once more from dilute alcohol and formed long prisms, m.p. 214–215° dec. It was dried for analysis 4 hours at 80° (0.05 mm.).

Anal. Calcd. for $C_{21}H_{23}N_2O_3$: C, 70.76; H, 7.92; N, 7.86. Found: C, 70.51; H, 8.00; N, 7.78.

The mother liquor from the first crystallization of recanescic alcohol was evaporated under reduced pressure and a small amount of an oily residue (*ca.* 40 mg.) obtained. This was treated in the usual manner with *p*-nitrobenzoyl chloride in pyridine. The derivative (*ca.* 15 mg.) was identical with material prepared from an authentic sample of 3,4,5-trimethoxybenzoyl alcohol[5] (m.p., mixed m.p. and X-ray patterns).

Partial Hydrolysis of Recanescine; Isolation of Methyl Recanescate *O*-Tosylate and 3,4,5-Trimethoxybenzoic Acid.—To a solution of 100 mg. of sodium in 25 ml. of absolute methanol was added 670 mg. of recanescine (free of solvent of crystallization). After boiling for 1 hour under reflux and concentration to 5 ml. *in vacuo*, the reaction mixture was acidified and extracted exhaustively with ether. The ethereal solution was evaporated to dryness, the residue dissolved in hot sodium hydroxide solution (*ca.* 10%), filtered and acidified. Beautiful prisms of 3,4,5-trimethoxybenzoic acid, m.p. 168°, slowly separated. This material was identical with the authentic sample of the acid (m.p., mixed m.p. and X-ray patterns).

The aqueous phase from ether extraction was made basic and extracted with chloroform, dried over anhydrous sodium sulfate and evaporated to dryness. The residue (400 mg.) was dissolved in 5 ml. of dry pyridine, 800 mg. of recrystallized, dry tosyl chloride added, and allowed to stand for three days at room temperature. After the usual work-up, the crude tosyl ester was recrystallized from boiling benzene with addition of charcoal. The yield was 215 mg. of material, m.p. 210–211° dec. It was recrystallized twice from the same solvent and dried for 4 hours at 100° (0.05 mm.) for analysis.

Anal. Calcd. for $C_{29}H_{34}O_6N_2S$: C, 64.66; H, 6.36; N, 5.20; S, 5.95. Found: C, 64.84; H, 6.50; N, 5.15; S, 5.88.

INDIANAPOLIS 6, INDIANA

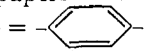
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Macro Rings. XI. Reactions in the 1,4-Decamethylenebenzene Series[1]

BY DONALD J. CRAM AND MARTIN CORDON

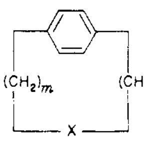
RECEIVED JANUARY 21, 1955

Syntheses, reactions and physical properties are described for compound I ($n = m = 4$) with X = —C≡C—, —C=CH— (*cis*), —CH_2CHOH— (both enantiomers) and for I ($m = 4$, $n = 3$) with X = $O{=}\underset{|}{C}{-}CH{=}CH{-}$.

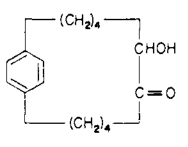
Previous papers[2] in this series have reported the preparation of I ($m = n = 4$) with X = CH_2CH_2, CHOHCO, CHOHCHOH, COCO (and its enol) and CH_2CO, as well as various derivatives of these substances. Of these compounds, only I ($m = 4$, $n = 3$) where X = CH=COHCO and its acetate possess ultraviolet spectral properties which cannot be predicted by simple addition of the aromatic and X chromophores. Other papers[3] have recorded the preparation of I with -X- =  in which m and n were systematically varied between 2 and 6. In this series, abnormal ultraviolet spectral properties were observed for those compounds in which n or $m < 4$, the spectra of the higher homologs being normal as compared to open chain models.

The objectives of this investigation were (1) to prepare and study the properties of I with $m = n = 4$ and X = C≡C or CH=CH (*cis*), and of I with $m = 3$, $n = 4$ and X = CH=CHCO; and (2) to prepare and resolve I ($m = n = 4$) with X = CH_2CHOH. This latter objective is a preliminary to solvolysis studies designed to determine if the π-electrons of the benzene become involved in ionization processes in the side chain.

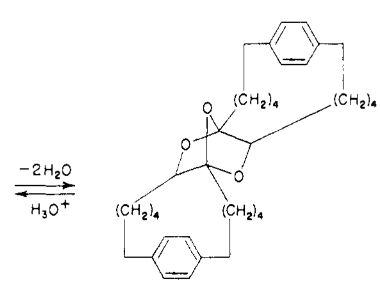
Preparation of Derivatives of 1,4-Decamethylenebenzene.—Acyloin II[2a] (the parent cyclic starting material) was found upon standing to undergo self-condensation to give material which upon treatment with acetic anhydride gave a substance whose properties are consistent with the bicyclic bis-ketal structure, III. The analysis and molecular weight of the compound indicated it to be



I



II



III

a dimer of the acyloin minus one mole of water. The infrared spectrum of the substance was devoid of bands in the hydroxyl or carbonyl regions, but possessed a strong band at 9.30 μ characteristic of ether linkages. The compound reacted very slowly with a solution of 2,4-dinitrophenylhydrazine in dilute acid, and with bismuth oxide in acetic acid.[4] Although a number of stereoisomeric forms of III are possible, no detailed structural assignment is possible. This bicyclic ketal probably arose by the action of the acetic anhydride on the simple dimer containing the cyclic hemiketal linkage IV, which function has been observed to arise from other acyloins.[5]

The acyloin II was oxidized (Bi_2O_3) to a mixture of α-diketone and enol[2a] which was heated with

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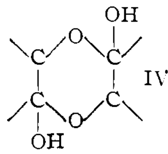
(1) This work was generously supported by a grant from the Upjohn Company.

(2) (a) D. J. Cram and H. U. Daeniker, THIS JOURNAL, **76**, 2743 (1954); (b) D. J. Cram and M. Cordon, *ibid.*, **77**, 1810 (1955).

(3) (a) D. J. Cram and H. Steinberg, *ibid.*, **73**, 5691 (1951); (b) H. Steinberg and D. J. Cram, *ibid.*, **74**, 5388 (1952); (c) D. J. Cram and N. L. Allinger, *ibid.*, **76**, 726 (1954); (d) N. L. Allinger and D. J. Cram, *ibid.*, **76**, 2362 (1954); (e) J. Abell and D. J. Cram, *ibid.*, **76**, 4406 (1954); (f) D. J. Cram and N. L. Allinger, *ibid.*, **76**, 6132 (1954).

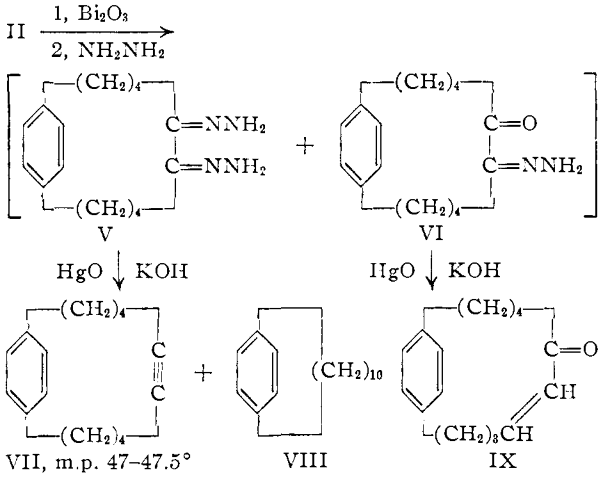
(4) W. Rigby, *J. Chem. Soc.*, 793 (1951).

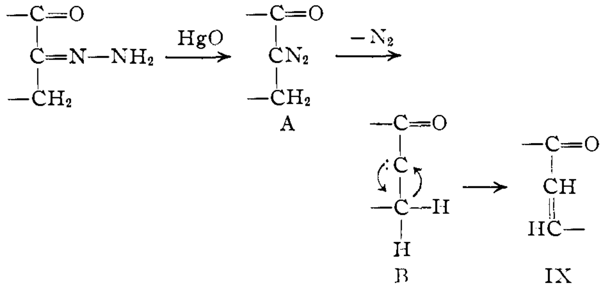
(5) J. C. Sheehan, R. C. O'Neill and M. H. White, THIS JOURNAL, **72**, 3376 (1950).

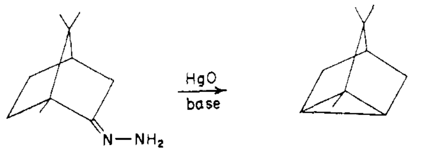


IV

excess 95% hydrazine. Since the product was an oil, it was treated directly with yellow mercuric oxide in the presence of sodium sulfate and potassium hydroxide in refluxing benzene.[6] Two compounds were isolated, the acetylene VII and the α,β-unsaturated ketone IX,[7] and evidence was obtained for the presence of hydrocarbon VIII. The best yield of acetylene VII was 12% (based on II), the compound arising from osazone V by decomposition of a bis-diazo intermediate. The hydrocarbon VIII presumably arose by a competing Wolff–Kishner reaction. The α,β-unsaturated ketone probably came from the monohydrazone VI, which was converted with mercuric oxide to a diazoketone A. This substance might have decomposed to give a resonance stabilized carbene B which went to the unsaturated ketone by a 1,2-hydrogen shift from the adjacent methylene group. An analogy for this type of sequence is found in the conversion of camphor hydrazone X by the action of mercuric oxide to tricyclene XI.[8] In this example a 1,3-shift of a hydrogen and a rearrangement of electrons leads to a three- rather than a two-membered ring observed in the present investigation. The generality of this procedure for the preparation of α,β-unsaturated ketones is being investigated.

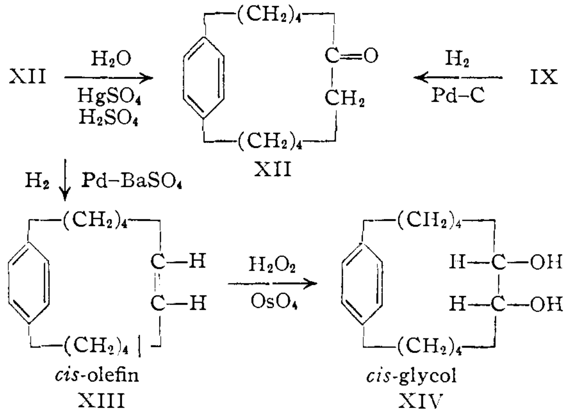




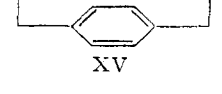


X XI

The cyclic acetylene VII and the unsaturated ketone IX were both converted to the same simple ketone XII by conventional methods, the ketone being characterized as its 2,4-dinitrophenylhydrazone and semicarbazone. These samples of ketone were demonstrated to be identical with "ketone C" obtained previously[2a] by the zinc–hydrogen chloride reduction of acyloin II, and with "ketone III" obtained by the dithiol reduction of acyloin II.[2b] The acetylene XII was reduced catalytically to *cis*-olefin XIII, which was hydroxylated with osmium tetroxide to give the *cis*-glycol XIV. The stereospecificity of the reduction[6b] and hydroxylation[6e] in medium sized rings allows glycol XIV to be assigned the *cis* configuration. The substance proved to be identical with the predominating "glycol IVA" obtained previously[2a] by catalytic reduction of acyloin II. Thus the configurations of both the *cis*(*meso*)- and *trans*-glycols become established.



Spectral Properties of the Unsaturated Derivatives of 1,4-Decamethylenebenzene.—The ultraviolet absorption spectra of *cis*-olefin XIII and acetylene VII proved to be essentially identical to that of the parent 1,4-decamethylenebenzene (VIII).[2a] These spectral results indicate that the π-electrons of the acetylenic and ethylenic linkages are too far away in these cycles to become involved with the π-electrons of the benzene ring. This result is consistent with the absence of transannular spectral effects of any consequence in compounds of structure XV when m and $n > 3$.[3f] The distance



XV

XVI

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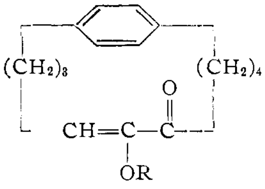
[6] (a) A. T. Blomquist, R. E. Burge, Jr., L. Huang Liu, J. C. Bohrer, A. C. Sucsy and J. Klein, THIS JOURNAL, **73**, 5510 (1951); (b) A. T. Blomquist, R. E. Burge, Jr., and A. C. Sucsy, *ibid.*, **74**, 3636 (1952); (c) A. T. Blomquist, L. Huang Liu and J. C. Bohrer, *ibid.*, **74**, 3643 (1952); (d) A. T. Blomquist and L. Huang Liu, *ibid.*, **75**, 2153 (1953); (e) V. Prelog, K. Schenker and H. H. Gunthard, *Helv. Chim. Acta*, **35**, 1598 (1952).

[7] This substance was purified and characterized as its 2,4-dinitrophenylhydrazone.

[8] M. Meerwein and K. van Emster, *Ber.*, **53**, 1815 (1920).

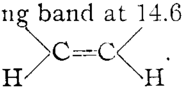
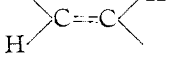
between the benzene ring and the site of unsaturation in the methylene belt in VII and XIII is probably less than the 3.7 Å. calculated for XV with $m = n = 4$, but greater than the 3.4 Å. which has been estimated as the normal van der Waals distance.[3f] These spectral results also suggest that in the olefin and acetylene, the ten-membered belt attached to the 1,4-positions of the benzene has not been pulled much tighter in these unsaturated compounds than in the parent compound containing the saturated belt (VIII). Had the belt been shorter, a shift in spectra of VII or XIII toward that of XVI would have been observed. Apparently the distance lost in altered bond lengths in VII and XIII has been gained in the increases in size of the two C–C–C bond angles.

The ultraviolet absorption spectrum of unsaturated ketone IX (see Experimental) resembles that of the keto enolacetate XVIIb, but is unlike that of the enol ketone XVIIa.

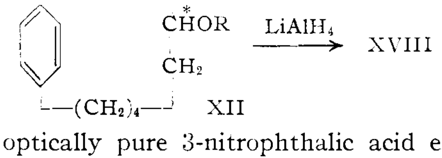


XVIIa, R = H
XVIIb, R = $COCH_3$

This result is expected since the acetylation of a hydroxyl group on this chromophore usually nullifies the effect of a hydroxyl on the spectrum.[9] The fact that all three spectra are abnormal (the spectra of the aromatic nucleus and the unsaturated ketone are not additive) is another example of transannular electronic effects becoming evident when the two chromophores are held together by one or more bridges containing three or less methylenes.[3f]

Bands characteristic of the functional groups of the above unsaturated compounds were observed in their infrared spectra. Acetylene VII possessed a weak band at 4.52 μ (—C≡C— stretching) characteristic of disubstituted acetylenes. Olefin XIII possessed a strong band at 14.60 μ characteristic of the *cis* linkage  . A weak band also was observed at 10.35 μ, probably due to a slight contamination with *trans*-olefin. The acetylene differed from its saturated parent (VIII) in the 12–13 μ region by having a medium band at 12.65 μ instead of an intense band at 12.36 μ which characterizes both VIII and olefin XIII. The unsaturated ketone IX gave two strong bands, one at 5.85 μ and one at 6.00 μ, with a shoulder at 5.92 μ. Normally these bands would have occurred at higher wave lengths and at different intensities, and the fact that the infrared spectrum of IX is abnormal correlates with the abnormal ultraviolet spectrum of the same substance. A band at 10.38 μ characteristic of  was also observed for IX whereas only a slight absorption was found in the 14–15 μ region. Apparently the α,β-unsaturated ketone possesses a *trans* configuration.

Preparation and Resolution of Alcohol XVIII.—Reduction of ketone XII with lithium aluminum hydride afforded alcohol XVIII which was characterized as its acid phthalate, 3-nitrophthalic acid ester, *p*-toluenesulfonate and 3,5-dinitrobenzoate. The first two derivatives did not melt sharply and the melting point varied depending on its mode of crystallization. The last two derivatives gave sharp and easily reproducible melting points. A partial and laborious resolution of the acid phthalate of XVIII was carried out through its brucine salt, but this method was abandoned in favor of one involving fractional crystallization of the strychnine salt of the 3-nitrophthalic acid ester of XVIII. This method was poor but appeared to yield essentially optically pure 3-nitrophthalic acid ester of the two enantiomers of XVIII, which were converted to their respective 3,5-dinitrobenzoates for characterization purposes. Table I records the melting points and rotations of these derivatives.



XII

TABLE I

MELTING POINTS AND ROTATIONS OF DERIVATIVES OF ALCOHOL XVIII

Compound	M.p., °C.	$[\alpha]^{22-23}D$ (3.3% $CHCl_3$)
(±)-3-Nitrophthalic acid ester	190–193	....
(−)-3-Nitrophthalic acid ester[a]	184–187	−14.1°
(+)-3-Nitrophthalic acid ester[b]	184–187	+14.3
(±)-3,5-Dinitrobenzoate	116–117	.....
(+)-3,5-Dinitrobenzoate[a]	98–99.5	+12.3
(−)-3,5-Dinitrobenzoate[b]	99–102	−11.3

[a] Derived from alcohol of the same configuration. [b] Derived from alcohol of the same configuration.

Experimental[10]

5-Hydroxy-6-keto[10]paracyclophane (II).[11]—This substance was prepared by the acyloin condensation of the appropriate diester in 76% yield, b.p. 164–166° (1 mm.). A small sample was converted to its oxime in 95% yield, m.p. 161–163° (white prisms from ethanol).

Anal. Calcd. for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.88. Found: C, 73.45; H, 8.81.

Dimeric Condensation Product (III) of Acyloin II.—A five-month old sample of acyloin II was treated with acetic anhydride by the procedure previously employed in preparing the acetate.[2a] Distillation of the uncrystallizable product gave ester (b.p. 160–162° at 0.8 mm., m.p. 47–49°) in 35% yield, and a pot residue which when dissolved in ethyl acetate deposited colorless platelets, m.p. 178–181° (23% yield). An analytical sample gave m.p. 184–186° (from ethyl acetate).

Anal. Calcd. for $C_{32}H_{42}O_3$: C, 80.97; H, 8.91; mol. wt., 474. Found: C, 80.90; H, 8.93; mol. wt. (Rast), 505.

5-[10]Paracyclophyne (VII).—Acyloin II (9.00 g.) and 10 g. of bismuth oxide were added to 40 ml. of glacial acetic acid, the mixture was stirred and heated at 110° for two hours. A small sample of material gave no acyloin test[4] at the end of this time. The mixture was filtered, 60 ml.

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(9) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1949, p. 195.

(10) Melting points are corrected, boiling points are not. The ultraviolet absorption spectra were taken on a Cary spectrophotometer, model 11 PMS in 95% ethanol unless otherwise specified. The infrared spectra were taken on a Model 21 Perkin–Elmer spectrophotometer.

(11) See D. J. Cram and J. Abell [THIS JOURNAL, **77**, 1179 (1955)] for an explanation of the system of nomenclature employed.

of water was added, and the yellow oil that separated was extracted into benzene. The benzene solution was washed with water, sodium bicarbonate solution, water and was dried. Evaporation of the solvent under reduced pressure gave a yellow oil (9 g.) which solidified to give a mixture of α-diketone and the corresponding enol ketone.[2a] Attempts to obtain crystalline bis-hydrazone from pure α-diketone failed, and therefore the above crude mixture was used directly in the next step. The material was dissolved in 15 ml. of absolute ethanol, 4 ml. of 95% hydrazine was added, and the mixture was heated at reflux for 1 hour. The ethanol was evaporated under reduced pressure, and the resulting oil in 50 ml. of benzene was added dropwise to 100 ml. of refluxing benzene containing 16 g. of yellow mercuric oxide, 13.6 g. of dry sodium sulfate and 0.6 g. of dry, powdered potassium hydroxide. Nitrogen was immediately evolved and mercury precipitated. Small additional amounts of mercuric oxide then were added until nitrogen was no longer evolved. The mixture was stirred and refluxed for 3 hours, cooled, filtered, and the filtrate was evaporated under reduced pressure. The residual orange oil was distilled at a pot temperature of 150–180° at 0.5 mm. to give 3.05 g. of a light yellow oil, $n^{25}_{\rm D}$ 1.5490. This material was chromatographed on 0.6 kg. of alumina (ethyl acetate washed, then heated for 3 days at 150° and cooled under vacuum) in a column (58 × 3.5 cm.) made up in pure pentane. The oil was absorbed on the column from 25 ml. of pure pentane, and the column was developed with pure pentane, 90–10-ml. fractions of the column filtrate being taken and evaporated through a short still. Fractions 24 to 69 gave 560 mg. of colorless oil that distilled (pot temperature of 125–130° at 0.8 mm.) to give 500 mg. of impure VIII,[2a] $n^{25}_{\rm D}$ 1.5445. Fractions 70–90 gave 900 mg. of white solid (VII), m.p. 45–46°. Recrystallization of a small sample of this material gave colorless needles, m.p. 47–47.5°.

Anal. Calcd. for $C_{16}H_{20}$: C, 90.51; H, 9.49. Found: C, 90.26; H, 9.56.

6-Keto-4-[10]paracyclophene (IX).—Development of the above chromatogram with ether gave an eluate which when evaporated gave an oil. This material distilled at a pot temperature of 150° at 0.5 mm. to give 0.725 g. of colorless oil (IX), $n^{25}_{\rm D}$ 1.5513. This material decolorized bromine in carbon tetrachloride, and gave a 2,4-dinitrophenylhydrazone test for a carbonyl group.

Anal. Calcd. for $C_{16}H_{20}O$: C, 84.15; H, 8.84. Found: C, 84.08; H, 8.69.

To possibly further purify this α,β-unsaturated ketone, 410 mg. of the substance was converted to 430 mg. of its 2,4-dinitrophenylhydrazone derivative, m.p. 170–172° (red-orange needles from ethyl acetate). Further recrystallizations of the substance did not alter its m.p.

Anal. Calcd. for $C_{22}H_{24}N_4O_4$: C, 64.69; H, 5.93. Found: C, 64.99; H, 6.15.

This derivative (430 mg.) was heated at 100° for 16 hours with 3 ml. of pyruvic acid and 3 ml. of acetic acid,[12] during which time yellow crystals separated. Water (30 ml.) was added to the cooled mixture along with 8 g. of sodium bicarbonate. The mixture was warmed until homogeneous, was cooled and extracted with ether. The ether extract was washed with water, dried, evaporated, and the residual yellow oil was flash distilled at a pot temperature of 150° and 0.5 mm. to give 150 mg. of oil (IX), $n^{25}_{\rm D}$ 1.5522.

Anal. Calcd. for $C_{16}H_{20}O$: C, 84.15; H, 8.84. Found: C, 84.40; H, 8.74.

This ketone (106 mg. of IX) was hydrogenated in the presence of 25 mg. of 10% palladium-on-charcoal in 2 ml. of methanol, 90% of one molar volume of hydrogen being consumed. The resulting mixture was filtered, diluted to 7 ml. with methanol, and 92 mg. of 2,4-dinitrophenylhydrazine and 0.15 ml. of concentrated hydrochloric acid was added. The resulting precipitate was collected and recrystallized from ethyl acetate–ethanol to give 140 mg. of derivative, m.p. 134–136°, m.m.p. with 2,4-dinitrophenylhydrazone of "ketone C,"[2a] 134–136°.

***cis*-5-[10]Paracyclophene (XIII).**—Palladium (5%)-on-barium sulfate (24 mg.) in 20 ml. of absolute methanol (containing 3 drops of quinoline) was stirred in an atmosphere of hydrogen at 29° and 755 mm. pressure. The above acetylenic compound (XII) (250 mg.) was added and stirred in an atmosphere of hydrogen until a sharp break in the rate of hydrogen uptake occurred (after 1.01 moles of hydrogen had been absorbed, acetylene = 1 mole). The mixture was filtered, the filtrate was evaporated to 10 ml. and diluted with water. The mixture was extracted with pure pentane, the extract was washed with dilute acid, base, water and dried. Evaporation of the pentane gave a colorless oil (XIII) which was flash distilled at a pot temperature of 160° (4 mm.) to give 190 mg. of olefin, $n^{25}_{\rm D}$ 1.5385.

Anal. Calcd. for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.61; H, 10.10.

***cis*-5,6-Dihydroxy[10]paracyclophane (XIV).**—The above olefin (70 mg. of XIII) was mixed with 1 ml. of dry pyridine and 80 mg. of osmium tetroxide.[6e] The resulting mixture was left at 0° for 48 hours, 8 ml. of methylene dichloride was added, and the mixture was shaken for 5 hours with 5 ml. of water containing 200 mg. of mannitol and 200 mg. of potassium hydroxide. The almost colorless organic layer was separated, washed with water, with dilute hydrochloric acid, again with water and was dried. The solution was evaporated to an oil which when dissolved in 2 ml. of ether gave a solution that deposited colorless needles when cooled, wt. 20 mg., m.p. 99.5–100.5. This substance gave m.m.p. of 99.5–101° with "diol IVa,"[2a] and m.m.p. of 79–85° with "diol IVb."[2a] Another 20 mg. of XVI (*cis*-diol) was isolated from the mother liquors, m.p. 98–99.5°, undepressed by admixture with "IVa."[2a]

5-Keto[10]paracyclophane (XII) by Hydration of Acetylene VII.—A mixture of 100 mg. of VII, one drop of concentrated sulfuric acid, 100 mg. of mercuric sulfate and 5 ml. of 80% aqueous acetic acid was heated at 100° for 4 hours.[13] The mixture was cooled, diluted with water and extracted with ether. The ether layer was washed with water, sodium bicarbonate solution (one-third of the product was lost by foaming), water and was dried. The ether was evaporated and the residual oil was warmed with 60 mg. of semicarbazide hydrochloride and 90 mg. of anhydrous sodium acetate in 2 ml. of 95% ethanol. After standing 10 hours, the mixture was diluted with water, and the solid that separated was twice recrystallized from 1 ml. of methanol to give 20 mg. of white rosettes, m.p. 170–172°, m.m.p. with the semicarbazone of "ketone C,"[2a] 169–171°.

5-Hydroxy[10]paracyclophane (XVIII).—A solution of 6.73 g. of 5-keto[10]paracyclophane[2b] in 70 ml. of dry ether was added to 1.5 g. of lithium aluminum hydride. The product was isolated by the usual extraction procedure to give 6.65 g. of an oil that solidified on standing at room temperature, m.p. 41–44°. A small sample of this material was distilled at a pot temperature of 150–160° at 0.9 mm., m.p. 43–47°.

Anal. Calcd. for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.74; H, 10.28.

The 3,5-dinitrobenzoate of the alcohol XVIII was prepared in the usual manner and recrystallized from ethanol, m.p. 116–117°.

Anal. Calcd. for $C_{23}H_{26}N_2O_6$: C, 64.77; H, 6.15. Found: C, 64.57; H, 6.02.

3-Nitrophthalic Acid Ester of 5-Hydroxy[10]paracyclophane.—Alcohol XVIII (16.64 g.) and 13.85 g. of 3-nitrophthalic anhydride were dissolved in 25 ml. of pyridine, and the solution was heated at 100° for 45 minutes. The mixture was left at 25° for 18 hours and then added to excess dilute sulfuric acid. The product was extracted with ether, the ether solution was washed with water, dried and evaporated to an oil. This material crystallized from ethyl acetate–pentane to give 22.4 g. (74%) of ester, m.p. 188–191°. Two recrystallizations of this material from ethyl acetate–pentane gave m.p. 190.5–193°. Another recrystallization from methanol gave m.p. 186–193.5°.

Anal. Calcd. for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.39. Found: C, 67.52; H, 6.24.

A similar procedure was applied for the preparation of the acid phthalate of alcohol XVIII. From 6.65 g. of alcohol was prepared 8.47 g. (78%) of ester as white rosettes, m.p. 95.5–101.5° (ethyl acetate–pentane). A sample was recrystallized twice from ethyl acetate–pentane and once from methanol–water to give an analytical sample, m.p. 97–103°.

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(12) A. C. Cope and B. D. Tiffany, THIS JOURNAL, **73**, 4158 (1951).

(13) R. J. Thomas, K. N. Campbell and G. F. Hennion, *ibid.*, **60**, 718 (1938).

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 $C_{23}H_{30}SO_3$: 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.

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

The Bromination of Tropinone[1]

BY ALEX NICKON[2]

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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–

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(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.

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(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.