SDS suspension. Thus, lowering BXP photosensitization of NAT lysis in SDS micellar suspension from that in homogeneous aqueous solution may be due to separation of NAT from BXP trapped in the micellar phase, where the superoxide is formed by the photoexcited BXP and diffuse out for the oxidation of NAT in aqueous phase.

In order to compare the effect of micellar composition on the BXP-sensitized photolysis of tryptophan under the same condition, tryptamine instead of NAT was used as a substrate. The tryptamine is located in both CTAB and SDS micellar phase as demonstrated by blue shift of emission maxima from that in aqueous solution (Table 2). This is in good agreement of previous results obtained by Rossi *et al.*[12] Under this condition, the relative photolysis of tryptamine sensitized by BXP was greater in SDS micellar phase than in aqueous solution, but much lower than in CTAB micelles (Figure 4). These results again implicate that the anion radical of BXP may play a major role in the photosensitization in micellar phase, and that the sensitizer is more reactive in hydrophobic environment. Similar results have been obtained for the photosensitizing action in surfactant solutions of chlorpromazine and furosemide.[13]

The mechanism of anion radical formation of BXP in micellar phase may be different from that in ethanol (Eqs. 1,2), since the surfactants would not function as electron donor.[14] It might be rather possible that the photoexcited molecule of BXP may accept electron from BXP remained in the group state and change into BXP as shown in the following equation.

$$BXP^* + BXP \rightleftharpoons (BXP\cdots BXP)^* \rightarrow BXP^{\cdot-} + BXP^{\cdot+} \qquad (5)$$

The micelle may serve as a "super cage" for maintaining high local concentrations of reactants in a restricted space for a longer time than in aqueous phase and subsequently induce efficient formation of some excimer. In fact, the photo-induced [2 + 2] dimerization of 2-phenylbenzoxazole, an analog of BXP, was detected in degassed cyclohexane by Roussilhe *et al*[15]., although the quantum yield of this reaction is low. Thus, it is not impossible to postulate that the excimer formation of BXP would be more efficient in micellar phase, and induce efficient electron transfer from BXP* to BXP. Nevertheless, the direct detection of transients produced from BXP in micellar phase should be necessary to explore this possibility. Such investigation is in progress in our laboratory by using laser flash photolysis technique.

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Cationic Cyclizations to Tricyclene Structures†

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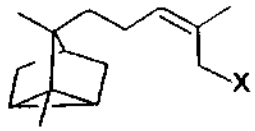
Various carbocation-mediated cyclizations to tricyclene structure (basically, tricyclo [2,2,1,$0^{2,6}$] heptane skeleton) were carried out, starting from protonated species of either 3-methyl-2,5-norbornadiene-2-carboxylic acid (**10**) or 3-methylene-5-norbornene-2-carboxylic acids (**18** and **19**). The resulting products were individually converted to π-iodotricyclene (**35**), a pivotal intermediate in almost all syntheses of tricyclene terpenes.

Introduction

The highly prized fragrance from isolate of *Santa ablum* Linn, East Indian sandalwood oil, is known to be derived from α-and β-santalols, **1** and **2**. Due to the highly condensed ring structures of these tricyclic sesquiterpenes and their importance, many synthetic achievements have been reported thus far[1].

† Dedicated to Professor Nung Min Yoon on the occasion of his 60th birthday.

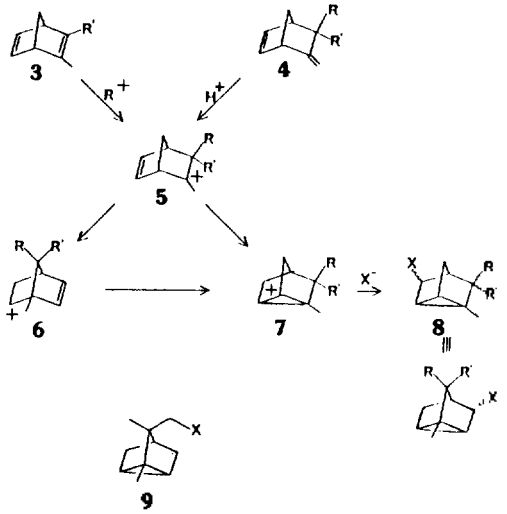


X=OH **1** α-Santalol

X=H **2** β-Santalol

Basically, these efforts were concerned with the construction of the existing 3-membered ring by photoisomerization of a bicyclo[3,2,1]-octenone[2], intramolecular C-H insertion of carbenes derived from substituted bicyclo[2.2.1]hetanones[3] or cyclization of 5-methylene-2-norbornes[4]. For some time, we have been engaged in simple construction of tricyclo[2,2,1,$0^{2,6}$]heptane rings by cationic cyclization, the details of which are described herein.

Game Plan. Our primary objective was to build up the tricyclene skeleton by cationic cyclization of carbocation **5**, which may be generated by Prins reaction[5] (or protonation) of substituted norbornadiene **3**[6], or protonation of methylenenorbornene derivatives **4**[4] (Scheme 1). The inherent advantage of this approach seemed to be that, once the cation **5** is formed, either direct cyclization or Waner-Meerwein rearrangement to **6** followed by cyclization would give the same cation **7** which would be captured internally or externally. Subsequent functional group elaboration would be initiated by the reduction at C-3, which would furnish the basic skeleton of tricyclene terpenes. In this regard, it is to be noted that numerous syntheses[1], except for the case by Monti[2], invariably utilized π-halotricyclene **9**. Consequently, our efforts were directed toward the convenient access to the compound **9**.



Scheme 1

Experimental

Genertal. All reactions involving organometallic reagents were carried out under an inert atmosphere of nitrogen. Diethyl ether and tetrahydrofuran were distilled from sodium metal and benzophenone and methylene chloride from calcium hydride immediately before use, and transferred using hypodermic syringes. Solutions of *n*-butyllithium were obtained from the Aldrich Chemical Co., and analysis of lithium reagent was carried out using titration with a standard solution of 2-butanol in THF with 1,10-phenanthroline as an indicator. A Varian EM-360A spectrometer was used to obtain ^{1}H-NMR spectra, and Schimadzu infrared spectrophotometer (IR-440) for IR spectra.

3-Methyl-2,5-norbornadiene-2-carboxylic acid (10). But-2-ynoic acid (7.5 g, 89.2 mmol) was dissolved in 60 mL (724 mmol) of freshly distilled cyclopentadiene. The reaction mixture was heated to reflux under nitrogen at 105°C in an oil bath. The bath temperature was raised to 155-160°C and stirring was continued overnight. The reaction mixture was allowed to cool to rt, to which were added 125 mL of 5% sodium carbonate solution and 60 mL of dichloromethane with vigorous stirring for 2 h. The aqueous layer was extracted off with dichloromethane three times, acidified with conc. hydrochloric acid, and then extracted with dichloromethane. The combined extracts were washed with water, dried over $MgSO_4$, and concentrated on a rotary evaporator. The residue was placed under vacuum at 60°C until it solidified. The yield was 6.98 g (52%), mp 42-45°C. TLC R_f 0.40 (50% ether in hexane). NMR (CCl_4) δ 6.80 (d, J=8Hz, 2H), 3.85 (s, 1H), 3.30 (s, 1H), 2.25 (s, 3H), 2.0 (s, 2H).

3-Methyl-2,5-norbornadiene-2-methanol (11). To lithium aluminum hydride (52 mg, 1.36 mmol) in 3 mL dry ether in an ice bath, a solution of 102 mg of bicyclic acid **10** (0.68 mmol) in 1 m*l* of dry ether was transferred at 0°C. After 30 min at 0°C (after the reaction was complete) 0.1 mL of water, 0.2 mL of 15% sodium hydroxide solution, and 0.1 m*l* of water were added consecutively. The solid was filtered off and the aqueous layer was extracted with ether. The combined extracts were dried over magnesium sulfate and the solvent was removed to give 61 mg (66%) of the alcohol (**11**). TLC R_f 0.29 (50% ether in hexane). NMR (CCl_4; TMS ref.) 6.85 (s, 2H), 4.03 (s, 2H), 3.40 (s, 1H), 3.20 (s, 1H), 1.90 (s, 2H), 1.65 (s, 3H).

3-Methylene-5-norbornene-2 (exo and endo)-carbonitrile (16). Cyanoallene (3.25 g, 150 mmol)[9] was added slowly to 9.92 g (150 mmol) of freshly prepared cyclopentadiene at rt. After refluxing for 3 h, the reaction mixture was distilled under reduced pressure to give 4.50 g (69%) of the product, **16**. bp 99°C/20 mm. TLC R_f 0.31 (20% ether in hexane). NMR (CCl_4) δ 6.20 (d, J=8Hz, 2H), 5.10 (d, J=8Hz 2H), 3.25 (s, 2H), 2.80 (s, H), 1.60 (q, J=8Hz, 2H).

2-(*exo*)-Methyl-3-metylyene-5-norbornene-2-(*endo*) carbonitrile (17). To a solution of 8.5 m*l* (60.9 mmol) of diisopropylamine in 140 m*l* of dry THF at −20°C, was added *n*-BuLi in hexane (9.5 *M*, 6.1 m*l*, 58 mmol) at−20°C, which was warmed up to −5°C stirred for 20 min. After cooling to −78°C, a solution of 3.8 g (29 mmol) of **16** in 10 m*l* of dry THF at −78°C was transferred to the above LDA solution. This was followed by stirring at −40°C for 1 h, and cooling the reaction mixture to −78°C. There was added 9.0 m*l* (145 mmol) of methyl iodide dropwise. The mixture was warmed to rt and stirred at the temperature for additional 1 h. After the reaction was complete, the reaction mixture was cooled to 0°C followed by addition of 30 m*l* of water. The aqueous layer was extracted with ether, and the combined extracts were dried over $MgSO_4$. The solvent was removed and the crude product was chromatographed to give 4.21 g (100%) of the pure product, **17**. TLC R_f 0.51 (40% ether in hexane). NMR ($CDCl_3$) δ 6.30 (t, J=1Hz, 2H), 5.10 (d, J=6Hz, 2H),

3.25 (s, 1H), 2.95 (s, 1H), 1.70 (s, 2H), 1.55 (s, 3H).

2(*exo*)-Methyl-3-methylene-5-norbornene-2(*endo*)-carboxylic acid (18) by Hydrolysis. A solution of 277 mg (1.91 mmol) of the nitrile **17** in 9.6 m*l* of 4 *M* NaOH solution was refluxed for 15 h. After the reaction was complete, the reaction mixture was cooled to 0°C, acidified with conc. hydrochloric acid and extracted with diethyl ether. The combined extracts were dried over magnesium sulfate and concentrated to yield 265 mg (60%) of the carboxylic acid, **18.** TLC R_f 0.31 (40% ether in hexane). NMR($CDCl_3$) δ 6.25 (br s, 2H), 5.10 (d, J=6Hz, 2H), 3.25 (br s, 1H), 3.0 (br s, 1H), 1.75 (s, 2H), 1.55 (s, 3H).

3-Methylene-5-norbornene-2(*exo*-and *endo*)-carboxylic acid (19). A solution of 2.01 g (15.3 mmol) of the nitrile **16** in 115 m*l* of 2 *M* NaOH solution was refluxed for 3 h, after which the reaction mixture was cooled to 0°C, acidified with conc. HCl, and extracted with ether. The combined extracts were dried over magnesium sulfate and concentrated to give 2.3 g (100%) of the carboxylic acid, **19**. TLC R_f 0.31 (50% ether in hexane). NMR(CCl_4) δ6.2 (s, 2H), 5.15 (s, 2H), 3.35 (br s, 1H), 3.2 (br s, 1H), 2.8 (s, 1H), 1.55 (br s, 2H).

2(*exo*)-Methyl-3-methylene-5-norbornene-2(*endo*)-carboxylic acid (18) by Methylation. To a solution of 25 mg (1.04 mmol) of NaH and 0.13 m*l* (0.94 mmol) of diisopropylamine in 3.1 m*l* of THF was added 138 mg (0.94 mmol) of carboxylic acid **19** at 0°C, which was heated to 60°C and stirring was continued for 15 min. Then the reaction mixture was cooled to 0°C and 1.5 m*l* (0.94 mmol) of n-BuLi was added and stirring at the temperature for additional 10 min. Then, the mixture was heated to 30°C min, to complete metalation. The solution was cooled and 0.06 m*l* (0.94 mmol) of CH_3I was added at 0°C. And stirring was continued for 15 h at rt. After the reaction was complete, the reaction mixture was cooled to 0°C followed by addition of 10 m*l* of water. The aqueous layer was acidified with 6 M HCl solution and extracted with ether. The combined extracts were dried over $MgSO_4$ and the solvent was removed to give 106 mg (71%) of the carboxylic acid, **18**.

3(*exo*)-Hydroxy-1-methyltricyclo[2,2,1,$0^{2,6}$]heptane-7(*syn*)-carboxylic Acid Lactone (20) from 19. A solution of 1.00 g (6 mmol) of **19** in 20 m*l* of 97% formic acid and a catalytic amount of conc. H_2SO_4 was refluxed for 4 h. After the reaction was complete, the reaction mixture was cooled to 0°C followed by addition of 10 m*l* of water, and extracted with diethyl ether. The combined extracts were dried over magnesium sulfate. The solvent was removed and the product was isolated by column chromatography to yield 657 mg (73%) of the lactone, **20**. TLC R_f 0.49 (60% ether in hexane). NMR(CCl_4) δ 4.60 (br s, 1H), 2.40 (s, 2H), 1.80 (s, 2H), 1.55-1.40 (dd, J=2Hz, 2H), 1.29 (s, 3H).

3(*exo*)-Hydroxy-1-methyltricyclo[2,2,1,$0^{2,6}$]heptane-7(*syn*)carboxylic Acid Lactone (20) from 10. 3-Methyl-2,5-norbornadiene-2-carboxylic acid **10** (1.04 g, 6.89 mmol) was dissolved in 14 m*l* 97% formic acid containing a drop of conc. H_2SO_4. The mixture was refluxed for 10 h, after which water (10 m*l*) was added at 0°C. Extraction with ether, washing with cold sat. $NaHCO_3$, and evaporation provided a residue, which was chromatographed on silica gel to furnish 0.581 g (56%) of the lactone **20**, the spectral data and chromatographilic mobility of which were identical with the material prepared from the acid **19**.

3(*exo* and *endo*)-Formyloxy-1,7-dimethyltricyclo[2,2,1,$0^{2,6}$]heptane-7(*syn*)-carbonitrile (22). A solution of 284 mg (1.95 mmol) of the diene nitrile **17** in 10 m*l* 97% formic acid in the presence of a catalytic amount of conc. H_2SO_4 was heated to reflux for 5 h, after which it was cooled to 0°C and 10 m*l* of water was added. The reaction mixture was extracted with diethyl ether and the combined extracts were washed with cold 5% NaOH solution. The organic layer was dried over magnesium sulfate and the solvent was removed to give 323 mg (87%) of the product, **22**. TLC R_f 0.40 (40% ether in hexane). NMR(CCl_4) δ8.0 (s, 1H), 5.25 (d, J=3Hz, 1H), 2.20 (br, 1H), 1.80 (br, 2H), 1.45 (s, 2H), 1.25 (d, J=2Hz, 3H), 1.2 (d, J=5Hz, 3H).

3(*exo*)-Hydroxy-1,7-dimethyltricyclo [2,2,1,$0^{2,6}$]heptane-7(*syn*)-carboxylic Acid Lactone (23). A mixture of 1.06 g (6.5 mmol) of the carboxylic acid **18** in 20 m*l* of 97% formic acid in the presence of a catalytic amount of conc. H_2SO_4 was heated to reflux for 15 h. After the reaction was complete, the reaction mixture at 0°C was quenched with 20 m*l* of water and extracted with diethyl ether. The combined extracts were washed with cold 5% NaOH solution, dried over magnesium sulfate and stripped off solvent to give 1.06 g (100%) ot the lactone, **23**. TLC R_f 0.37 (40% ether in hexane), NMR($CDCl_3$) δ4.80 (br s, 1H), 2.25 (br s, 1H), 1.85 (s, 2H), 1.55 (br s, 2H), 1.20 (s, 3H), 1.15 (s, 3H).

1-Methyltricyclo[2,2,1,$0^{2,6}$]heptane-7-carboxylic Acid (26). To a solution of 100 mg (0.67 mmol) of the lactone **20** in 3.3 m*l* of CH_2Cl_2 was added 0.1 m*l* (0.87 mmol) of $TiCl_4$ at 0°C. The reaction mixture was cooled to −78°C, treated with 0.43 m*l* (2.26 mmol) of Et_3SiH (dropwise) and allowed to warm up to rt. Stirring was continued for 4 h at rt. After the reaction was complete, it was cooled to 0°C, followed by addition of 10 m*l* of water, acidified with conc. hydrochloric acid and extracted with ether. The combined extracts were back extracted again with 5% NaOH solution, which was subsequently acidified, extracted with ether, dried over magnesium sulfate and concentrated to give 68.3 mg (67%) of the tricyclic acid, **26.** TLC R_f 0.54 (60% ether in hexane). NMR ($CDCl_3$) δ 2.29 (d, J=1.5Hz, 1H), 2.15-2.35 (m, 1H), 1.83 (d, J=11Hz, 1H), 1.29 (s, 3H), 1.15-1.6 (m, 3H), 1.08 (d, J=5Hz, 1H), 0.95 (d, J=5Hz, 1H). IR(CCl_4) 1700, 1425, 1420, 1300, 1295, 1240, 1230, 1220 and 855 cm^{-1}.

1,7-Dimethyltricyclo[2,2,1,$0^{2,6}$]heptane-7-carboxylic Acid (27) by Reduction. To a solution of 3.1 g (23.5 mmol) of aluminum chloride in 20 m*l* of dry CH_2Cl_2 at 0°C were added 1.28 g (7.83 mmol) of the lactone **23** in 5 m*l* of CH_2Cl_2 and 1.88 m*l* of triethylsilane (11.8 mmol). Stirring was continued for 10 min at 0°C and then at rt for another 4 h. The reaction mixture was cooled to 0°C and 20 m*l* of water was added very slowly. The aqueous layer was extracted with diethyl ether. The extracts were back extracted with 5% NaOH solution, the extracts of which were acidified with conc. hydrochloric acid and extracted with ether. The combined extracts were dried over magnesium sulfate and the solvent was removed to give 803 mg (62%) of the teresantalic acid, **27**. TLC R_f 0.43 (40% ether in hexane), NMR(CCl_4) δ1.9-2.1 (m, 1H), 1.58, 1.77 (br d, J=5Hz, 2H), 1.23 (s, 3H), 1.15 (s, 3H), 1.0-1.09 (m, 3H), 0.86 (br d, J=6Hz, 1H). IR(CCl_4) 1700, 1445, 1405, 1290, 1200, 1155, 1140, 1080, 1040, 975, 940 and 855 cm^{-1}.

1,7-Dimethyltricyclo[2,2,1,$0^{2,6}$]heptane-7-carboxylic Acid (27) by Methylation. To LDA solution prepared from diisopropylamine (0.20 m*l*) and n-butyllithium (1.33 M, 1.10 m*l*, 1.43 mmol) at 0°C in 2 m*l* THF was added the

tricyclic acid **26** (75 mg, 0.49 mmol) in 1 m*l* THF. The mixture was allowed to warm up to rt and heated to 50°C for 1 h. After cooling to −30°C and addition of 0.43 m*l* of 1.33 M n-butyllithium (0.49 mmol), the reaction mixture was allowed to warm up, heated to 50°C for 1 h and cool to −5°C. After addition of 0.18 m*l* (2.85 mmol) of methyl iodide, stirring was continued for 20 h at rt. After addition of 10 m*l* H_2O and acidification with 1 N HCl, the mixture was extracted with water. And the combined extracts were dried over $MgSO_4$ and stripped off the solvent. The residue was chromatographed on SiO_2 to give 10.1 mg (13%) of the starting material and 50.2 mg (71%) of the methylated acid **29** whose spectral data were identical with those of the product prepared independently.

Methyl 1,7-dimethyl-3 (*endo*)-iodotricyclo[2,2,1,$0^{2,6}$] heptane-7 (*syn*)-carboxylate (28). To a solution of 200 mg (1.22 mmol) of the lactone **23** in 3 m*l* of CCl_4 was added 0.87 m*l* (6.09 mmol) of trimethylsilyl iodide at rt. The reaction mixture was heated to reflux for 1 h. After it was cooled to 0°C 2 m*l* of dry methanol was added. This was followed by heating to reflux for 1 h. When the transesterification was complete, 10 m*l* of water was added at 0°C. The reaction mixture was extracted with ether and the combined extracts were washed with 10% sodium thiosulfate solution. The extracts were dried over magnesium sulfate and concentrated to give 250 mg (69%) of the product, **28**. TLC R_f 0.63 (40% ether in hexane). NMR(CCl_4) δ 3.6 (s, 3H), 2.1 (s, 1H), 1.9 (s, 1H), 1.75 (s, 1H), 1.55 (br, 2H), 1.2 (s, 3H), 1.15 (s, 3H), 0.86 (br, 1H).

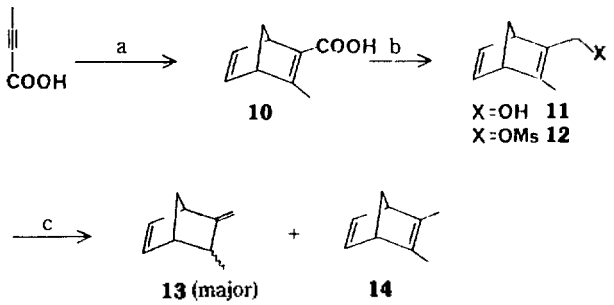
1,7-Dimethyltricyclo [2,2,1,$0^{2,6}$]heptane-7-methanol (30). To a solution of 1.55 g (9.33 mmol) of teresantalic acid **27** in 23 m*l* of dry THF was added 2.97 m*l* of borane methyl sulfide (9.43 *M*, 25.5 mmol) at 0°C. The reaction mixture was stirred at rt for 3 h. After the reaction was complete, 10 m*l* of water was added slowly at 0°C. The reaction mixture was acidified with 10% HCl solution and extracted with diethyl ether. The combined extracts were dried over magnesium sulfate and the solvent was removed to give 1.42 g (100%) of the teresantalol, **30**. TLC R_f 0.29 (40% ether in hexane). NMR (CCl_4) 3.60 (br, 2H), 1.85 (br, 5H), 1.5 (br, 1H), 1.30 (br, 1H), 1.15 (d, J = 3Hz, 3H), 0.9 (d, J = 4Hz, 3H).

1,7-Dimethyltricyclo [2,2,1,$0^{2,6}$] heptane-7-methanol Tosylate (34). A solution of 1.54 g (10.1 mmol) of teresantalol **20** in 20 m*l* of dry pyridine at 0°C was treated with 5 g (26.2 mmol) of *p*-toluensulfonyl chloride, which was stirred at rt for 20 h. Subsequently it was poured into 20 g of ice water, and extracted with diethyl ether. The combined extracts were washed with 10% HCl solution, and dried over magnesium sulfate. The solvent was removed to give 2.8 g (91%) of the tosylate, **34**. TLC R_f 0.54 (40% ether in hexane). NMR(CCl_4) δ 7.7 (d, J = 8Hz, 2H), 7.25 (d, J = 8Hz, 2H), 3.8 (m, 2H), 2.4 (s, 3H), 1.85-1.1 (7H), 0.9 (s, 3H), 0.85 (s, 3H).

1,7-Dimethyl-7-iodomethyltricyclo [2,2,1,$0^{2,6}$] heptane (35). A mixture of 511 mg (1.67 mmol) of the tosylate **34** and 1.11 g (6.67 mmol) of potassium iodide in 3.4 m*l* of dry DMF was heated to reflux for 5 h. After addition of 10 m*l* of sat. NaCl solution at 0°C the mixture was extracted with diethyl ether and the combined extracts were washed with brine. The organic layer was dried over magnesium sulfate and the solvent was removed to give 347 mg (75%) of the iodide, **35**. TLC R_f 0.71 (20% ether in hexane). NMR(CCl_4) δ 3.4 (d, J = 9Hz, 1H), 2.9 (d, J = 9Hz, 1H), 1.9-1.2(7H), 1.05 (s, 3H), 0.9 (s, 3H).

Results and Discussion

Starting Material. The known preparation of 2-methyl-2,5-norboradiene by the metalation-methylation sequence[7] did not provide any usable quantity of the material. Instead, Diels Alder reaction of cyclopentadiene (8 equiv) with 2-butynoic acid (bath temp 155°, 8 h) provided 3-methyl-2,5-norbornadiene carboxylic acid **10**[8] in 52% yield. Reduction with $LiAlH_4$ (2 equiv) in ether afforded 66% yield of the corresponding allylic alcohol **11**, which was mesylated (MsCl, Et_3N, CH_2Cl_2: 100%). Unfortunately, various reduction procedures for the mesylate **12** invariably yielded the S_N2' products **13** as major products with only minor quantity of the desired dimethylnorbornadiene **14**. Whether this reflects the thermodynamic stability of *exo*-methylene compounds **13** as compared to the norbornadiene **14** is not clear. Having been unable to prepare the methylated norbornadienes in usable quantities, the opportunity to examine Prins reaction vanished.



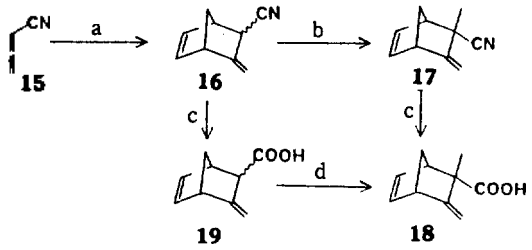
[a]Cyclopentadiene, 155°C, 8 h. [b]MsCl, Et_3N, CH_2Cl_2. [c]$LiAlH_4$, ether, 30°C.

Scheme 2

Additionally, the known cyanoallene, **15**, prepared from propargyl bromide and KCN in the presence of CuCN[9], was refluxed with 1 equiv cyclopentadiene for 3 h to give a ca. 1:1 mixture of *exo*-and *endo*-3-methylene-5-norbornecarbonitrile 16, bp 99°C/20 mm, in 69% yield, which was methylated with 2.4 equiv methyl iodide (THF, rt, 1 h) following the treatment with LDA (1 equiv) at −5°C to give exclusively *exo*-methylated nitrile **17** in quantitative yield (Scheme 3). The stereochemical proof was ascertained at the cyclization stage described below. Subsequent hydrolysis of the nitrile **17** proved to be highly erratic: Hydrolysis in refluxing 4 N NaOH solution furnished the known carboxyic acid **18**[10] in somewhere between **10** and 60%. The reaction proceeded very slowly presumably on the steric ground. However, as the reaction time increased, the yield decreased drastically, which might be closely related to the pronounced tendency of decarboxylation of β,γ-unsaturated carboxylic acids, although it was not attempted to identify the side product formed (Scheme 3).

On the other hand, the unmethylated nitriles **16** upon basic hydrolysis afforded, at a faster rate (3 h), quantitative yield of the corresponding carboxylic acid **19** (in a ca. 1:1 ratio of *exo* and *endo* isomers) under the same condition. Apparently, the sodium salt of carboxylic acid **19** was stable

under this condition. Methylation at α position was accomplished (71%) by the following sequence of the carboxylic acid dianion chemistry[11]: formation of sodium salt by NaH (1.1) with added i-Pr_2NH(1.0) in THF at 60°C, subsequent generation of the corresponding dianion upon addition of 1.0 equiv n-BuLi and stirring at 30°C for a brief period (10 min), and finally methylation with methyl iodide at 23°C for 15 h. The spectroscopic data of the resulting carboxylic acid **18** were identical with those of material prepared independently (*vide supra*).



[a]Cyclopentadiene, Δ, 3 h. [b]LDA, THF, -5°C then 2.4 equiv MeI. [c]NaOH, H_2O, Δ. [d]NaH(1.1), i-Pr_2NH(1.0), THF, 60° then n-BuLi, 0° → 30°C, then MeI (1.0), rt.

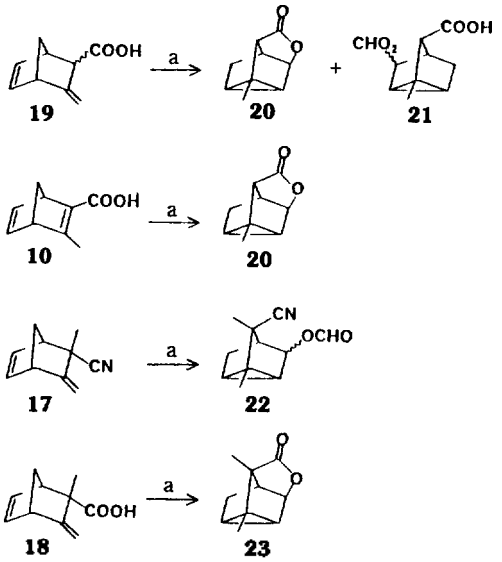
Scheme 3

Cyclization. With several potential candidates for cyclization in hand, the standard condition developed by Corey and Sutherland[6] was applied; a solution of the substrate in 97% formic acid containing a catalytic amount of concentrated sulfuric acid (substrate concentration; 0.2-0.3 M)) was refluxed until the starting material was completely consumed (Scheme 4). Ethereal extraction, washing with cold 5% NaOH solution and subsequent purification provided good yields of cyclized products in all cases.

With a 1:1 mixture of methylenenorbonenecarboxylic acid **19**, surprisingly, 73% yield of tetracyclic lactone **20** was obtained (4 h), indicating the attendent epimerization of carboxy group in **19** during the reaction. This is especially true considering the fact that the lactone **20** would be formed from *endo* isomer and the formate of the regioisomeric hydroxy acid, **21**, which was actually isolated, resulted from the *exo* oriented carboxylic acid of **19**. Apart from the epimerization, the cyclization itself was rather predictable in view of the results obtained by other workers[4]. More pleasing was that even norbornadienecarboxylic acid **10** was found to undergo cyclization to the same lactone **20** in 56% yield (10 h). This is, to our knowledge, the first instance of this type of compound like **10** undergoing cationic cyclization.[4]

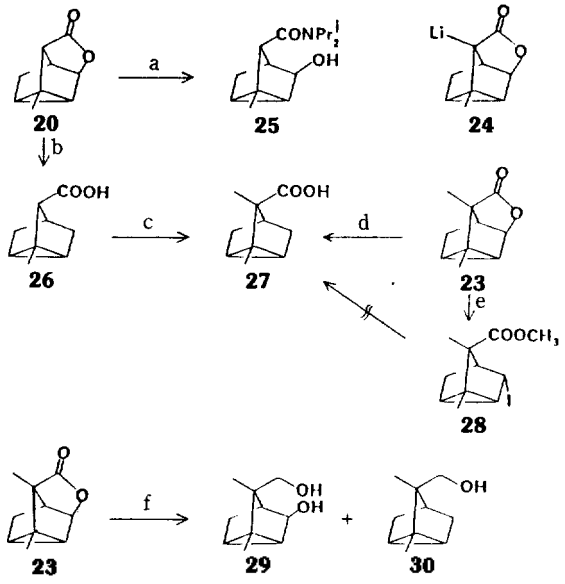
Also, the endo nitrile **17** underwent cyclization to give the formate **22** in 82% yield (5 h). And the methylated carboxylic acid **18** afforded quantitative yield of the lactone **23** in 15 h, a result already reported by Barnett et al.[10] But the difference is that the endo carboxylic acid **18**, the starting material in this reaction, was elaborately separated from the exo isomer by chemical means (Barnett) but in our case prepared stereospecifically (*vide supra*).

Methylation and Reduction. Next came the task of methylation of **20** to a certain equivalent form of **23** and deoxygenation at C-3. In case of the non-methylated lactone **20**, the order of methylation and reduction could be reversed (Scheme 5). In any case attempts to methylate the lactone **20** were birefly made; reaction with LDA (1.5 equiv) to generate the metallated lactone 24 (Note that the corresponding enolate structure cannot be written because of the non-planarity.) invariably produced the hydroxy amide **25**. Instead, deoxygenation at C-3 was tried next. In this regard, it is to be noted that the position is a bisected cyclopropylcarbinyl where the corresponding cation is especially stable[12]. In such cases, so called ionic reduction employing Et_3SiH and trifluoroacetic acid seemed to be convenient.[13] However, such a general method did not work at all. Eventually, a combination of Et_3SiH (3 equiv) and $TiCl_4$ (1.3 equiv) in CH_2Cl_2 at 23°C for 4 h was effective for the reduction to give a carboxylic acid **26** in 67% yield, which was methylated to give tere-



[a]HCO_2H, cat. H_2SO_4, Δ.

Scheme 4



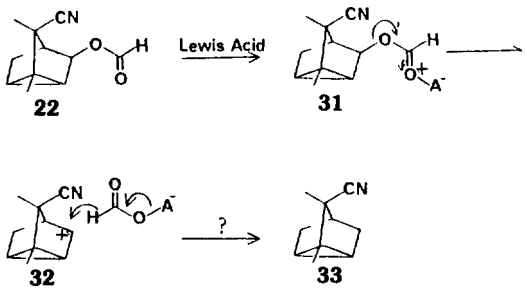
[a]LDA (1.5), THF -78→0°C then MeI. [b]Et_3SiH, $TiCl_4$, CH_2Cl_2, 4 h. [c]1. LDA, THF 0→50°C, 2.n-BuLi, -30→50°C, 3. MeI(5.8), -5→23°C, 20 h. [d]Et_3SiH(1.5), $AlCl_3$(3), CH_2Cl_2, 23°C, 4 h. [e]Me_3SiI(6.0), CCl_4, Δ, 1 h. [f]$AlCl_2H$, ether.

Scheme 5

santalic acid **27**, a natural product[1], in 82% yield (13% recovery of **26**) through the sequence of (1) LDA (3 equiv), THF, 0 → 50°C, (2) n-BuLi (1 equiv), −30° → 50° and (3) MeI (5.8 equiv), −5° → 23°C (20 h) (Scheme 5).

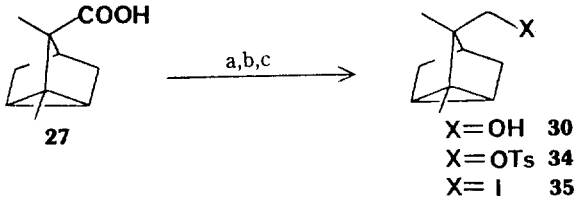
Also, the methylated lactone **23**, obtained by cyclization of **18**, was reduced by Et_3SiH (1.5 equiv) and $AlCl_3$ (3.0 equiv) in CH_2Cl_2 at 23° for 4 h to obtain 62% yield of teresantalic acid **26**, which was identical in all respects with the meterial prepared above. Prior to this event, the lactone **23** was treated with 6.0 equiv Me_3SiI in CCl_4 (reflux, 1 h) followed by methanol quench to obtain 69% yield of the iodo ester **28**, the reduction of which never materialized under a variety of conditions (Scheme 5). Additionally, an attempt was made stepwise reduce the lactone **23** first at C-3 followed by reduction of the resulting carboxylate in one pot utilizing the high Lewis-acidic character of Cl_2AlH.[14a] In the event, reduction with Cl_2AlH in ether, generated from $AlCl_3$ (10.0 equiv) and $LiAlH_4$ (5 equiv)[14d], at refluxing temperature provided a 2:1 mixture of the diol **29** resulting from initial attack at the carbonyl group and the monoalcohol **30** which we eventually intended to have (vide infra) (Scheme 5). Although the chances would seem to be greater with unsolvated Cl_2AlH[14b], this matter has not been pursued further (Scheme 5).

Finally, we were lead to believe that the formate **22** could be reduced upon treatment with a Lewis acid even in the absence of an added hydride donor since formate ion, HCO_2^-, is known to be a good hydride donor[15]. The following Scheme (Scheme 6) was the basic of our conjecture.



Scheme 6

However, even prolonged heating with a variety of Lewis acids sometimes even with externally added hydride donor, Et_3SiH, did not show any sign of reduction.



[a]BMS(2.7), THF, 3 h. [b]TsCl(2.6), Py, 20 h. [c]KI(4.0), DMF, Δ, 5 h.

Scheme 7

Functional Group Modification. With teresantalic acid **27**, reduction with borane-methyl sulfide (2.7 equiv) in THF at 23°C (3 h) afforded the corresponding alcohol **30** in quantitative yield, which was tosylated with p-toluenesulfonyl chloride (2.6 equiv, pyridine, 23°C, 20 hr; 91%) (Scheme 7). The resulting tosylate was converted to the corresponding iodide **35** in 75% yield by the reaction with 4.0 equiv KI in refluxing DMF for 5 h.

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