaks at 3080 ($-\overset{|+}{\underset{|}{\text{N}}}\text{—H}$) and 1720 cm.$^{-1}$ (C═O), as well as maxima at 3470 and 1640 cm.$^{-1}$.

*Anal.* Calcd. for $C_{10}H_{18}ClNO_5$: C, 44.86; H, 6.78; N, 5.23. Found: C, 44.93; H, 6.81; N, 5.09.

**The picrate** crystallized as yellow needles from water, m.p. 216–216.5° dec. (reported[23] 206°).

**10-Methyl-10-azabicyclo[4.3.1]decane.**—A mixture of 15.9 g. (0.095 mole) of 10-methyl-10-azabicyclo[4.3.1]decan-8-one, 20 g. (0.36 mole) of potassium hydroxide, 15 ml. of 100% hydrazine hydrate and 150 ml. of triethylene glycol was heated under reflux for 1.5 hours. The solution was then distilled until the pot temperature reached 190°. The mixture was heated under reflux an additional 2.5 hours and then distilled until the vapor temperature reached 165° (90 mm.). The distillates were combined and extracted with ether. The extracts were dried, concentrated and distilled, b.p. 114–119° (37 mm.), yield 12.8 g. (88%). The product was redistilled for analysis from sodium, b.p. 93.5° (14 mm.), $n^{24}_D$ 1.4931.

*Anal.* Calcd. for $C_{10}H_{19}N$: C, 78.36; H, 12.50. Found: C, 78.36; H, 12.33.

The infrared spectrum (5% in carbon tetrachloride) was transparent in the 3 and 6 μ regions and exhibited an N-$CH_3$ peak at 1389 cm.$^{-1}$. The ultraviolet spectrum in absolute ether exhibited a single maximum at 217 mμ (log ε 3.04).

**The perchlorate** crystallized as a mixture of short colorless needles and colorless plates from absolute ethanol, m.p. 259–261° dec. with previous softening and charring (immersed at 230°). The infrared spectrum (Nujol) was transparent in the 6 μ region and exhibited a peak at 3120 cm.$^{-1}$ ($-\overset{|+}{\underset{|}{\text{N}}}\text{—H}$).

*Anal.* Calcd. for $C_{10}H_{20}ClNO_4$: C, 47.33; H, 7.95; N, 5.52. Found: C, 47.23; H, 7.77; N, 5.44.

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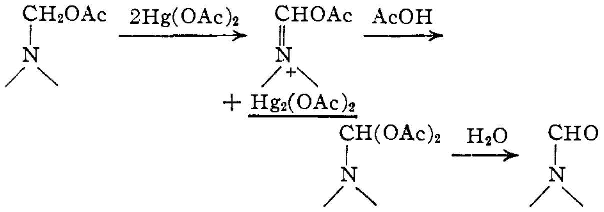
[24] The conformations VIII, XVI and XVII are arbitrarily written with one ring in the chair form and the other in a form which minimizes the steric interaction between the hydrogens of the two rings (see footnote, p. 1816, in P.B.D. de la Mare, W. Klyne, D. J. Millen, J. G. Pritchard and D. Watson, *J. Chem. Soc.*, 1813 (1956)).

[25] One explanation for the isolation of some N-formyl product may be pictured as



$$\underset{\diagup\ \diagdown}{\overset{CH_2OAc}{\underset{|}{N}}} \xrightarrow{2Hg(OAc)_2} \underset{\diagup\,+\,\diagdown}{\overset{CHOAc}{\underset{\|}{N}}} + \underline{Hg_2(OAc)_2} \xrightarrow{AcOH} \underset{\diagup\ \diagdown}{\overset{CH(OAc)_2}{\underset{|}{N}}} \xrightarrow{H_2O} \underset{\diagup\ \diagdown}{\overset{CHO}{\underset{|}{N}}}$$

[26] For example, compounds of the epialloyohimhine, or reserpine series,[6] if subjected to prolonged mercuric acetate treatment under non-epimerizing (at C-3) conditions, might be expected to undergo oxidation at one of the two α-methylene positions (C-5, C-21). At both positions, one of the hydrogens can be *trans* to an N-mercurated complex, and we have now observed that even an α-methyl group can be attacked when it provides the only hydrogen meeting the steric requirements for desaturation.

[27] All melting points are corrected. Microanalyses were performed by Mr. Jozsef Nemeth and his associates, and the infrared absorption spectra were determined by Mrs. Louise Griffing and Mr. James Brader, using a Perkin–Elmer automatic recording infrared spectrometer, model 21.

[28] A. C. Cope, H. L. Dryden, Jr., C. G. Overherger and A. A. D'Addieco, THIS JOURNAL, **73**, 3416 (1951).

[29] A. Piccinini, *Gazz. chim. ital.*, **32**, 260 (1902).

[30] J. English, Jr., and G. W. Barher, THIS JOURNAL, **71**, 3310 (1949).

**The picrate** crystallized as long yellow needles from 33% aqueous dimethylformamide, m.p. 276.5–277° dec. (immersed at 268°).

*Anal.* Calcd. for $C_{16}H_{22}N_4O_7$: C, 50.26; H, 5.80; N, 14.65. Found: C, 50.45; H, 5.79; N, 14.74.

**Condensation of 2,6-Lutidine and Chloral.**—A mixture of 150 g. (1.06 moles) of chloral and 211 g. (1.98 moles) of 2,6-lutidine was heated at 110° for 33.5 hours. The excess lutidine was distilled at 80° (20 mm.). The residue was extracted with three 400-ml. portions of boiling petroleum ether (60–90°). The extract was treated with Darco and concentrated, yielding 171 g. (63%) of a light yellow solid, m.p. 102–103°. The product crystallized from petroleum ether (60–90°) in small colorless prisms and melted at 106–106.5°.

*Anal.* Calcd. for $C_9H_{10}Cl_3NO$: C, 42.46; H, 3.96; N, 5.50. Found: C, 42.64; H, 3.96; N, 5.45.

The infrared spectrum in Nujol exhibited broad O–H stretching absorption centered at 3130 cm.$^{-1}$ and had other peaks (selected) at 1170 and 1098 cm.$^{-1}$ (three adjacent arom. H's), and at 786 and 756 cm.$^{-1}$ ($-CCl_3$), consistent with the structural assignment as **2-(2′-hydroxy-3′,3′,3′-trichloropropyl)-6-methylpyridine**.

**11-Methyl-11-azabicyclo[5.3.1]hendecane.**—The reduction of 11-methyl-11-azabicyclo[5.3.1]hendecan-4-one[21] was carried out by the method described above for the lower ring homolog. The yield was 91%, b.p. 102° (16 mm.), $n^{24}$D 1.4880. The infrared spectrum (10% in carbon tetrachloride) was transparent in the 6 $\mu$ region and exhibited a peak at 1397 cm.$^{-1}$ ($N-CH_3$). The ultraviolet absorption spectrum in ether exhibited a single maximum at 215 m$\mu$ (log $\epsilon$ 3.03).

*Anal.* Calcd. for $C_{11}H_{21}N$: C, 78.97; H, 12.66; N, 8.37. Found: C, 78.78; H, 12.71; N, 8.25.

**The perchlorate** crystallized as a mixture of colorless long needles and flat striated plates from absolute ethanol, m.p. 239–245°. The infrared spectrum in Nujol was transparent in the 6 $\mu$ region and exhibited a peak at 3185 cm.$^{-1}$ (s) $(-\overset{|+}{\underset{|}{N}}-H)$.

*Anal.* Calcd. for $C_{11}H_{22}ClNO_4$: C, 49.34; H, 8.28; N, 5.23. Found: C, 49.43; H, 8.11; N, 5.00.

**The picrate** crystallized as a mixture of long yellow needles and large yellow plates from water, m.p. 215–216°.

*Anal.* Calcd. for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10; N, 14.14. Found: C, 51.62; H, 6.22; N, 14.14.

**Oxidations with Mercuric Acetate. 1. N-Methylgranatanine.**—A mixture of 10.3 g. (0.074 mole) of purified N-methylgranatanine, 100 g. (0.31 mole) of mercuric acetate, 35 ml. of glacial acetic acid and 600 ml. of water was heated on a steam-bath for 6 hours and then under reflux for 14 hours. Although no solid had appeared in the hot solution, a precipitate of mercurous acetate separated when the mixture was cooled in ice. The solid was collected and dried, weight 9.1 g. (24% of a two-electron oxidation). The filtrate was saturated with hydrogen sulfide, filtered and concentrated under reduced pressure to *ca.* 50 ml. This was treated with 150 ml. of 1:1 ethanol–ether, and 20 ml. of 70% perchloric acid was added slowly. The resulting mixture was cooled in ice for 1 hour. The precipitate was filtered and washed thoroughly with anhydrous ether. The salt thus obtained weighed 8.0 g. (45% recovery) and decomposed at 270°. The infrared spectrum in Nujol was almost identical with that of the perchlorate salt of N-methylgranatanine. The amine liberated from the filtrate boiled at 73–74° (22 mm.) and weighed 4.3 g. (42% additional recovery). The infrared spectrum of a 5% solution in carbon tetrachloride was identical with that of **N-methylgranatanine**.

**2. 10-Methyl-10-azabicyclo[4.3.1]decane. a. 7% Acetic Acid Solvent.**—A mixture of 3.8 g. (0.025 mole) of 10-methyl-10-azabicyclo[4.3.1]decane, 31.6 g. (0.99 mole) of mercuric acetate and 150 ml. of 7% aqueous acetic acid was heated on a steam-bath for 21 hours. A precipitate of mercurous acetate was visible after 1.5 hours of heating. The mixture was cooled in ice and filtered. The mercurous acetate collected weighed 15.0 g. (117% of a two-electron oxidation). The amine product was isolated in the usual manner, b.p. 90–94° (16 mm.), weight 2.03 g. (equivalent to 53% recovery if calcd. as starting material), $n^{23}$D 1.4981. The infrared spectrum of a liquid film was transparent in the 6 $\mu$ region and exhibited peaks at 3260 (N–H) and 1388 cm.$^{-1}$ ($N-CH_3$).

The perchlorate salt was made in ether. It was an oil which solidified easily when triturated with ether, m.p. 203–215° dec. (immersed at 180°). The infrared spectrum of the crude salt in Nujol exhibited peaks at 3110 $(-\overset{|+}{\underset{|}{N}}-H)$, 1607 ($>\overset{+}{N}H_2$) and 1383 cm.$^{-1}$ ($N-CH_3$), and showed a very weak maximum at 3535 cm.$^{-1}$. The salt was separated into two components by fractional crystallization from a 1:1 mixture of *t*-butyl alcohol and petroleum ether (60–90°). The less soluble component was recrystallized twice from absolute ethanol, and separated as a mixture of colorless needles and plates, m.p. 259–262° dec. (immersed at 240°). A mixture of this salt and the perchlorate of **10-methyl-10-azabicyclo**[4.3.1]decane melted at 260–262° dec. (immersed at 240°) and the infrared spectra of the two salts were identical.

The more soluble component (estimated 40% crude yield) was recrystallized several times from 1:1 *t*-butyl alcohol–petroleum ether (60–90°) and separated as irregular colorless prisms, m.p. 240–242° dec. (immersed at 230°). A mixture of this salt and the perchlorate of **10-azabicyclo**[4.3.1]decane (see below) melted at 241–243° dec. (immersed at 230°).

**b. Glacial Acetic Acid Solvent.**—A mixture of 3.82 g. (0.025 mole) of 10-methyl-10-azabicyclo[4.3.1]decane, 31.9 g. (0.10 mole) of mercuric acetate and 150 ml. of glacial acetic acid was heated under reflux for 2 hours. Mercurous acetate precipitated after 5 minutes of heating. The reaction mixture was cooled and filtered. The mercurous acetate weighed 15.9 g. (122% of a two-electron oxidation). The filtrate was saturated with hydrogen sulfide and filtered. The new filtrate was concentrated at reduced pressure to *ca.* 15 ml., treated with 10 ml. of absolute ethanol and 50 ml. of ether, and 70% aqueous perchloric acid was added until the solution was acid to congo red. The dark oil which separated solidified when cooled in ice, weight 2.11 g. (34% yield). This salt was dissolved in water and extracted with chloroform, which removed most of the colored impurities. The aqueous solution was concentrated to give a nearly colorless residue, m.p. 264–266° dec. The **perchlorate of 10-azabicyclo**[4.3.1]decane was recrystallized three times from 1:1 *t*-butyl alcohol–petroleum ether (60–90°), small colorless irregular prisms, m.p. 245–246° (charring). The infrared spectrum in Nujol exhibited peaks at 3105 $(-\overset{|+}{\underset{|}{N}}-H)$ and 1607 cm.$^{-1}$ ($>\overset{+}{N}H_2$).

*Anal.* Calcd. for $C_9H_{18}ClNO_4$: C, 45.09; H, 7.57; N, 5.84. Found: C, 45.31; H, 7.52; N, 5.82.

The perchlorate salt was dissolved in water, the solution was made strongly basic with concentrated aqueous sodium hydroxide solution and was extracted with five 15-ml. portions of ether. The extracts were dried, concentrated and distilled. The colorless amine, **10-azabicyclo**[4.3.1]**decane**, was sublimed at 93–94° (20 mm.), m.p. 43–45°. The infrared spectrum (10% solution in carbon tetrachloride) was transparent in the 3 and 6 $\mu$ regions and exhibited no band attributable to an $N-CH_3$ grouping.

*Anal.* Calcd. for $C_9H_{17}N$: N, 10.06. Found: N, 9.78.

**The picrate** of **10-azabicyclo**[4.3.1]decane crystallized from absolute ethanol as long orange needles, m.p. 255–256° dec.

*Anal.* Calcd. for $C_{15}H_{20}N_4O_7$: C, 48.91; H, 5.47; N, 15.31. Found: C, 49.10; H, 5.33; N, 15.08.

The filtrate remaining after removal of the perchlorate salt (see above) was concentrated at reduced pressure, treated with 10% aqueous sodium bicarbonate solution and extracted with five 15-ml. portions of ether. The extracts were dried, concentrated, and distilled. A semi-solid compound, **10-formyl-10-azabicyclo**[4.3.1]decane, was obtained, b.p. 81° (0.2 mm.), weight 0.76 g. (18% yield). The infrared spectrum (10% in carbon tetrachloride) was transparent in the 3 $\mu$ region and exhibited weak peaks at 2770 ($O{=}\underset{|}{C}{-}H$ stretching) and 1739 cm.$^{-1}$ and had a very strong carbonyl band at 1665 cm.$^{-1}$ (amide).

*Anal.* Calcd. for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.38. Found: C, 71.19; H, 10.00; N, 8.12.

**Formylation of 10-Azabicyclo[4.3.1]decane.**—A solution of 110 mg. (0.74 mmole) of 10-azabicyclo[4.3.1]decane in 2 ml. of chloroform was cooled in ice and treated with a solution of 120 mg. (0.81 mmole) of chloral, freshly distilled from 36 *N* sulfuric acid, in 2 ml. of chloroform. The mixture was allowed to stand at 25° for 9 hours and was heated under reflux for an additional 12 hours. The solution was concentrated under reduced pressure and distilled. A semi-solid distillate was collected, b.p. 104–106° (1.0 mm.), which weighed 84 mg. (64%). The infrared spectrum (10% in carbon tetrachloride) was identical with that of the neutral compound obtained by the mercuric acetate oxidation of 10-methyl-10-azabicyclo[4.3.1]decane in glacial acetic acid.

**Lithium Aluminum Hydride Reduction of 10-Formyl-10-azabicyclo[4.3.1]decane.**—A solution of 500 mg. (3.00 mmoles) of the formamide in 10 ml. of ether was added slowly to a cooled slurry of 120 mg. (3.16 mmoles) of lithium aluminum hydride in 10 ml. of ether. This mixture was stirred at 25° for 17 hours, cooled in ice, and treated with 0.5 ml. of water. The mixture was stirred for 30 minutes and decanted from a small amount of oil. The ether solution was treated with a saturated solution of picric acid in ether. The picrate crystallized from 33% aqueous dimethylformamide as yellow needles and melted at 275–275.5° dec. (immersed at 268°), yield 480 mg. (42%). A mixture of this salt and the picrate of 10-methyl-10-azabicyclo[4.3.1]decane melted at 275.5–276° dec. (immersed at 269°).

3. **11-Methyl-11-azabicyclo[5.3.1]hendecane.**—A mixture of 5.21 g. (0.031 mole) of 11-methyl-11-azabicyclo[5.3.1]hendecane, 39.6 g. (0.13 mole) of mercuric acetate and 250 ml. of 5% aqueous acetic acid was heated on a steam-bath for 19.5 hours. Mercurous acetate precipitated after 1 hour. The mixture was cooled in ice and filtered. The mercurous acetate weighed 28.1 g. (174% of a two-electron oxidation). The filtrate was saturated with hydrogen sulfide and filtered. This filtrate was concentrated under reduced pressure to *ca.* 15 ml. This residue was treated with 10 ml. of absolute ethanol and 500 ml. of ether, and was made acid to congo red by the addition of 70% aqueous perchloric acid. No precipitate appeared, so an additional 500 ml. of ether was added. An oil separated which solidified when cooled in ice. This weighed 0.3 g. It was recrystallized from absolute ethanol as very small colorless prisms, m.p. 232–235° dec. A mixture of this salt and the perchlorate salt of **11-methyl-11-azabicyclo[5.3.1]hendecane** melted at 233–236° dec. The infrared spectrum in Nujol was identical with that of the perchlorate salt of 11-methyl-11-azabicyclo[5.3.1]hendecane.

An additional 500 ml. of ether was added to the filtrate, and the solid which separated was collected by filtration. It was recrystallized from 1:1 *t*-butyl alcohol–petroleum ether (60–90°), weight 3.16 g. **The perchlorate of 11-azabicyclo[5.3.1]hendecane** was recrystallized from 1:1 *t*-butyl alcohol–petroleum ether (60–90°) as colorless needles, m.p. 203.5–204.5° dec. The infrared spectrum in Nujol exhibited strong peaks at 3180, 3085 $(-\overset{|+}{\underset{|}{N}}-H)$ and 1596 cm.$^{-1}$ $(>\overset{+}{N}H_2)$.

*Anal.* Calcd. for $C_{10}H_{20}ClNO_4$: C, 47.33; H, 7.95; N, 5.52. Found: C, 47.50; H, 7.84; N, 5.42.

The remaining filtrate from the perchlorates was concentrated, made strongly basic with concentrated aqueous sodium hydroxide solution, saturated with potassium carbonate, and extracted with three 15-ml. portions of ether. The extracts were dried, concentrated and distilled. The amine, impure 11-azabicyclo[5.3.1]hendecane, 1.65 g., bringing the total yield to about 60% of theory, was redistilled for infrared analysis, b.p. 99–100° (16 mm.), $n^{26}D$ 1.4957. The infrared spectrum (10% in carbon tetrachloride) was transparent in the 3 and 6 $\mu$ regions and exhibited no peak which could be attributed to an $N-CH_3$ grouping.

**The picrate** crystallized from absolute ethanol as yellow platelets, m.p. 244.5–245° dec.

*Anal.* Calcd. for $C_{16}H_{22}N_4O_7$: C, 50.26; H, 5.80; N, 14.65. Found: C, 50.54; H, 5.78; N, 14.23.

**11-Acetyl-11-azabicyclo[5.3.1]hendecane.**—A mixture of 870 mg. (5.7 mmoles) of 11-azabicyclo[5.3.1]hendecane, 900 mg. (8.8 mmoles) of acetic anhydride and 25 ml. of dry benzene was heated under reflux for 21 hours. The solvent was removed, and 25 ml. of ice-water was added to the residue. The oil which separated was extracted with ether, the extracts were dried and concentrated, and the residue was sublimed at 0.1 mm. The **acetamide** was obtained as colorless irregular prisms, m.p. 56–57°, yield 990 mg. (89%). The compound was resistant to hydrolysis. The infrared spectrum (10% in chloroform) exhibited peaks at 1612 (amide (C=O), 1374 and 1388 cm.$^{-1}$ $(C-CH_3)$ and was transparent in the 3 $\mu$ region.

*Anal.* Calcd. for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.98; H, 10.85; N, 7.09.

**11-Benzenesulfonyl-11-azabicyclo[5.3.1]hendecane.**—**The benzenesulfonamide**, made in the usual manner, was insoluble in both acid and base. It crystallized as large flat colorless plates from absolute ethanol, m.p. 179.5–180°. The compound was resistant to hydrolysis.

*Anal.* Calcd. for $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.65; H, 7.98; N, 4.63.

**Formic Acid–Formaldehyde Methylation of 11-Azabicyclo[5.3.1]hendecane.**—The amine generated from 40 mg. of the picrate of 11-azabicyclo[5.3.1]hendecane, m.p. 244.5–245°, by solution in 6 *N* hydrochloric acid, exhaustive extraction with ether, concentration, basification and extraction with ether, was treated with 5 ml. of 88% formic acid and 100 mg. of 36% aqueous formalin solution. This mixture was allowed to stand at 25° for 10 hours and was warmed on a steam-bath for an additional 14 hours. This solution was cooled in ice, made strongly basic with concentrated aqueous sodium hydroxide solution, saturated with potassium carbonate, and extracted with four 15-ml. portions of ether. The extracts were dried and concentrated. A saturated solution of picric acid in ether was added to the residue. The picrate, which crystallized as yellow needles, m.p. 211–213° dec., in admixture with the picrate of 11-methyl-11-azabicyclo[5.3.1]hendecane melted at 211–212.5° dec.

**Blank Mercuric Acetate Oxidations. a. Formic Acid.**—A mixture of 10.2 g. (0.032 mole) of mercuric acetate, 500 mg. (0.011 mole) of 98% formic acid and 70 ml. of 5% aqueous acetic acid was heated on a steam-bath for 2 hours. A dark-gray precipitate of mercurous acetate separated in less than 5 minutes. The mixture was cooled in ice and filtered. The mercurous acetate collected weighed 5.50 g. (100% of a two-electron oxidation). **b. Formaldehyde.**—A mixture of 12.8 g. (0.040 mole) of mercuric acetate, 540 mg. (0.0067 mole) of 37% formalin solution and 70 ml. of 5% aqueous acetic acid was heated on a steam-bath for 8 hours. A precipitate of mercurous acetate was visible after 3 hours of heating. The solution was cooled in ice and filtered. The mercurous acetate collected weighed 4.2 g. (61% of a four-electron oxidation).

**Tropinone Perchlorate.**—An authentic sample of tropinone was sublimed at 0.1 mm. The infrared spectrum (5% in carbon tetrachloride) was transparent in the 3 $\mu$ region and exhibited a strong carbonyl absorption maximum at 1720 cm.$^{-1}$ and a strong $N-CH_3$ maximum at 1353 cm.$^{-1}$. The perchlorate separated as microscopic crystals from absolute ethanol, m.p. 221.5–222° dec. The infrared spectrum in Nujol exhibited maxima at 3185 $(-\overset{+|}{\underset{|}{N}}-H)$, 1730 cm.$^{-1}$, (C=O) and 1372 cm.$^{-1}$ $(N-CH_3)$.

*Anal.* Calcd. for $C_8H_{14}ClNO_5$: C, 40.09; H, 5.89; N, 5.85. Found: C, 40.24; H, 6.13; N, 5.65.

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