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(16) Alternatively, **15a,b** may be converted to the corresponding diazo compounds. The carbonium ions **17** and **18a,b** may be cyclic oxonium ions.
(17) The sterochemistry of diazo hydroxides **14** and **15a,b** is not known. NMR showed that the acetate and nitroso groups of **6** and **9b** were anti and that **9a** was a mixture of syn and anti isomers.
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An Abbreviated Stereorational Synthesis of [10.10]Betweenanene

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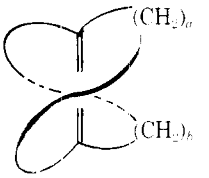
[*a.b*]Betweenanenes (I) are a novel class of fused bicyclic *trans*-cycloalkenes in which the double bond is common to both rings.[1] This unique geometric arrangement requires the bridging chains to crisscross above and below the double bond, at least for smaller values of *a* and *b*, thereby effectively burying it and sharply diminishing its reactivity. Cahn, Ingold, and Prelog, in their treatise on molecular chirality,[2] appear to have been the first to recognize these types of structures [they called them "bis(*trans*-polymethylene)ethylenes"] and pictured [6.6]betweenanene[3] as a hypothetical example of a molecule possessing planar chirality.

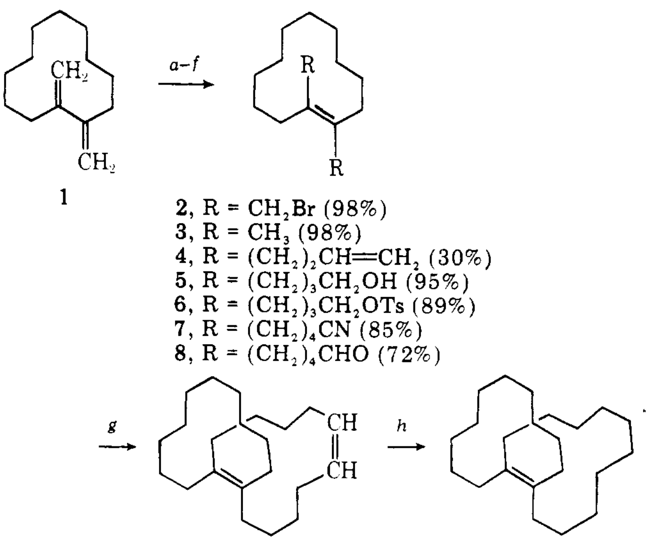


I

II

We independently perceived the betweenanene structure (I) some ten years ago in connection with studies involving photoinitiated ionic additions to cycloalkenes.[4] Recently, we completed a stereochemically definitive synthesis of [10.10]betweenanene (I, $a = b = 10$), the first known bis(*trans*-polymethylene)ethylene, and its cis isomer II ($a = b = 10$).[1] At about the same time, Nakazaki and co-workers reported the photoisomerization of bicyclo[10.8.0]eicos-1(12)-ene (II; $a = 10$, $b = 8$) to [10.8]betweenanene (I; $a = 10$, $b = 8$), thus demonstrating an alternative approach to betweenanenes.[5] More recent efforts in our laboratory have been aimed at developing efficient stereocontrolled routes to functionalized betweenanenes for planned studies of the chemical and physical properties of selected members of this unique class of cycloalkenes. This note describes a recent step in this direction.

Scheme I



1

2, R = CH_2Br (98%)
3, R = CH_3 (98%)
4, R = $(CH_2)_2CH{=}CH_2$ (30%)
5, R = $(CH_2)_3CH_2OH$ (95%)
6, R = $(CH_2)_3CH_2OTs$ (89%)
7, R = $(CH_2)_4CN$ (85%)
8, R = $(CH_2)_4CHO$ (72%)

9 (40%) 10 (93%)

[a] Br_2, $CHCl_3$. [b] $CH_2{=}CHCH_2MgCl$, THF, HMPA. [c] $(SiAm)_2BH$, THF; H_2O_2, NaOH. [d] *p*-TsCl, C_5H_5N. [e] NaCN, Me_2SO. [f] $(i\text{-}Bu)_2AlH$, ether; H_2O, NH_4Cl. [g] $TiCl_3$, Zn(Cu), DME. [h] H_2/Pt-C, EtOAc.

The synthesis, outlined in Scheme I, originates with 1,2-dimethylenecyclododecane (1), available in quantity from cyclododecanone via aminomethylation, Wittig condensation, quaternization, and Hoffman elimination.[6] Bromination of diene 1 afforded the *trans*-dibromide 2 as a solid in 98% yield. Analogous bromination of 2,3-dimethyl-1,3-butadiene has been shown to yield *trans*-2,3-dimethyl-1,4-dibromo-2-butene.[7] Proof for the stereochemistry of dibromide 2 was secured through its reduction with K-selectride[8] in 98% yield to *trans*-1,2-dimethylcyclododecene.[9]

After numerous trials with Grignard and organolithium reagents, as well as organocuprates, in various solvents, we found that allylmagnesium chloride in tetrahydrofuran–hexamethylphosphoramide gave the highest yield of triene 4 (30%). In all cases reduction–elimination to diene 1 predominated. This behavior stands in sharp contrast to that of the aforementioned 1,4-dibromo-2,3-dimethyl-2-butene, which couples almost quantitatively with allylmagnesium chloride.[10]

Further elaboration of the butenyl side chains of triene 4 was effected along standard lines by hydroboration–oxidation to diol 5 and cyanide displacement of the tosylate derivative 6. The dinitrile 7, thus obtained in over 80% overall yield, was reduced with diisobutylaluminum hydride to the dialdehyde 8 in 72% yield. Cyclization was effected by the recently reported titanium reagent of McMurry[11] to afford the [10.10]-betweenadiene 9 in 40% yield. While no attempt was made to ascertain the stereochemistry of the disubstituted double bond in this diene, a prominent peak at 970 cm^{-1} in its infrared spectrum suggests a predominance of the trans isomer.[11,12] Hydrogenation over platinum yielded [10.10]betweenanene (**10**), identical with material previously synthesized.[1] While further improvements are expected, the sequence described above represents a sixfold improvement in overall yield compared with our original route.[1]

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Experimental Section[13]

(*E*)-1,2-Bis(bromomethyl)cyclododecene (2). To a solution of 5.80 g (30.2 mmol) of 1,2-dimethylenecyclododecane[6] (1) in 18 mL of chloroform at −10 °C was added dropwise with stirring a solution of 1.6 mL (30.8 mmol) of bromine in 16 mL of chloroform. After 1.5 h, the mixture was washed with saturated aqueous sodium bisulfite, dried, and concentrated under reduced pressure to give 10.4 g (98%) of solid dibromide **2**, which was of suitable purity for use in the subsequent coupling reaction. Recrystallization from pentane gave 6.37 g of white solid: mp 56–57 °C; δ_{Me_4Si} ($CDCl_3$) 4.15 (AB, J_{AB} = 9 Hz, CH_2Br), 2.35 (m, allylic CH_2), and 1.2 (envelope, ring CH_2).

(*E*)-1,2-Dimethylcyclododecene (3). To a stirred solution of 0.10 g (0.29 mmol) of dibromide **2** in 5 mL of tetrahydrofuran (THF) at −80 °C was added 1.3 mL (0.65 mmol) of 0.50 M potassium tri-*sec*-butylborohydride[8] in THF via hypodermic syringe. The solution was allowed to stir with warming for 2 h, whereupon 2.5 mL of 20% sodium hydroxide and 2.5 mL of 30% hydrogen peroxide were added at 0 °C. After 2 h, the product was isolated by ether extraction to give 0.055 g (98%) of (*E*)-1,2-dimethylcyclododecene, identified by spectral and chromatographic comparison with an authentic sample:[9] δ_{Me_4Si} ($CDCl_3$) 1.70 (s, vinyl CH_3) and 1.2 (envelope, ring CH_2).

(*E*)-1,2-Di-3-butenylcyclododecene (4). To a stirred solution of 0.07 g (0.20 mmol) of dibromide **2** in 1 mL of hexamethylphosphoric triamide at room temperature was added dropwise 1 mL (0.5 mmol) of 0.50 M allylmagnesium chloride in THF. After 4 h, the product was isolated by extraction with hexane and filtration through 20 g of neutral alumina. Distillation afforded 0.025 g (65%) of dimethylenecyclododecane (**1**), bp 40–65 °C at 0.02 torr, and 0.16 g (30%) of triene **4**: bp 70– 120 °C at 0.02 torr; δ_{Me_4Si} ($CDCl_3$) 5.8–5.0 (vinyl H), 2.1 (allylic CH_2), and 1.4 (envelope, ring CH_2).

Anal. Calcd for $C_{20}H_{34}$: C, 87.51; H, 12.49. Found: C, 87.21; H, 12.84.

(*E*)-1,2-Bis(4-hydroxybutyl)cyclododecene (5). To a stirred solution of 4.4 mL of 2-methyl-2-butene in 50 mL of THF was added 16.5 mL of 1.0 M diborane in THF. After 15 min, 1.48 g of triene **4** in 5–10 mL of THF was added. The reaction mixture was stirred at room temperature for 3.5 h and treated with 4.8 mL of water. After 3.7 mL of 40% aqueous sodium hydroxide had been added, 6.2 mL of 30% aqueous hydrogen peroxide was added over a 10-min period with continuous stirring. Occasional cooling was necessary to control the exothermic reaction. The resulting mixture was heated at 45–50 °C for 5 h. After cooling, the organic layer was separated and the water layer was extracted with ethyl acetate. Filtration and removal of solvent gave 3.3 g of a colorless oil. The 3-methyl-2-butanol was removed by vacuum distillation, leaving a colorless solid residue of 1.8 g (95%) which was normally used without further purification. Recrystallization from hexane gave material with mp 95–98 °C: IR (film) 3370, 2950, 2890, 1470, 1060 cm^{-1}; δ_{Me_4Si} ($CDCl_3$) 1.05–1.75 (m, CH_2), 1.75–3.00 (m, allylic CH_2 and OH), 3.58 (m, CH_2–O).

Anal. Calcd for $C_{20}H_{38}O_2$: C, 77.36; H, 12.33. Found: C, 77.62; H, 12.35.

(*E*)-1,2-Bis(4-cyanobutyl)cyclododecene (7). A solution containing 1.8 g of crude diol **5** in 10–15 mL of pyridine was added to a stirred solution of 2.5 g of *p*-toluenesulfonyl chloride in 18 mL of pyridine. After 1 h at 0 °C, the mixture was placed in a freezer overnight and then poured onto ice and extracted with ether. Filtration and removal of solvent gave 3.5 g of a colorless ditosylate **6**, which was used without further purification: IR (film) 2950, 2880, 1600, 1370, 1180 cm^{-1}.

This sample of ditosylate **6**, 2 g of sodium cyanide, and 40 mL of dimethyl sulfoxide were heated under argon with stirring at 135 °C for 1 h. After being cooled, the mixture was poured into water and extracted with ether. Filtration and removal of solvent gave 1.69 g of dinitrile **7** as a light yellow oil which was used without further purification: IR (film) 2950, 2880, 2250, 1460, 1120 cm^{-1}.

The dicarboxylic acid derivative, mp 150–152 °C, was prepared by saponification using potassium hydroxide in ethylene glycol at 190 °C for 5 h.

Anal. Calcd for $C_{22}H_{38}O_4$: C, 72.09; H, 10.75. Found: C, 71.99; H, 10.39.

[10.10]Betweenanene (10). To a stirred solution of 0.82 g (5.0 mmol) of dinitrile **7** in 80 mL of ether at 0 °C was added dropwise 6.0 mL of 1 M diisobutylaluminum hydride in hexane. After 3 h, 50 mL of saturated aqueous ammonium chloride was added to the cold solution followed, after 20 min, by 50 mL of 5% aqueous hydrochloric acid. The product was isolated by ether extraction, giving 0.60 g (72%) of dialdehyde **8** sufficiently pure for use in the next step: δ_{Me_4Si} ($CDCl_3$) 9.7 (t, *J* = 2 Hz, –CHO) and 2.38 (m, CH_2CHO).

To a well-stirred mixture of 4.1 g of zinc–copper couple and 4.2 g of titanium trichloride in 40 mL of refluxing 1,2-dimethoxyethane was added a solution of 0.44 g (1.32 mmol) of dialdehyde **8** in 50 mL of DME over a 34-h period.[11] Heating was continued for an additional 14 h, whereupon the cooled mixture was filtered, concentrated under reduced pressure, and eluted through 20 g of silica gel with hexane to afford 0.16 g (40%) of diene **9**: δ_{Me_4Si} ($CDCl_3$) 5.4 (m, vinyl H), 2.1 (m, allylic H), and 1.4 (envelope, ring CH_2).

A solution of 0.15 g (0.50 mmol) of the above diene **9** in 8 mL of ethyl acetate was stirred for 2 h at room temperature with 0.1 g of 5% platinum-on-carbon under a hydrogen atmosphere. Filtration followed by concentration and chromatography (silica gel) afforded 0.14 g (93%) of solid [10.10]betweenanene (**10**), mp 63.5–64.5 °C, after recrystallization from acetone: δ_{Me_4Si} ($CDCl_3$) 2.8–1.8 (m, allylic CH_2) and 1.25 (envelope, ring CH_2).

Anal. Calcd for $C_{22}H_{40}$: C, 86.76; H, 13.24. Found: C, 86.90; H, 13.33.

The sample thus obtained was identical with material previously synthesized by an independent route.[1]

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Registry No.—**1**, 41613-91-3; **2**, 69309-09-7; **3**, 56491-46-4; **4**, 63240-80-2; **5**, 63240-82-4; **6**, 63240-84-6; **7**, 63240-86-8; **8**, 69309-10-0; **9**, 69309-11-1; **10**, 63269-60-3; allylmagnesium chloride, 2622-05-1; (*E*)-1,2-bis(4-carboxybutyl)cyclododecene, 63240-88-0.

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(13) The apparatus described by W. S. Johnson and W. P. Schneider ("Organic Syntheses", Collect. Vol. 4, Wiley, New York, 1963, p 132) was used to maintain an argon atmosphere. The isolation procedure consisted of thorough extractions with the specified solvent, washing the combined extracts with water and saturated brine solution, and drying the extracts over anhydrous sodium sulfate. The solvent was removed from the filtered extracts under reduced pressure on a rotary evaporator. Microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, Ill. Nuclear magnetic resonance spectra were recorded with Varian CFT-20 or Perkin-Elmer R20B spectrometers. Signals are reported as the chemical shift downfield from tetramethylsilane (Me_4Si) in parts per million of the applied field. Coupling constants are reported in hertz. Melting points were determined on a calibrated Thomas capillary melting point apparatus. Melting points are not corrected.

Facile Synthesis of Codeine from Thebaine[1]

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The conversion of thebaine (**1**) to codeine (**2**) has recently received attention since the former alkaloid could have become the principal domestic raw material for the analgesic