H, 3.24. Found: C, 59.10; H, 3.52. Satisfactory analytical data could not be obtained due to hygroscopicity. For NMR data, see Table I.

pK_{R^+} Measurement. The pK_{R^+} values were determined for the cations **2** (X = H), **8a–d**, and **12** in CH_3CN–H_2O (1:1 by vol) at 25 °C according to the spectrophotometric method previously reported.[23] All the cations and the corresponding neutralized compounds were stable in this solvent during the measurement. After each measurement, the reversibility was confirmed by regeneration of the cation's spectrum upon acidifying the neutralized solution. The UV–vis spectrum was recorded on each cation in 10–15 solutions of buffers spaced through a pH range of 2–3 units on each side of the pK_{R^+}. The pH values were read on a Horiba Model H pH meter calibrated with standard buffers before use.

Cyclic Voltammetry. Cyclic voltammograms were obtained at the scan rate of 0.1 V/s by the use of a Hokuto-Denko HA104 potentiostat, a HB107A function generator, a Hitachi 057 X-Y recorder, and a three-electrode cell composed of platinum wire working and counter electrodes and a Ag/0.01 M $AgNO_3$ (CH_3CN) reference electrode. All the sample solutions were 1 mM in cations and 0.1 M in tetra-*n*-butylammonium perchlorate as a supporting electrolyte in CH_3CN. Irreversible cathodic peaks were observed for all cations. The peak potentials were read and corrected with reference to ferrocene ($E_{1/2}$ +0.083 V) added as an internal standard after each measurement.

Acknowledgment. We thank Professor Kohei Tamao of Kyoto University for providing us with Ni(dppp)Cl_2. Financial support from Yazaki Memorial Foundation of Science and Technology is gratefully acknowledged. This work was also partly supported by a Grant-in-aid from the Ministry of Education, Science, and Culture, Japan.

Supplementary Material Available: Two-dimensional NMR spectra of 1-aryl-8-tropylionaphthalenes **8a–d** (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Perchlorotriphenylene: A Compound with Severe Molecular Twisting?

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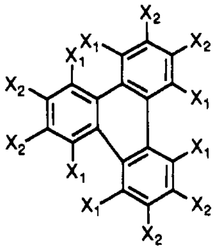
Perchlorotriphenylene has been reported several times in the literature. However, there is inconclusive evidence that this compound has actually been prepared. Severe molecular twisting to relieve steric interactions of "ortho" chlorines may preclude any stable existence. The compound is discussed in context with other severely twisted molecules, and methods are proposed for its synthesis.

Perchlorotriphenylene, $C_{18}Cl_{12}$, is a member of a family of compounds whose general structure is:



The parent triphenylene, $C_{18}H_{12}$, has more than 1300 mentions in the literature, and perfluorotriphenylene, $C_{18}F_{12}$, has received nine references.[1–9] The crystal structures of both triphenylene[10] and perfluorotriphenylene[4] show distortions from planarity in the solid state, due to steric interactions of the "ortho" hydrogens or fluorines (X_1 in the general structure).

This distortion from planarity caused by the twisting of a molecule to achieve a measure of stability is well documented (especially by Ballester[11] in his review on perchloro organic chemistry). A few examples are shown in the structures of hexadecafluoro-1-phenyltriphenylene,[9] decachlorophenanthrene,[12] octachloronaphthalene and tetrabenznaphthalene,[13] octafluorodibenzothiophene,[14] perchloro-1,1-diphenylethylene,[15] and perchlorobifluorenylidene,[16] which has a 67° twist around the ethylene bond. 9-18-Diphenyltetrabenz[*a,c,h,j*]anthracene[17] has been synthesized with the anthracene molecule twisted by 65.7° end to end, and the same paper postulates that helical complexes with twists of 90° or even 180° might be synthesized.

With this background of stable twisted molecules, it is

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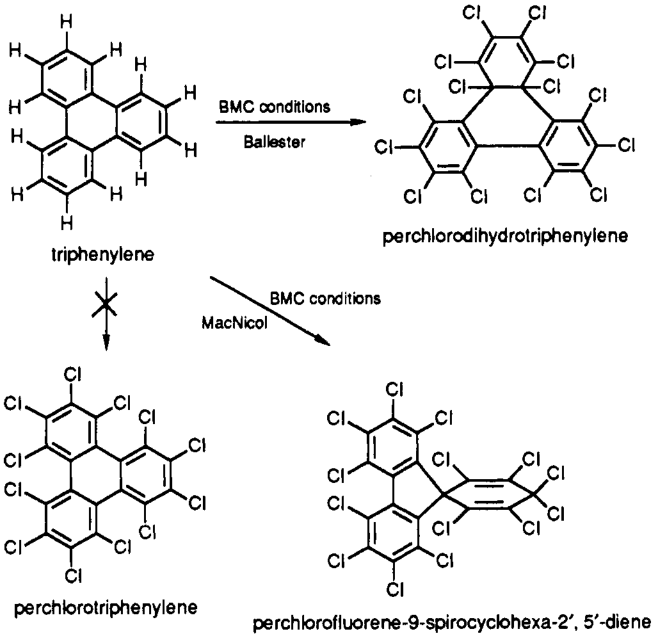
surprising that very little has been written on perchlorotriphenylene, whose distortions from planarity would be expected to be no more severe than say the compound in ref 17. We are of the opinion that even though perchlorotriphenylene has six references[7,18–22] in the literature, it has not been proved conclusively that the compound exists.

Both Massey[7] and Zitko[21] state that perchlorotriphenylene has been prepared and reference the patent[20] which describes the fluorination of perchlorotriphenylene by SbF_5 to a "mixture of cyclic perchlorofluoro compounds of average empirical formula between $C_{18}Cl_3F_{19}$ and $C_{18}Cl_3F_{21}$". Neither the patent nor its corresponding Chemical Abstract describes the actual preparation of perchlorotriphenylene. Stilmar in ref 18 and Downing in ref 19 (reporting Stilmar's work) are the earliest statements of this fluorination of perchlorotriphenylene. The method[18] of chlorination is one of passing chlorine into the starting organic material at 200–300 °C in the presence of 1% $FeCl_3$. The chlorinated material was then fluorinated directly via treatment with SbF_5 and/or AgF_2. Downing is a little more succinct, "The aromatic compounds...were exhaustively chlorinated...". The isolation and characterization of perchlorotriphenylene is not described in either reference. The paper of MacNicol[22] sheds a little light on the matter. Deciding to prepare perchlorotriphenylene for his work on inclusion compounds, MacNicol chlorinated triphenylene under BMC conditions (mixtures of $AlCl_3$ and S_2Cl_2 in SO_2Cl_2). Ballester[15] has described these conditions as "most powerful" in terms of its perchlorination capacity. Instead of the desired product, a new chlorocarbon, perchlorofluorene-9-spirocyclohexa-2′,5′-diene was isolated and its structure confirmed by a X-ray crystal determination. The spiro configuration of one ring relieves the steric congestion which would be inherent in perchlorotriphenylene. A minor product of this reaction was perchloro-*o*-terphenyl, whose molecular arrangement is strain free.

Ballester[23] has also undertaken the chlorination of triphenylene under BMC conditions, but the state product is "probably" perchlorodihydrotriphenylene. The product's structure was determined by elemental analyses and infared spectrum. Is it possible that Ballester had prepared the spiro compound of MacNicol? Also, what was the compound prepared in 1947 during the chlorination of triphenylene?

Stilmar was dealing with mixtures of compounds which were first chlorinated and the product mixtures subsequently fluorinated. From the final product mix was isolated a chlorofluorocarbon which did indeed have the basic "triphenylene" structure. The presence of F's in the "ortho" X_1 position relieves the strain by their smaller Van der Waals radii interactions.

The question we asked ourselves was "Can perchlorotriphenylene be prepared?". In attempting to answer this question, we tried several possible routes to the synthesis of perchlorotriphenylene: (i) slight decomposition of 1,2,3,4-tetrachloronaphthalene–bis(hexachlorocyclopentadiene)adduct,[24–27] where the loss of the elements of CH_2Cl_2 would yield the desired product; (ii) careful chlorination of triphenylene using chlorosulfonic acid[28] and under BMC conditions,[22] (iii) coupling of 1,2-diiodotetrachlorobenzene via an Ullmann-type[29] reaction. This was the method used to prepare the analogous perfluorotriphenylene;[4] (iv) coupling of 1,2-diiodotetrachlorobenzene via Ni(0)-catalyzed reactions.[30]



Summary of Results

(i) Thermal decomposition of 1,2,3,4-tetrachloronaphthalene–bis(hexachlorocyclopentadiene) adduct up to 250 °C yielded only the breakdown products of hexachlorocyclopentadiene and 1,2,3,4-tetrachloronaphthalene.

(ii) Utilizing the chlorination procedures used by Cremlyn and Cronje,[28] triphenylene was stirred with chlorosulfonic acid in the presence of chloroform and/or iodine or without solvent. IR and mass spectral analysis of the materials isolated from the various reactions indicated the presence of perchlorofluorene-9-spirocyclohexa-2′,5′-diene.[22]

Mass spectral analysis of the product from chlorinating triphenylene under BMC conditions showed mass clusters corresponding to the spiro complex of McNicol.[22]

(iii) Coupling of 1,2-diiodotetrachlorobenzene via Ni(0)-catalyzed reactions of Semmelhack et al.[30] yielded products identified as unreacted starting material and possibly the spiro complex.

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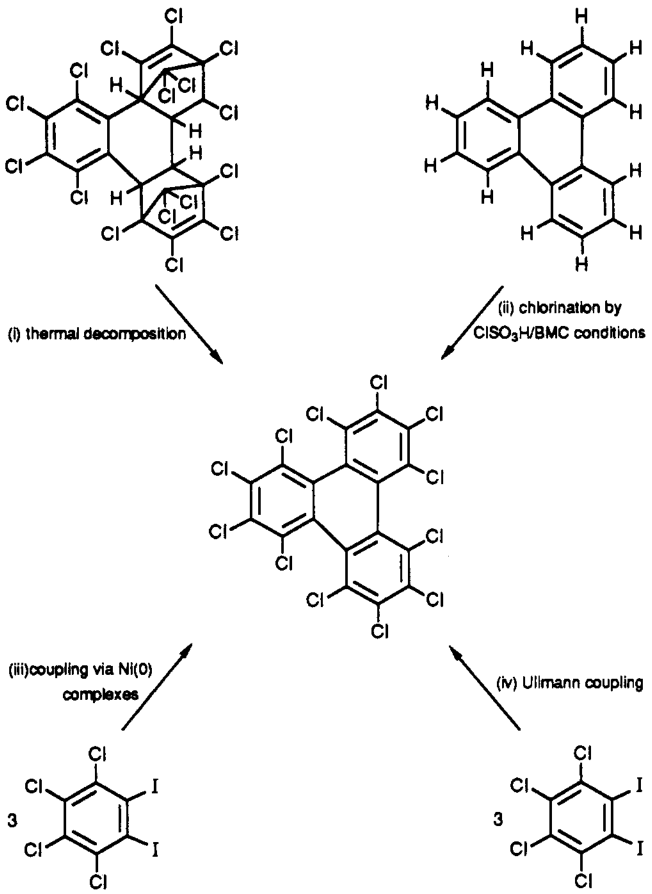

(iv) Ullmann[29] coupling of 1,2-diiodetetrachlorobenzene gave a product identified by IR and mass spectral analysis as perchlorofluorene-9-spirocyclohexa-2′,5′-diene.

In the Ullmann reaction, secondary products were identified as $C_{12}Cl_8I_2$ and $C_{12}Cl_9I$ formed by partial coupling of the starting 1,2-diiodotetrachlorobenzene. Mass clusters centered at $m/z = 640$ corresponding to $C_{18}Cl_{12}^+$ were assumed to be daughter ions derived from the highest cluster at $m/z = 711$ by loss of Cl_2.

Conclusion

Perchlorotriphenylene would be too highly distorted to be formed, and in order to diminish the twist of the molecule, perchlorofluorene-9-spirocyclohexa-2′,5′-diene is the preferred perchlorinated derivative of triphenylene.

Experimental Section

(i) Decomposition of 1,2,3,4-Tetrachloronaphthalene–Bis(hexachlorocyclopentadiene) Adduct. A sample of the white crystalline adduct was heated slowly in air. No change was apparent in the material (samples taken at intervals and checked by IR spectroscopy for any breakdown) until 205 °C when darkening occurred and a liquid began to distill over. The breakdown products were identified (by comparison with authentic samples) as hexachlorocyclopentadiene and 1,2,3,4-tetrachloronaphthalene.

(ii) Chlorination of Triphenylene via the Method of Cremlyn and Cronje.[28] (a) Triphenylene (1.0 g, 4.38 mmol), iodine (8.34 g, 32.8 mmol), and chlorosulfonic acid (25 mL) were placed in a 100-mL round-bottom flask fitted with a reflux condenser that had been previously flame dried. The stirred mixture was heated at 60 °C for approximately 6 h. The mixture was then stirred at rt overnight. The reaction mixture was then poured carefully onto ice. The solids were filtered, washed with hot water, 30% Na_2SO_3, and 10% NaOH, and then refiltered. This afforded 1.73 g of brown material. Repeated mass analysis of this material and a sublimed portion yielded a base cluster at $m/z = 256$ which was assigned as S_8^+.

(b) Triphenylene (1.0 g, 4.38 mmol) and 25 mL of chlorosulfonic acid were placed in a flame-dried 100-mL round-bottom flask fitted with a reflux condenser. The mixture was heated for approximately 6 h at 60 °C with stirring and further stirred at rt overnight. The mixture was poured onto ice, and the solids were filtered and washed with hot water and 10% NaOH. A total of 0.95 g of brown material was obtained. Nothing conclusive could be gathered from the mass spectrum of this material, though mass clusters up to $m/z = \sim 600$ were observed.

(c) Triphenylene (1.0 g, 4.38 mmol) was dissolved in approximately 75 mL of chloroform, freshly distilled and dried over molecular sieves. This solution was heated to reflux, while 25 mL of chlorosulfonic acid was added dropwise. The mixture was heated at reflux for 6 h and then stirred at rt overnight. The mixture was poured onto ice, and the solids were filtered off and washed several times with chloroform. The organic layers were collected and dried, and the solvent was then removed yielding 1.34 g of a yellow material. A mass spectrum of this material and a sublimed portion yielded a highest mass cluster at $m/z = 711$, corresponding to $C_{18}Cl_{14}^+$. Detailed mass spectrum of products (mass number, m/z of clusters*, assignment, % intensity of base cluster): 711, $C_{18}Cl_{14}^+$, 18.6; 676, $C_{18}Cl_{13}^+$, 100; 641, $C_{18}Cl_{12}^+$, 60.4; 605, $C_{18}Cl_{11}^+$, 18.6; 569, $C_{18}Cl_{10}^+$, 57.3; 535, $C_{18}Cl_9^+$, 14.3; 500, $C_{18}Cl_8^+$, 35.5; 464, $C_{18}Cl_7^+$, 8.5; 428, $C_{18}Cl_6^+$, 21.7; 394, $C_{18}Cl_5^+$, 49.0; 358, $C_{18}Cl_4^+$, 9.1; 321, $C_{18}Cl_3^+$, 5.1; 285, $C_{18}Cl_2^+$, 16.5; 250, $C_{18}Cl^+$, 17.2; 214, C_{18}^+, 15.3.

(iii) Chlorination of Triphenylene under BMC Conditions.[22] Triphenylene (1.0 g, 4.38 mmol) dissolved in 25 mL of freshly distilled sulfuryl chloride, SO_2Cl_2, and 1 mL of sulfur monochloride, S_2Cl_2, was added dropwise over a 30-min period to a boiling solution of 0.3 g aluminum chloride, $AlCl_3$ in 75 mL of sulfuryl chloride, SO_2Cl_2. The mixture was heated at reflux for approximately 8 h. The solvents were removed, and water was added followed by a strong solution of sodium hydrogen carbonate. The mixture was heated on a steam bath for 1 h and then strongly acidified with concd HCl. The solids formed were collected, dried, and recrystallized from toluene giving a pale yellow product (yield 1.63 g). Mass and IR spectral analysis of this material indicated the presence of perchlorofluorene-9-spirocyclohexa-2′,5′-diene. Detailed mass spectrum of products (mass number, m/z of clusters,* assignment, % intensity of base cluster): 711, $C_{18}Cl_{14}^+$, 21.6; 676, $C_{18}Cl_{13}^+$, 100; 641, $C_{18}Cl_{12}^+$, 65.7; 606, $C_{18}Cl_{11}^+$, 19.4; 569, $C_{18}Cl_{10}^+$, 66.3; 535, $C_{18}Cl_9^+$, 14.3; 499, $C_{18}Cl_8^+$, 39.7; 463, $C_{18}Cl_7^+$, 6.5; 427, $C_{18}Cl_6^+$, 18.7; 393, $C_{18}Cl_5^+$, 43.0; 357, $C_{18}Cl_4^+$, 6.1; 321, $C_{18}Cl_3^+$, 8.7; 285, $C_{18}Cl_2^+$, 30.4; 250, $C_{18}Cl^+$, 26.0.

(iv) Coupling Reactions Utilizing Ni(0) Catalysis.[30] (a) In a glovebag under N_2, zinc (0.42 g, 6.4 mmol) triphenylphosphine (0.506 g, 1.9 mmol) and potassium iodide (0.05 g, 0.3 mmol) were added to a 50-mL three-neck round-bottom flask. Bis(triphenylphosphine)nickel(II) chloride $Ni(PPh_3)_2Cl_2$ (0.21 g, 0.32 mmol) was added and the mixture dissolved in 20 mL dry DMF. The solution was stirred under N_2 for 1 h (color changes of green to red brown were observed). 1,2-Diiodotetrachlorobenzene, $C_6Cl_4I_2$ (1.5 g, 3.2 mmol), was then added. The mix was stirred under N_2 for 24 h (after 3 h the color had turned "green-brown"). After this time, the contents of the reaction flask were poured into 75 mL of H_2O. A fine white precipitate formed which was filtered off. The filtrate was extracted with ether, washed with H_2O and brine, and dried over anhyd $MgSO_4$. The dried ether was evaporated under vacuo, giving a red oily material.

The filtered precipitate was dried over P_4O_{10} in a vacuum desiccator.

(b) Tetrakis(triphenylphosphine)nickel, $Ni(PPh_3)_4$ (1.0 g, 0.9 mmol), was dissolved in 25 mL of dry DMF under N_2. 1,2-Diiodotetrachlorobenzene (0.42 g, 0.9 mmol) was added and the mixture warmed to 60 °C and stirred for 48 h under N_2. The color of the reaction mixture changed from an initial red-brown to lime green. A similar workup to reaction (iva) above was undertaken.

Mass and IR spectral analysis of the products of the above two attempted coupling reactions indicated only unreacted starting materials and possibly the presence of the spiro compound.

(c) A series of reactions was undertaken using 1,2-diiodotetrachlorobenzene and powdered Ni sealed in evacuated glass ampules. These were heated variously up to 200 °C for usually 24 h but also up to 72 h duration. No reaction took place, and only starting material was isolated.

(v) Coupling Reaction of 1,2-Diiodotetrachlorobenzene under Ullmann[29] Conditions. Copper powder (0.5 g, 7.06 mmol) was placed in a glass ampule attached to a vacuum line and flame heated. 1,2-Diiodotetrachlorobenzene (0.5 g, 1.07 mmol) was added and the ampule sealed off and removed from the vacuum line. The sealed ampule with its contents under vacuo was heated at 180–200 °C for 24 h. The contents were then washed with ether (until colorless) and filtered, and the ether was removed under vacuo. A brown solid was obtained.

IR and mass spectral analysis indicated the product to be perchlorofluorene-9-spirocyclohexa-2′,5′-diene. Detailed mass spectrum of products (mass number, *m*/*z* of clusters,* assignment, % intensity of base cluster): 711, $C_{18}Cl_{14}^+$, 7.2; 681, $C_{18}Cl_{13}^+/C_{12}Cl_8I_2^+$, 48.8; 640, $C_{18}Cl_{12}^+$, 68.3; 609, $C_{18}Cl_{11}^+$, 8.8; 590, $C_{12}Cl_9I^+$, 65.1; 570, $C_{18}Cl_{10}^+$, 37.6; 555, $C_{12}Cl_8I^+$, 79.9; 536, $C_{18}Cl_9^+$, 4.7; 500, $C_{18}Cl_8^+$, 36.6; 468, $C_6Cl_4I_2^+/C_{18}Cl_7^+$, 60.3; 428, $C_{12}Cl_8^+/C_{18}Cl_6^+$, 100; 393, $C_{12}Cl_7^+/C_{18}Cl_5^+$, 21.2; 356, $C_{12}Cl_6^+/C_{18}Cl_4^+$, 65.0; 341, $C_6Cl_4I^+$, 20.1; 321, $C_{12}Cl_5^+/C_{18}Cl_3^+$, 20.3; 286, $C_{12}Cl_4^+/C_{18}Cl_2^+$, 40.2; 250, $C_{12}Cl_3^+/C_{18}Cl^+$, 24.6; 214, $C_{12}Cl_2/C_6Cl_4^+/C_{18}^+$, 52.1; 177, $C_{12}Cl^+/C_6Cl_3^+$, 37.9; 127, I^+, 17.2.

*Mass number, *m*/*z*, assignment of highest peak within the respective clusters. Mass spectra run on a Kratos MS50 in the EI mode.

Acknowledgment. The authors thank the reviewers for their very useful comments and suggestions. Thanks are extended to the UNB Research Fund and the UNB Faculty Development Fund.

Registry No. Perchlorotriphenylene, 137695-68-2; 1,2,3,4-tetrachloronaphthalene–bis(hexachlorocyclopentadiene) adduct, 80789-64-6; triphenylene, 217-59-4; hexachlorocyclopentadiene, 77-47-4; 1,2,3,4-tetrachloronaphthalene, 20020-02-4; perchlorofluorene-9-spirocyclohexa-2′,5′-diene, 102611-22-3; 1,2-diiodotetrachlorobenzene, 40707-59-3.

A Convergent Synthetic Approach to a Chiral, Nonracemic CDEF Analogue of Nogalamycin

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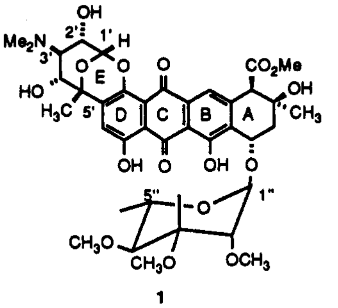
An approach to the synthesis of the CDEF rings of nogalamycin is described. The synthesis involves two key cycloadditions: (1) The regioselective addition of (2*S*)-2,3-*O*-cyclohexylideneglyceronitrile oxide with furan to yield the furoisoxazoline 7 and (2) the regioselective Bradsher cycloaddition of 7 with isoquinoline salt 8, induced by a pressure of 6 kbar, to attach the amino sugar moiety to the aromatic ring.

Nogalamycin (1) and its congeners are notable members of the anthracycline family.[2] Nogalamycin was isolated from *Streptomyces nogalater* var, nogalater sp. n. by Wiley et al.[3] It has a nogalose unit attached to ring A at C-7 and an amino sugar joined to the aromatic ring D via a glycosidic and a C–C bond, forming a benzoxocin ring system. The structure of nogalamycin, with the exception of the A-ring stereochemistry and the configuration of the amino glucose residue, was determined by Wiley et al.[4] The absolute stereochemistry of nogalamycin was established by Arora using X-ray crystallography in 1982.[5] Other recently reported anthracyclines, with the nogalamycin-type *DEF*-benzoxocin, are decilorubicin,[6] arugomycin,[7,8] and viriplanin.[9]

Nogalamycin is active against Gram-positive microorganisms, L1210 leukemia and KB cell carcinoma in vitro.[2] It has broad spectrum activity and less cardiotoxicity compared to daunomycin, adriamycin, and related compounds.[2,4] Despite its promise, nogalamycin's unacceptable toxicity precluded its clinical use.[2] A semisynthetic derivative, 7-*con*-*O*-methylnogarol 2 showed superior antitumor activity in comparison to the parent compound 1.[2,10] Crystallographic studies,[11] modeling and NMR work[12] have confirmed a proposal by Arora that the chromophore intercalates into DNA, with the amino sugar and nogalose interacting in major and minor grooves, respectively.[5]

Although the total synthesis of nogalamycin has not yet been achieved, a number of synthetic model studies have been reported[13-20] and the syntheses of both (+)- and (±)-7-*con*-*O*-methylnogarol 2 have been described.[19,21-24]



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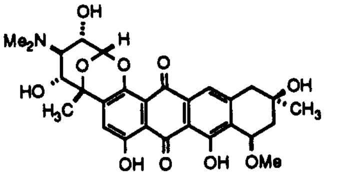

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In this paper, we describe an approach to the synthesis of *CDEF*-benzoxocin model of nogalamycin, 3, using the

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† Hoffman-LaRoche.

[1] The synthetic chemistry is taken entirely from the Ph.D. dissertation of H.Y., CUNY, 1990, and was supported by NIH CA 39351 and PSC/CUNY grants (R.W.F.). The crystallography laboratory at Hunter College is supported by NIH GM 41359 (G.J.Q.) and NIH RR 03037. Portions of this work were presented at the Northeast Regional Meeting of the American Chemical Society, June 18–21, 1989; Abstract no. 190.

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