Nmr spectra were determined on a Varian Associates HA-100 spectrometer on solutions in $CDCl_3$ with TMS as internal standard. Microanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich. Mass spectra were measured on a Hitachi-Perkin-Elmer RMU-6E spectrometer.

Extraction and Preliminary Fractionation.—The dried ground roots and rhizomes (5.5 kg) of *S. abyssinica* were continuously extracted with hot 95% ethanol during 24 hr, and the extract was concentrated *in vacuo* to 1 l. The concentrate was dissolved in chloroform and extracted twice with 5% HCl (total of 4 l.). The organic phase was separated and evaporated to yield fraction A (74 g). The acid solution was decanted from an insoluble tar (101 g), adjusted to pH 5.0 with NH_4OH, and extracted twice with chloroform (1 l.). The resultant chloroform solution of weak bases yielded fraction B (73 g) upon evaporation. An excess of NH_4OH added to the remaining aqueous phase precipitated the strong bases which were extracted twice with chloroform (1 l.) to give fraction C (25 g).

Stephabyssine (1a).—A portion of extract C (15 g) was chromatographed over 400 g of silica gel (0.05–0.2 mm, Merck) in chloroform. Elution was begun with 1% methanol–chloroform, and subsequent to a dark-colored forerun, eluate (2 l.) was collected and evaporated. The residue was twice crystallized from aqueous ethanol to give stephabyssine (**1a**) (271 mg): mp 178–180°; $[\alpha]_D$ −58.9° (*c* 0.87, $CHCl_3$); λ_{max}^{KBr} 2.82, 5.77 μ; λ_{max}^{MeOH} 284 nm (ε 3300); *m/e* (%) 331 (M^+, 26), 316 (2.5), 231 (100), 198 (19); nmr τ 3.32 (s, 2 H, aromatic), 3.98 (s) and 4.87 (s) (2 OH), 4.98 (d, 1 H, *J* = 6 Hz), 6.11 (s, 3 H, OCH_3), 7.41 (s, 3 H, NCH_3).

Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.15; H, 6.29; N, 4.43.

Stephabyssine Hydrochloride.—Stephabyssine (40 mg) was stirred with 10% hydrochloric acid (1 ml) for 4 hr, the mixture evaporated to dryness *in vacuo*, and the residue crystallized twice from chloroform–carbon tetrachloride to give the hydrochloride (41 mg) as colorless plates: mp 247–250° dec; $[\alpha]^{25}D$ −32.5° (*c* 0.41, 60% aq EtOH); λ_{max}^{KBr} 3.05, 3.99, 5.79, 7.78, 8.73 μ.

Anal. Calcd for $C_{18}H_{21}NO_5 \cdot HCl$: C, 58.78; H, 6.03; N, 3.81. Found: C, 58.77; H, 6.03; N, 3.81.

Methylation of Stephabyssine (1a) to Metaphanine (1b).—Anhydrous potassium carbonate (200 mg) was added to a suspension of stephabyssine (50 mg) in methanol (1.5 ml) containing methyl iodide (0.3 ml). The mixture was allowed to stand 18 hr and then filtered and the solid washed thoroughly on the filter with water followed by a little methanol. Recrystallization from chloroform–ether gave colorless prisms (24 mg), mp 230–232° dec, charactarized by melting point, optical rotation, and ir, nmr, and mass spectrum as metaphanine by comparison with reported values.[9]

Stephaboline (2) Hydrochloride.—Elution was continued with 2, 3, 4, 5, and 6% methanol–chloroform (2 l. each); the eluates containing 5 and 6% methanol were combined and after evaporation the residual material was rechromatographed on 80 g of neutral alumina (activity I, Merck) overlaid with 10 g of basic alumina (activity I, Merck). After preliminary elution with chloroform (300 ml), 300-ml portions of chloroform containing 2, 4, and 5% ethyl acetate were passed through the column. The ethyl acetate containing eluates were combined and the solvents evaporated; the residue was taken up in 50% benzene–chloroform (20 ml) and allowed to stand overnight. Recrystallization of the precipitate from methanol–chloroform gave stephaboline hydrochloride (48 mg): mp 230–232° dec; $[\alpha]^{25}D$ +23.1 (*c* 0.44, MeOH), −45° (*c* 0.8, pyridine); λ_{max}^{KBr} 2.92, 2.99, 3.10, 3.71, 7.82 μ; λ_{max}^{MeOH} 283 nm (ε 2940).

Anal. Calcd for $C_{18}H_{23}NO_5 \cdot HCl$: C, 58.46; H, 6.54; N, 3.79; Cl, 9.59. Found: C, 58.58; H, 6.47; N, 3.64; Cl, 9.39.

Stephaboline (2).—Potassium carbonate (100 mg) was added to a solution of stephaboline hydrochloride (20 mg) in 50% aqueous methanol (2 ml), the mixture stirred 10 min, and 10 ml of water added. After 16 hr the precipitate was collected and crystallized from aqueous methanol to give stephaboline (11 mg): mp 186–188° dec; $[\alpha]^{25}D$ +34.7° (*c* 0.47, MeOH); λ_{max}^{EtOH} 281 nm (ε 2760); λ_{max}^{KBr} 2.79, 3.07, 6.64, 9.15, 9.57 μ; *m/e* (%) 333 (M^+, 17), 257 (12), 230 (100), 215 (9), 198 (33), 196 (16); nmr τ (pyridine-d_5) 3.34 (s, 2 H, aromatic), 4.06 (s), 4.81 (s), and 5.24 (s), (3 × 1 H, OH), 5.04 (d, 1 H, *J* = 6 Hz), 5.62 (dd, 1 H, *J* = 5 Hz, *J* = 11 Hz), 6.32 (s, 3 H, OCH_3), 7.23 (s, 3 H, NCH_3).

Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.84; H, 7.02; N, 3.98.

Stephaboline Methiodide.—A suspension of stephaboline (60 mg) in chloroform (8 ml) containing methyl iodide (2 ml) was stirred for 24 hr. The colorless prisms were filtered and recrystallized from methanol–ethyl acetate (42 mg): mp 230–232° dec; $[\alpha]^{25}D$ +19.6° (*c* 0.51, MeOH); λ_{max}^{KBr} 2.98, 6.20, 7.81, 9.42 μ.

Anal. Calcd for $C_{18}H_{23}NO_5 \cdot CH_3I$: C, 48.01; H, 5.51; N, 2.95. Found: C, 48.02; H, 5.59; N, 3.04.

Borohydride Reduction of Stephabyssine.—Sodium borohydride was added in eight portions (50 mg each) during 2 hr to a stirred suspension of stephabyssine (450 mg) in 50% aqueous methanol (15 ml). After a further 0.5 hr, 20% aqueous methanol (10 ml) was added and the mixture stirred 2 hr. The crystalline precipitate was collected, washed with 10% aqueous methanol, and recrystallized from methanol to give colorless needles (330 mg) of **2**, characterized by melting point, mixture melting point, and nmr comparison with stephaboline.

Prostephabyssine (3a).—Extract B (48 g) was stirred with 80% ethyl acetate–chloroform (500 ml) until no further material dissolved. After removal of the insoluble components the solvents were evaporated, and the residue was chromatographed over 1.5 kg of silica gel (0.2–0.05 mm, Merck). After elution with chloroform (4 l.), followed by chloroform containing 1, 2, and 4% methanol (4 l. of each), chromatography was continued with chloroform containing 6% methanol (8 l.). After evaporation of the solvents from the latter eluate, the residue was stirred with ethyl acetate (100 ml), the mixture filtered, and the filtrate evaporated. The residue in chloroform was applied to preparative layer silica gel plates (20 × 20 cm, 0.2 cm absorbent layer, Merck F_{254}) which were subsequently eluted with 4% methanol–chloroform. The principal low R_f band was collected and then extracted with 20% methanol–chloroform, and the filtered extract was evaporated to dryness to give prostephabyssine (**3a**) (200 mg) as a pale yellow glass, $\lambda_{max}^{CHCl_3}$ 2.84, 5.98, 6.10 μ.

Prostephabyssine Methiodide.—A solution of prostephabyssine, (**3a**, 80 mg) in benzene (1 ml) containing methyl iodide (0.5 ml) was refluxed 20 min and allowed to stand overnight at room temperature. Recrystallization of the precipitate from methanol–benzene gave colorless prisms (47 mg): mp 196–198° dec; $[\alpha]^{25}D$ −105° (*c* 1.98, MeOH); λ_{max}^{MeOH} 282 nm (ε 3810); λ_{max} 2.95, 5.90 μ.

Anal. Calcd for $C_{19}H_{23}NO_5 \cdot CH_3I$: C, 49.29; H, 5.34; N, 2.87. Found: C, 49.04; H, 5.22; N, 2.84.

Acid Hydrolysis of Prostephabyssine (3a) to Stephabyssine (1a).—A solution prostephabyssine (**3a**, 41 mg) in 50% acetone–methanol (2 ml) containing 5% hydrochloric acid (0.6 ml) was warmed on the steam bath for 5 min. After removal of the volatile materials *in vacuo* the residue was basified with ammonium hydroxide and extracted with chloroform (20 ml). After evaporation of the chloroform, the residue was twice crystallized from methanol–acetone to give colorless needles of **1a** (24 mg), characterized as stephabyssine by melting point, mixture melting point, and ir and nmr comparison with an authentic sample.

Registry No.—**1a**, 36871-84-8; **1a** HCl, 36871-85-9; **2**, 36871-86-0; **2** HCl, 36921-52-5; **2** MeI, 36871-87-1; **3a**, 36871-88-2; **3a** MeI, 36921-53-6.

The West Synthesis of Hexabromocyclopentadiene

GARY A. UNGEFUG

Hydrocarbons and Monomers Research Laboratory, The Dow Chemical Company, Midland, Michigan 48640

CARLETON W. ROBERTS*[1]

Textile Department, Clemson University, Clemson, South Carolina 29631

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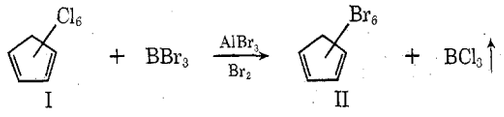
Until the publication of the West procedure for the synthesis of hexabromocyclopentadiene (II) from

(1) To whom inquiries should be directed.

hexachlorocyclopentadiene (I) by an exchange reaction,[2,3] the standard synthesis of II involved the bromination of cyclopentadiene using sodium hypobromite.[4] The West procedure has been modified[5-7] and clarified and we wish to describe these modifications.

The original literature procedure[2,3] gives a low-melting product with chlorinated impurities; the modified procedure described here is a convenient laboratory synthesis of a high-purity product with residual chlorine levels less than 0.2%.

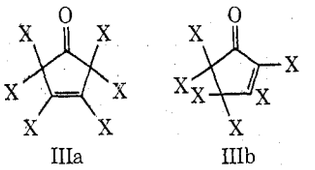


I II

Some of the minor products were isolated from the above reaction to gain a further understanding of their formation and to help determine the best way to purify the crude product. Their amounts varied with the source of starting material (I), suggesting that the minor products may arise from impurities in I.

The most abundant side product (5%) is a colorless ketone C_5Br_6O, mp 185–188° dec. Structure IIIa, X = Br, is proposed on the basis of its failure to react with ethanol after 1 hr of reflux and on the similarity of its infrared spectrum with that of IIIa, X = Cl. Structure IIIb would be expected to give an enol ether on heating in ethanol.

Further confirmation is found in the uv of IIIa. The uv spectrum of III does not have the absorption for a conjugated ketone which is found at 270 nm for the Diels–Alder dimer of tetrabromocyclopentadienone (VIII). The two spectra are quite different, while the uv spectrum of IIIb, X = Cl, is very similar to the

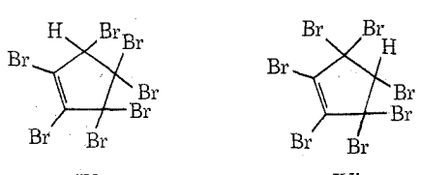


IIIa IIIb

X = Cl
X = Br

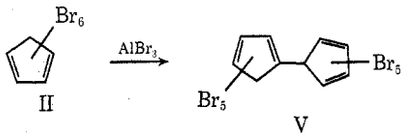
spectrum of the Diels–Alder dimer of tetrachlorocyclopentadienone.[8,9]

A product formed in lesser amounts (C_5HBr_7, mp 136–140°) is formally the result of addition of HBr to C_5Br_6. Either structure IVa or IVb is consistent with the present data.



IVa IVb

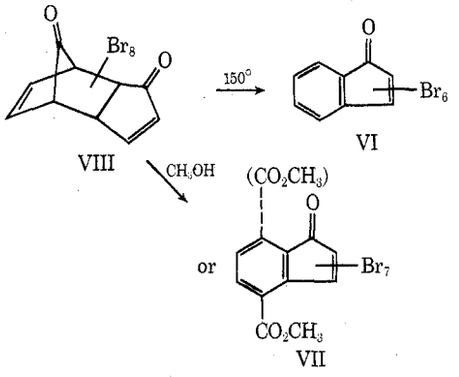
A dimer $C_{10}Br_{10}$, mp 139–141° (V), was isolated in less than 1% yields. Compound V was isolated by



II V

McGregor from the reaction of II with aluminum bromide and from the cuprous bromide coupling of II.[6]

Hexabromoindone (VI)[9] and ester VII were isolated in less than 1% yields. Both VI and VII probably arise from dimer VIII. Pews has shown that dimer



VII

VIII can be pyrolyzed to VI at 150° and ester VII is produced by reaction of VII with methanol.[10] Methanol was used as a recrystallization solvent during product separation.

Experimental Section

Infrared spectra were obtained with Beckman IR-9 and Perkin-Elmer 137 spectrometers. The mass spectra were obtained on a CEC-21-110B(direct probe) instrument. Nuclear magnetic resonance spectra were obtained on Varian A-60 and HA-100 spectrometers. Thin layer chromatography (tlc) plates were prepared from silica gel G containing 0.04% of Rhodamine 6G.

Preparation of Hexabromocyclopentadiene (II) from Hexachlorocyclopentadiene (I).[2]—(Caution: Run this reaction in a well-ventilated hood. All of the reagents and the exhaust gases are toxic. On two occasions this reaction has become so vigorous that the mixture foamed out of the flask. A large bucket of ice water was kept on hand while mixing the reagents and adding the catalyst. A dish was placed under the reaction pot so that ice water could be poured over the sides of the flask if the temperature should rise too rapidly. A large bulb (2 l.) was placed on top of the condenser to help contain foam. The two runaways occurred when the catalyst was added faster than directed by the procedure below. Reactants were mixed cautiously since impure I will react violently with boron tribromide.)

Hexachlorocyclopentadiene (474 g, 1.73 mol, Hooker Chemical Co.), boron tribromide (1108 g, 4.70 mol, Trona Division, American Potash and Chemical Corp.), and bromine (420 ml) were added *via* an additional funnel to a 2-l., three-necked flask equipped with magnetic stirring, a reflux condenser, a thermometer, and a dry nitrogen inlet. The nitrogen flow was adjusted to a rate that would sweep out evolved gases with a minimum loss of bromine. Aluminum bromide (10 g) was preweighed in 1-g lots into rubber-stoppered vials under a nitrogen atmosphere in a glove bag. The vials were stored in a desiccator. Five 1-g aluminum bromide samples were added one at a time to the reaction mixture at about 20-min intervals. The temperature was watched closely during addition of catalyst. If a rapid increase in temperature occurred, ice water was poured on the sides of the flask. If the temperature rose steadily without decreasing during the 20-min period after addition of catalyst,

(2) P. T. Kwitowski and R. West, *J. Amer. Chem. Soc.*, **88**, 4541 (1966).
(3) R. West and P. T. Kwitowski, *ibid.*, **90**, 4697 (1968).
(4) F. Straus, L. Kollek, and W. Heyn, *Chem. Ber.*, **63B**, 1868 (1930).
(5) R. G. Pews and C. W. Roberts, *J. Org. Chem.*, **34**, 2029 (1969).
(6) S. D. McGregor and C. W. Roberts, *ibid.*, **35**, 3576 (1970).
(7) G. A. Ungefug, S. D. McGregor, and C. W. Roberts, *ibid.*, **36**, 352 (1971).
(8) E. T. McBee, D. K. Smith, and H. E. Ungnade, *J. Amer. Chem. Soc.*, **77**, 559 (1955).
(9) R. G. Pews, *Org. Prep. Proced. Int.*, **3**, 37 (1971).
(10) R. G. Pews, personal communication.

the next catalyst addition was delayed until the reaction cooled to 35°. The mixture was stirred for 20 hr at 20–25°; the remaining five 1-g samples of aluminum bromide were added one at a time at 20-min intervals. The mixture was heated at 50° for 13 days.

The mixture was cooled to room temperature. Solvent and excess boron tribromide were removed by vacuum distillation into a series of two Dry Ice–acetone cooled traps. Vacuum was produced by a water aspirator connected to a large safety trap. Solvent removal was speeded by warming the flask with an oil bath set no higher than 40°. The residual reaction mixture was poured on ice, stirred, and then dissolved in methylene chloride. The organic solution was washed with water, 5% sulfuric acid, and water, and then dried with magnesium sulfate.[11] The solvent was removed under vacuum. Hexane was added and the solvent was removed under vacuum to force out remaining bromine and methylene chloride. Although not all of the material dissolved at this point, the mixture was not filtered. The methylene chloride insoluble and hexane insoluble material was mostly C_5Br_6O. The crude yield of II was 851 g.

The crude II was dissolved in 3.5 l. of hot hexane and cooled to room temperature to give a dark solution and additional C_5Br_6O. The solution was split into two equal fractions and each was absorbed on a 3-kg silica gel column (Davison, 200 mesh) and eluted with hexane. The hexane eluent was poured back into the column until the yellow product band began to come off. Six 2-l. fractions were collected from each column. The solvent was removed under vacuum. All of the fractions were combined, since their ir spectra were identical.

Recrystallization from methanol gave 734 g (78%) of high-purity hexabromocyclopentadiene (II), mp 88–90°, with total chlorine 0.05% by X-ray fluorescence.

Hexabromo-3-cyclopenteneone (IIIa).—Ketone IIIa, C_5Br_6O (9 g), was separated from the hexane solution of crude II prepared above as nearly colorless crystals, and after elution of II from the silica gel column with hexane, the remaining material was eluted with benzene. The benzene was evaporated under vacuum, and the residue was recrystallized from chloroform to yield 33 g of white crystals. An analytical sample was prepared by three recrystallizations from chloroform: mp 185–188° dec; tlc (carbon tetrachloride with wick) one spot, R_f 0.49; uv $\lambda_{max}^{cyclohexane}$ 241 nm (ϵ 14,700), no other max to 400 nm; ir (split mull) C=O at 1841 (w), 1789 (s), 1768 (m), C=C at 1563 cm^{-1} (s).

Anal. Calcd for C_5Br_6O: C, 10.81; Br, 86.31. Found: C, 10.80; Br, 86.70.

Isolation of Other By-products.—Crude II prepared as indicated above was absorbed on silica gel for purification. After elution of II with hexane the remaining material was eluted with hexane–benzene by slowly increasing the percentage of benzene to 50%. Fifteen fractions of 1–2 l. were collected from each column, and the solvent was removed under vacuum. Each fraction was analyzed by tlc. Those fractions having only one or two components were purified further. The only compounds isolated were those which were separated by chance. Many unknown mixtures were discarded.

Fractions 1–9, 2–9, and 2–10 were absorbed on a 350-g silica gel column and eluted with hexane. Nine fractions with a volume increasing from 250 to 2000 ml were collected. Fractions 6–9 were combined. Recrystallization from hexane gave clumps of brown crystals and of off-white crystals. The crystals were separated by hand.

Two recrystallizations of the brown crystals from hexane–methylene chloride gave 0.9 g of V as amber crystals, mp 139–141° dec, tlc (hexane with wick) one spot, R_f 0.35. This material was identical with a sample of $C_{10}Br_{10}$ previously described.[6]

Recrystallization of the off-white crystals from hexane–methylene chloride gave 0.4 g of IV as off-white crystals: mp 135–137° dec; tlc (hexane with wick) one spot, R_f 0.35; ir (CCl_4) CH at 2961 (w), C=C at 1566 (m), max at 1152 cm^{-1} (s); nmr ($CDCl_3$) single line at δ 5.56; mass spectrum, weak P^+ at m/e 614; uv $\lambda_{max}^{cyclohexane}$ 244 nm (ϵ 13,000).

Anal. Calcd for C_5HBr_7 (620.5): C, 9.68; H, 0.16; Br, 90.16. Found: C, 10.0; H, <0.3; Br, 90.4.

Column fractions 1–15, 2–14, and 2–16 were combined and recrystallized from hexane–methylene chloride. The first crop (0.5 g) was eluted from a 12 × 2.5 cm silica gel column with benzene to give 0.4 g of brown solid. Two recrystallizations from methylene chloride–carbon tetrachloride gave 0.2 g of VI as yellow crystals, mp 190–192°, identical with a sample of VI prepared by Pews.[9]

Column fractions 1–16, 17, 18, and 2–17, 18, 19 were re crystallized from methanol–methylene chloride to give a mixture of colorless and yellow crystals. Two recrystallizations from methylene chloride–carbon tetrachloride gave 0.3 g of VII as white crystals, mp 172–174° with decomposition and formation of a solid remelting about 215° dec, tlc (benzene with wick) one spot, R_f 0.47. This material was identical with a sample of VII prepared by Pews.[10]

Registry No.—II, 14310-17-9; IIIa (X = Br), 36976-60-0; IVa, 36976-61-1; IVb, 36976-62-2.

Acknowledgment.—The authors are grateful to L. Shadoff for the mass spectral data, to R. Nyquist for the infrared spectra, to J. Heeschen and T. Evans for the nmr data, to L. Swim and P. North for the elemental analyses, and to J. Simek for the uv spectra.

(11) Chlorine-containing impurities in earlier preparations from halogen exchange with methylene chloride during work-up. Slow work-up can drive the product back to very high values of chlorine-containing impurities if the aluminum bromide is not destroyed. A volatile solvent that does not react with aluminum bromide is desired. Benzene gives brominated benzene impurities which are very difficult to remove. Bromine was added as a solvent when early runs at room temperature set up solid. Excess boron tribromide is used on the assumption that $BBrCl_2$ is vented along with BCl_3. When high-purity starting material [purified by vacuum distillation, center cut, bp 108° (10 mm); $n^{25}D$ 1.5625; glc indicated 98% purity] I was used, the crude product could be passed through a single 3-kg column for purification.

The Synthesis of Cyclic *N*-Cyanoguanidines

C. M. BALTZER AND C. G. MCCARTY*

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506

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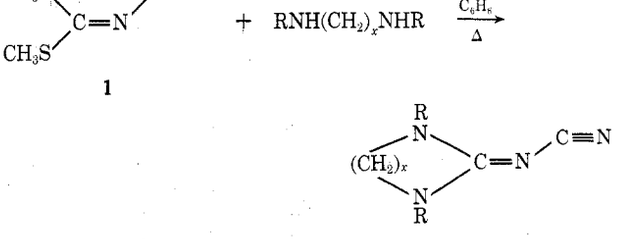
The observation that dimethyl cyanoimidodithiocarbonate (**1**) reacts readily with primary and secondary amines to give *N*-cyanoguanidines[1] prompted us to examine the possible use of **1** with diamines for the synthesis of cyclic *N*-cyanoguanidines. Such cyclic guanidines, not previously reported in the literature, may prove to be as interesting as some of their acyclic analogs which have been studied as hypotensive agents[2] and potential antimalarials.[3]

The reactions of **1** with the various primary and secondary diamines proceed quite readily at the reflux temperature of dry benzene to yield cyclic guanidines with the general formula **2** (Table I).



1

2, R = H, CH_3; x = 2, 3

(1) C. G. McCarty, J. E. Parkinson, and D. M. Wieland, *J. Org. Chem.*, **35**, 2067 (1970).
(2) S. M. Gadekar, S. Nibi, and E. Cohen, *J. Med. Chem.*, **11**, 811 (1968).
(3) E. L. May, *J. Org. Chem.*, **12**, 437 (1947).