Anal. Calcd. for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.74; H, 7.69.

p-Toluenesulfonate of 5-Hydroxy[10]paracyclophane (XX).—A mixture of 500 mg. of alcohol XVIII, 450 mg. of *p*-toluenesulfonyl chloride and 2 ml. of pyridine was allowed to stand at 25° for 28 hours. The resulting ester was isolated in the usual way, chunky white crystals separating from pentane at −15°, wt. 600 mg. (72%), m.p. 56–58°. Two recrystallizations from pentane gave m.p. 57.5–58.7°.

Anal. Calcd. for $C_{28}H_{30}SO_3$: C, 71.48; H, 7.82. Found: C, 71.27; H, 7.71.

Resolution of 5-Hydroxy[10]paracyclophane (XVIII).—A mixture of 24.12 g. of the 3-nitrophthalic acid ester of XVIII and 18.90 g. of strychnine was dissolved in 100 ml. of chloroform, and 500 ml. of methanol was added. The salt that separated (32.4 g.) was collected and recrystallized five times from chloroform–methanol and four times from chloroform–acetone to yield 0.68 g. of salt with a constant rotation, $[\alpha]^{27}D$ −22.2° (*c* 3.3, $CHCl_3$). This salt was converted to the 3-nitrophthalic acid ester in the usual way, which was recrystallized from ethyl acetate–pentane, m.p. 182–186°. Recrystallization of the material from methanol gave m.p. 184–186.7°, $[\alpha]^{29}D$ −14.1 (*c* 3.3, $CHCl_3$). Recycling of the various crops gave more pure strychnine salt which gave a total of 0.92 g. of (−)-3-nitrophthalic acid ester. This material was hydrolyzed in the usual way to alcohol XVIII which was converted to its 3,5-dinitrobenzoate, wt. 0.62 g., m.p. 98–99.5° (two crystallizations from 95% ethanol), $[\alpha]^{25}D$ +12.3° (*c* 3.3, $CHCl_3$).

Anal. Calcd. for $C_{23}H_{26}N_2O_6$: C, 64.77; H, 6.15. Found: C, 64.65; H, 6.04.

The mother liquors from the original separation of the salt and from the first recrystallization were combined and evaporated. The residue (*ca.* 25 g.) was recrystallized six times from chloroform–methanol to yield 5.18 g. of salt of constant rotation, $[\alpha]^{26}D$ −5.50° (*c* 3.3, $CHCl_3$). This material was converted to the 3-nitrophthalic acid ester in the usual way, wt. 2.74 g., m.p. 184–186.8° (from ethyl acetate–pentane), $[\alpha]^{24}D$ +14.3° (*c* 3.3, $CHCl_3$). This material was hydrolyzed in the usual way to 1.2 g. of alcohol (m.p. 33–37.5°, unrecrystallized) which was converted directly to the 3,5-dinitrobenzoate, m.p. 99–102° (from ethyl acetate–pentane), wt. 2.5 g., $[\alpha]^{22}D$ −11.3° (*c* 3.3, $CHCl_3$).

Anal. Calcd. for $C_{23}H_{26}N_2O_6$: C, 64.77; H, 6.15. Found: C, 65.01; H, 6.13.

LOS ANGELES 24, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BRYN MAWR COLLEGE]

The Bromination of Tropinone[1]

BY ALEX NICKON[2]

RECEIVED FEBRUARY 7, 1955

Tropinone combines with bromine to form an insoluble complex that changes to 2-bromotropinone hydrobromide on standing. Chemical evidence and spectroscopic studies show that the bromine substituent is oriented *cis* to the amine bridge.

The selective bromination of tropinone (I) has not been achieved. In 1896, Willstätter[3] reported that under a variety of conditions this ketone formed a tetrabromo derivative (m.p. 164°), but he was unable to isolate less highly substituted products. Our attempts to effect monobromination in acetic acid solution, in the presence or absence of sodium acetate, likewise afforded only the tetrabrominated product. During the experimentation, we observed (as did Willstätter) that under certain brominating conditions a transient, solid complex appeared. An investigation of this aspect of the reaction eventually provided us with a route to 2-bromotropinone (II), and we now wish to report these results.

When a methanolic solution of bromine was added to the amino-ketone in dry ether, a 1:1 complex of the two reagents precipitated quantitatively as a faint yellow solid (m.p. *ca.* 50°, dec.), which can be collected on a Büchner funnel. This addition compound is unstable, but the onset of decomposition varies with the purity and environmental conditions. Some batches began to decompose within a few minutes, whereas others survived for several hours.

When a suspension of the complex in acetic acid was treated with a little sulfuric acid or boron trifluoride, the solid dissolved and 2-bromotropinone hydrobromide (IIa) soon precipitated in 40–50% yield. The formation of the bromo-ketone by these acid-catalyzed treatments was not always reproducible. However, when the addition compound was simply allowed to stand immersed in dry ether for several days, the material spontaneously changed to the white hydrobromide salt IIa in consistently good yield (92%). By mild basification of this stable hydrobromide salt, the free 2-bromotropinone (IIb) was obtained as a crystalline solid (m.p. 75.5–76.5°), which is sensitive to alkali. Treatment of the free bromo-ketone IIb with ethereal hydrogen bromide regenerated the hydrobromide salt IIa. Four criteria were used to establish that the bromine substituent at C.2 is oriented *cis* to the nitrogen bridge (*i.e.*, β-configuration[4]).

First, a comparison of the infrared spectra of 2-bromotropinone (IIb) and tropinone (I) in carbon disulfide disclosed that no significant displacement of the carbonyl band had occurred on bromination (*cf.* 1722 and 1718 cm.$^{-1}$, respectively). According to the investigations by Jones, *et al.*,[6] and by Corey[7] and his co-workers on halo-ketones, the infrared evidence is interpreted to mean that the carbon–

(1) A portion of this work is taken from the author's Ph.D. thesis, Harvard, 1953; the remainder was carried out at Bryn Mawr College, 1953.

(2) At present Postdoctoral Fellow of the Canadian National Research Council, Ottawa 2, Canada.

(3) R. Willstätter, *Ber.*, **29**, 2228 (1896).

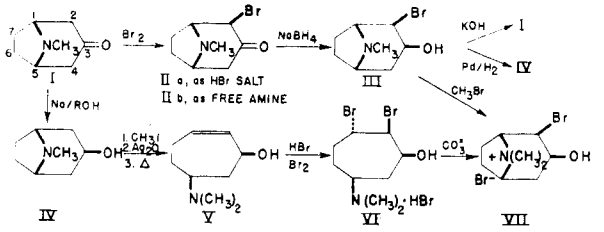
(4) The proposal by Fodor and Nádor[5] for the use of α- and β-prefixes to designate configurations in tropane alkaloids is modelled upon steroid usage and is adopted in this paper. When the two-dimensional formula is viewed from the direction of the amine bridge, substituents below the plane are α, those above the plane, β. Thus, a β-substituent is *cis* with respect to the nitrogen.

(5) G. Fodor and K. Nádor, *J. Chem. Soc.*, 721 (1953).

(6) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

(7) E. J. Corey, *ibid.*, **76**, 175 (1954), and references cited there.

bromine bond is nearly perpendicular to the plane defined by the carbonyl carbon and the two contiguous carbon atoms (*i.e.*, an axial[8] bromine in a chair-shaped cyclohexanone ring). For the case at hand this condition is satisfied by a *cis* relationship between the bromine and the nitrogen bridge.[9]



A second criterion comes from the ultraviolet spectrum of the bromo-ketone IIb, which exhibits a maximum in ethanol at 306 μ (ϵ 90). The corresponding carbonyl absorption in the parent compound tropinone (I) is too weak to be detected. However, the λ_{max} values (*ca.* 280–290 mμ) recorded in the literature for normal six-membered ketones[10,11] make it evident that introduction of the bromine into tropinone has created a significant spectral displacement. Since the data compiled by Cookson[11] clearly show that a bathochromic shift and intensified absorption are characteristic changes produced when a halogen is substituted axially next to an isolated carbonyl group, the β-configuration of the C.2 bromine in II again is indicated.[9]

The third approach to the stereochemical problem is based upon the following chemical transformations. On reduction with aqueous sodium borohydride the bromo-ketone salt IIa yielded the crystalline bromohydrin III.[12] Catalytic hydrogenolysis (Pd/C) smoothly removed the bromine from III and gave pseudotropine (IV). From the known configuration of this last compound,[6,13] the hydroxyl group of the bromohydrin must be β. To determine the steric relationship of the bromine to the hydroxyl, the bromohydrin III was heated with ethanolic potassium hydroxide. This reaction gave an oil shown to be crude tropinone (I) by a comparison of infrared spectra and by conversion to the hydrochloride and picrate derivatives. According to Bartlett's[14] generalization that under appropriate alkaline conditions *cis*-halohydrins generate ketones whereas *trans*-halohydrins give epoxides, the halogen in 2-bromopseudotropine (III) is oriented *cis* to the hydroxyl function and hence has the β-configuration.[15]

The fourth proof makes use of a sequence of reactions originally developed by Willstätter.[16] We repeated this sequence and have applied it to our problem in the following manner. On quaternization followed by Hofmann elimination, pseudotropine (IV) was converted to the des-base V.[17] Addition of a mole of bromine to a hydrobromic acid solution of this des-base gave a dibromide salt that was not crystalline. Direct neutralization of the acidic reaction mixture liberated the amine dibromide which then immediately cyclized to the crystalline quaternary salt VII (40–50% over-all yield from V). This last compound has an infrared spectrum (Nujol) identical to that given by the methobromide salt obtained on treatment of 2-bromopseudotropine (III) with methyl bromide.

Attention is now drawn to the stereochemical aspects of these reactions. First, the *cis* relation between the hydroxyl and the nitrogen group in V follows from the known configuration of the precursor IV. The bromination in aqueous acidic medium should produce *trans*-dibromides,[18] two of which are possible. Of these two, the one that undergoes cyclization to form VII must have the stereochemistry shown in VI. This conclusion follows from a consideration of the mechanism of the ring closure (VI → VII), a process which entails rearward displacement of an α-disposed bromine by the β-oriented amine grouping. It follows that the C.2 bromine is β-oriented, and this must apply also to the bromohydrin III and to the bromo-ketone II.

(8) D. H. R. Barton, O. Hassel, K. Pitzer and V. Prelog, *Nature*, **172**, 1096 (1953).

(9) The assignment of configuration from spectroscopic data is valid provided that the six-membered portion of the tropane ring system adopts the normal chair conformation [R. N. Jones, THIS JOURNAL, **75**, 4839 (1953)]. Except in those special cases where chelation effects might interfere [S. Archer and T. R. Lewis, *Chemistry & Industry*, 833 (1954)], there is ample support that this provision is upheld. Thus the behavior of tropinone on reduction, the relative stabilities of tropine and pseudotropine to alkali [R. C. Cookson, *ibid.*, 337 (1953); A. K. Bose and D. K. R. Chaudhuri, *Nature*, **171**, 652 (1953)], and the relative rates of saponification of the benzoates and nitrobenzoates of tropine and pseudotropine [F. L. J. Sixma, C. M. Siegmann and H. C. Beyerman, *Proc. K. Ned. Acad. Wet.*, **54B**, 452 (1951)], are in harmony with conformational predictions. Likewise, the epimerizations that recently have been elucidated for cocaine and related compounds [S. P. Findlay, THIS JOURNAL, **76**, 2855 (1954); O. Kovacs G. Fodor and I. Weisz, *Helv. Chim. Acta*, **37**, 892 (1954) and references cited there] are consistent with normal puckering of the tropane skeleton. Finally, an X-ray analysis has revealed that crystalline tropine hydrobromide exists in the chair conformation [J. W. Visser, J. Manassen and J. L. de Vries, *Acta Cryst.*, **7**, 288 (1954)].

(10) L. Dorfman, *Chem. Revs.*, **53**, 47 (1953).

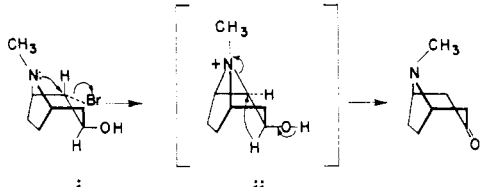
(11) R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

(12) Isomerization of the bromine in this reaction is unlikely since sodium borohydride in general does not effect such epimerizations during reductions.

(13) (a) A. Nickon and L. F. Fieser, THIS JOURNAL, **74**, 5566 (1952); (b) B. L. Zenitz, L. M. Martini, M. Priznar and F. C. Nachod, *ibid.*, **74**, 5564 (1952); (c) E. Hardegger and H. Ott, *Helv. Chim. Acta*, **36**, 1186 (1953), and references cited there.

(14) P. D. Bartlett, THIS JOURNAL, **57**, 224 (1935).

(15) It is of interest that the alkaline treatment of 2-bromopseudotropine (III) to form tropinone (I) can be rationalized on the basis of an α-oriented bromine (see i) if we assume that the bridged nitrogen can participate first in the manner shown to give an intermediate resembling ii. The action of alkali on such an intermediate could lead



i ii

to the ketone. Taken by itself, therefore, this chemical evidence would be insufficient.

(16) R. Willstätter, *Ann.*, **326**, 1 (1903).

(17) The formation of V as the major product appears to be another striking example of the stereospecificity of Hofmann eliminations. In this case the preferred coplanarity of the four relevant centers is attained only when a C.2 hydrogen is involved [J. McKenna, *Chemistry & Industry*, 406 (1954).]

(18) Stereochemical complications that might arise from any participation effects by nitrogen or hydroxyl are not to be expected under the acidic conditions employed [*cf.* S. Winstein and L. Goodman, THIS JOURNAL, **76**, 4368, 4373 (1954)].

We also have confirmed Willstätter's[16] findings that tropine (epimer of IV) undergoes an identical series of transformations, which may be represented by IV → V → VI → VII except that in each case the hydroxyl has the α-configuration. Moreover, in this epimeric series the dibromide salt corresponding to VI (α-OH) is a crystalline compound that was characterized and cyclized separately to the bicyclic salt VII (α-OH). This parallelism in behavior between the two epimeric series supports the contention, made above, that both the bromination (V → VI) and the internal cyclization (VI → VII) proceed by straightforward mechanistic paths.

Experimental[19]

Tropinone (I), Pseudotropine (IV), Tropine (Epimer of IV).—These three compounds were obtained as described in a previous publication.[13a] The tropinone had ν^{CS_2} 1718 cm.$^{-1}$; no ultraviolet maximum was detected around 285 mμ in ethanol.

Isolation of Tetrabromotropinone.—When one equivalent of bromine was added to a solution of tropinone in glacial acetic acid, a precipitate of the tropinone–bromine complex appeared within 2–3 min. The mixture stood uncovered for 1 hr., during which time the solid material redissolved and hydrogen bromide was copiously evolved. After the solution stood for an additional hour, it was poured into a large excess of water, which precipitated a small amount of crystalline material. The aqueous mixture was heated to the boiling point and then filtered. The crude crop after one crystallization from aqueous ethanol appeared as faint yellow platelets, m.p. 160–163° dec. (reported[3] 164°), ν^{CS_2} 1776 cm.$^{-1}$. Paucity of material precluded further purification; however, an analysis on these crystals indicated that four bromine atoms had been introduced.

Anal. Calcd. for $C_8H_9ONBr_4$ (454.84): Br, 70.29. Found: Br, 70.89.

Repetition of the procedure in the presence of 1.1 moles of sodium acetate resulted in no initial perbromide formation. The mixture was processed as described above, but the only product isolated was the tetrabromo derivative.

Tropinone–Bromine Perbromide.—Gradual addition of a solution of 3.2 g. (1.1 equiv.) of bromine in 10 cc. of commercial anhydrous methanol to a stirred solution of 50 cc. of commercial anhydrous ether containing 2.5 g. of tropinone resulted in the precipitation of a faint-yellow, granular solid. This substance was collected immediately and washed well with more ether. The yield (5.4 g.), based on a 1:1 ratio of tropinone to bromine, was quantitative; m.p. 51° (transition, sealed tube). The complex is insoluble in ether, benzene, methanol, and carbon tetrachloride, but is readily dissolved by acetone. It decomposes on standing and should be utilized immediately.

2β-Bromotropinone Hydrobromide (IIa). (a) By Sulfuric Acid Catalysts.—Addition of 2 cc. of concentrated sulfuric acid to a suspension of 5.0 g. of the complex in 25 cc. of glacial acetic acid caused the mixture to warm, and a nearly colorless solution was formed within 1–2 min. Hydrogen bromide was briskly evolved. When the walls of the flask were scratched vigorously tiny white crystals soon appeared. After being allowed to stand for 30 min. the solid was collected and washed with small portions of acetic acid and then with anhydrous ether; yield 1.85 g., m.p. 178° dec. We obtained a second crop (0.80 g.) by allowing the mother liquor and washings to stand overnight; total yield 2.65 g. (53%). This method was not always reproducible. After crystallization from an anhydrous mixture of methanol–ether, the 2β-bromotropinone hydrobromide had m.p. 192° dec. (vacuum, tube introduced at 180° and heated at 3° per min.); ν^{nujol} 1728 cm.$^{-1}$.

Anal. Calcd. for $C_8H_{13}ONBr_2$ (299.03): C, 32.13; H, 4.38. Found: C, 32.64; H, 4.43.

(19) All melting points are corrected, unless specified otherwise. The author is grateful to Dr. W. Y. Huang (Harvard) and Mr. R. Lauzon (N.R.C.) who recorded some of the spectra. These were determined on Perkin–Elmer (model 21) infrared, and on Cary (model 11M) recording ultraviolet, spectrophotometers.

(b) By Boron Trifluoride Catalysis.—The complex (1.0 g.) was suspended in 25 cc. of glacial acetic acid containing 1.0 cc. of boron trifluoride etherate. After several minutes the material suddenly started to dissolve. Within a minute or two a finely divided solid began to precipitate from the clear, nearly colorless solution; evolution of hydrogen bromide was observed. Next day the solid was collected, washed sparingly with glacial acetic acid and finally with anhydrous ether; 0.42 g. (42%), m.p. 181–183° dec. (vacuum). Several trials were performed in which the relative amounts of catalyst, complex and acetic acid were varied. These experiments all gave lower yields (15–35%). In some cases where the perbromide failed to dissolve after 15 min., brief heat treatment then initiated the reaction.

(c) By Spontaneous Transition.—The perbromide (2.0 g.) covered with anhydrous ether (100 cc.) was permitted to stand at room temperature for 14 days in a stoppered flask. Every 2 or 3 days during this period the supernatant liquid was decanted and replaced by fresh ether. When a little of the white solid no longer turned gummy on exposure to the atmosphere, the whole batch was washed (by decantation) with several portions of anhydrous ether, collected on a Büchner funnel, and again thoroughly washed with ether; yield of crude IIa was 1.85 g. (92.5%), m.p. 171–173° dec. (vacuum).

2β-Bromotropinone (IIb).—A purified sample of IIa (1.0 g., m.p. 190–192° dec. (vacuum)) was added to aqueous sodium carbonate, and the solution rapidly extracted twice with chloroform. The organic layer was filtered through anhydrous sodium sulfate, and evaporated in vacuum. The residual oil was crystallized from a small volume of petroleum ether (b.p. 30–60°); m.p. 69–73° (0.43 g.). For analysis the bromo-ketone was crystallized twice more, then sublimed in vacuum at a bath temperature of 60–70°; transparent prisms, m.p. 75.5–76.5° (Pyrex tube); ν^{CS_2} 1722 cm.$^{-1}$, λ^{EtOH} 306 mμ (ε 90).

Anal. Calcd. for $C_8H_{12}ONBr$ (218.11): C, 44.05; H, 5.55. Found: C, 44.22; H, 5.56.

The free bromo-ketone is sensitive to alkali and gradually decomposes on storage.

2β-Bromopseudotropine (III).—Crude 2-bromotropinone hydrobromide (m.p. 171–172°, 0.897 g.) was dissolved in 20 cc. of water. Sodium borohydride (0.150 g.) was introduced cautiously, and the solution was permitted to stand overnight at room temperature. Extraction with four 30-cc. portions of chloroform followed by evaporation of the solvent afforded 0.486 g. of crude, somewhat sticky bromohydrin. Preliminary purification was effected by chromatography over acid-washed alumina with eluents that ranged from pure benzene to a mixture of 80% benzene and 20% ether. The solid fractions (0.41 g., 62%) melted in the region 120–125°. Repeated crystallization from anhydrous ether gave transparent needles, m.p. 125–125.5°, ν^{CS_2} 3561 cm.$^{-1}$.

Anal. Calcd. for $C_8H_{14}ONBr$ (220.12): C, 43.65; H, 6.41. Found: C, 43.83; H, 6.46.

Conversion of III to Pseudotropine (IV).—Palladium-charcoal (0.1 g.) was added to a solution of III (0.044 g., m.p. 123–125°) in 10 cc. of commercial absolute ethanol, and the mixture reduced with hydrogen at atmospheric pressure for 5 hr. The catalyst was removed by filtration, and the filtrate taken to dryness. The residual solid (pseudotropine hydrobromide) was dissolved in 2 cc. of water that contained 0.2 g. of sodium hydroxide. Extraction with chloroform and evaporation of the solvent left a solid (m.p. 102.5–107°), which had m.p. 107.5–109° after crystallization from benzene–petroleum ether (b.p. 30–60°). A mixture melting point with authentic pseudotropine was undepressed. The initial crude crops as well as the crystallized material exhibited an infrared spectrum identical to that of genuine pseudotropine (chf.).

Conversion of III to Tropinone (I).—To 6 cc. of commercial anhydrous ethanol was added 0.018 g. of potassium hydroxide and a crude batch (m.p. 115–123°) of III (0.065 g.). The solution was refluxed for 4.5 hr., and then taken nearly to dryness in a vacuum desiccator. The residue was extracted with several 3-cc. portions of anhydrous ether. Careful evaporation of the filtered extracts gave 0.031 g. (75%) of a colorless oil that was shown to be crude tropinone by the following criteria. The hydrochloride salt, prepared with dry hydrogen chloride in ether, had m.p. 183.5–185°

dec., which was not depressed by genuine tropinone hydrochloride (m.p. 188°[20]). The crude picrate (m.p. 207° dec.), prepared in benzene, did not depress the m.p. of authentic tropinone picrate (m.p. 215°[20]). Finally, the infrared spectrum (chf.) of the oil was superposable on that of pure tropinone over the entire region with but minor exceptions.

Hofmann Degradation of Pseudotropine (IV).—A warm aqueous solution of pseudotropine methiodide (obtained with methyl iodide in ether) was treated with one equivalent of silver oxide and digested at 50° for 1 hr. The cooled mixture was filtered and the filtrate distilled at atmospheric pressure; after removal of the water the portion with b.p. 230–245° was collected. Redistilled twice in vacuum, the des-base V was a colorless, viscous liquid, b.p. 110–112° (2 mm.). On refrigeration the oil formed a hygroscopic solid (m.p. 41–44°, sealed tube).

The corresponding benzoate was prepared with benzoic anhydride in refluxing benzene (8 hr.) and converted to the hydrochloride salt as described by Willstätter.[16] This derivative had m.p. 169° (reported 166–167°) and was crystallized from an anhydrous mixture of alcohol–ether.

Bromination and Cyclization to 2-Bromopseudotropine Methobromide (VII).—To the des-base (V, 0.50 g.) obtained above, in 2 cc. of water was added 1.2 g. of 34% hydrobromic acid. This solution then was cooled in ice and shaken vigorously while a solution of bromine (0.54 g.) in chloroform (5.0 g.) was introduced slowly at a rate governed by the rate of discharge of the bromine color (10–20 min.). Sodium bisulfite was added to decolorize unchanged bromine, and the cold mixture was made alkaline with solid sodium carbonate and shaken well. The chloroform layer was separated, the aqueous layer was promptly extracted with more chloroform, and the combined organic layers were filtered through anhydrous sodium sulfate. Warming the filtrate effected cyclization of the des-base dibromide, and crystals of 2β-bromopseudotropine methobromide started to precipitate almost immediately. After concentration to a volume of 8 cc. the mixture was cooled and the solid collected; 0.33 g., m.p. 240° dec. (vacuum, dependent on rate of heating). Crystallization from ethanol improved the appearance but did not alter the m.p. (reported 237–238°[16]).

(20) R. Willstätter, *Ber.*, **29**, 393 (1896).

Conversion of the Bromohydrin III to the Methobromide Salt VII.—An anhydrous ethanolic solution of III (m.p. 120–124°) was treated with excess methyl bromide, and the stoppered flask allowed to stand 24 hr. The transparent rhombs that formed were collected, washed with a little ethanol, then with ether; m.p. 245° dec. Additional material was obtained by concentration of the mother liquor and precipitation with ether. The 2β-bromopseudotropine methobromide prepared this way and the one prepared by the cyclization procedure described above gave infrared spectra (in Nujol) that were superposable.

Hofmann Degradation of Tropine (Epimer of IV).—Tropine was degraded to the corresponding des-base (epimer of V) by the same procedure as was used for pseudotropine. After being redistilled twice, the olefin had b.p. 110–111° (2 mm.) and was a viscous oil with a faint yellow tinge.

The hydrochloride salt of the corresponding benzoate ester was obtained by heat treatment of the des-base with benzoyl chloride for a few minutes. The mixture stood overnight and then was diluted with ether. Crystallized from ethanol–ether (both anhydrous) the solid had m.p. (uncor.) 175–177° (reported 171–172°[16]).

Preparation of the Epimer of VI.—The des-base obtained from tropine was treated with bromine as described above for the pseudo series. During the bromine addition the chloroform layer became filled with a white solid. The cold mixture was filtered and the solid washed with cold chloroform then with dry ether; 0.46 g., m.p. 168° dec. Recrystallized from ethanol this hydrobromide salt had m.p. 178–178.5° dec. (reported 178°[16]).

Cyclization of the Dibromide Salt to the Epimer of VII.—The epimer of VI (0.40 g.) was added to a funnel containing 4 cc. of water, 5 cc. of chloroform and 0.6 g. of sodium carbonate, and the mixture shaken. The aqueous phase was extracted again with chloroform, and the combined organic layers were filtered through sodium sulfate and boiled down on a steam-cone for 15 min. The solid that precipitated was collected and dried; 0.18 g., m.p. 236° dec. Recrystallized from dry alcohol–ether, the 2β-bromotropine methobromide had m.p. 237° dec. (dependent on rate of heating); reported m.p. *ca.* 233°.[16] The preparation of this compound was performed also without isolation of the intermediate dibromide salt as was done in the pseudo series.

BRYN MAWR, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Azo Compounds.[1] A Re-examination of the Structure of the Product from the Reaction of Heptane-2,6-dione with Hydrazine Sulfate and Sodium Cyanide in Dilute Solution

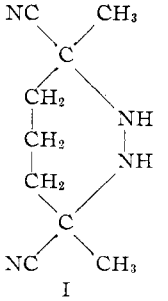
BY C. G. OVERBERGER AND BURTON S. MARKS[2]

RECEIVED JANUARY 18, 1955

The reaction betweenheptane-2,6-dione, hydrazine sulfate and sodium cyanide has been re-examined. It has been shown that the product is II, 1-amino-2,6-dicyano-2,6-dimethylpiperidine instead of I, 3,7-dicyano-3,7-dimethylhomopiperidazine, previously reported.

In previous work[3] we had reported that the reaction between heptane-2,6-dione, hydrazine sulfate and sodium cyanide had resulted in the formation of I.

Structure I was proposed based on the following evidence. Oxidation of the product with bromine in ethanol gave a quantitative evolution of nitrogen and three well characterized products, indicative of biradical formation on decomposition of an unstable azo intermediate. The analogous behavior of linear hydrazines of similar structure to form azo compounds on oxidation and the known mechanism of the decomposition of linear azo compounds of this



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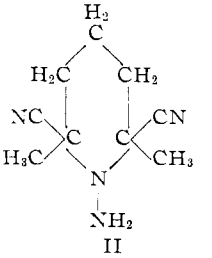

II

(1) This is the 12th in a series of articles on the preparation and decomposition of azo compounds. For the 11th paper in this series see C. G. Overberger, W. F. Hale, M. B. Berenbaum and A. B. Finestone, THIS JOURNAL, **76**, 6185 (1954).

(2) A portion of a thesis submitted by Burton S. Marks in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

(3) (a) C. G. Overberger, T. B. Gibbs, Jr., S. Shibnik, P. Huang and J. J. Monagle, THIS JOURNAL, **74**, 3290 (1952); (b) C. G. Overberger, P. Huang and T. B. Gibbs, Jr., *ibid.*, **75**, 2082 (1953).