(3 × 50 mL). The combined ether fractions were concentrated to afford oily **9** (1.42 g, 91%), which after chromatographic purification (CH_2Cl_2–MeOH, 97:3, R_f = 0.23) gave solid **9** (1.15 g, 74%). Ultimately the material was triturated with diethyl ether: mp 100–101 °C. $\Delta\epsilon$ (260 nm, MeOH): −0.57. $[\alpha]^{20}_D$: +12.5° (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$): (Tables I and II), δ 3.80 (s, 3 H, CO_2Me), 6.70 (d, J = 8.4 Hz, 1 H, NH), 7.0–7.3 (m, 5 H, Ar H), $J_{3\alpha,3\beta}$ = 14.2 Hz, $J_{5',6'}$ = 5.1 Hz. Anal. Calcd for $C_{18}H_{20}N_2O_3$ (MW 312.37): C, 69.21; H, 6.45; N, 8.97. Found: C, 69.4; H, 6.8; N, 9.0.

Registry No. **1**, 129918-83-8; **2**, 129918-88-3; **3**, 67501-00-2; (*S*)-**4**, 19460-86-7; (*R*)-**4**, 130008-09-2; **5**, 55314-19-7; **6**, 129918-87-2; **7**, 129918-84-9; **8**, 129918-85-0; **9**, 129918-86-1; *i*-PrNHMe, 4747-21-1; $(i\text{-Pr})_2NH$, 108-18-9; *i*-$PrNH_2$, 75-31-0; H-Phe-OMe·HCl, 7524-50-7.

Preparation of Chiral Inducers Having the Bicyclo[3.1.1]heptane Framework. Assignment of Diastereomer Configuration by NMR and Comparison of Calculated and Observed Coupling Constants[1]

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Several bicyclo[3.1.1] compounds have been prepared for possible uses in asymmetric synthesis, including 10-phenyl-α-pinene and the diastereomeric (1*S*,2*S*,5*S*)-10-phenylmyrtanols. The geometry and NMR properties of bicyclo[3.1.1] compounds have been investigated by using molecular mechanics and NMR coupling constants.

Among commercially available resolved compounds having the bicyclo[3.1.1] framework, (+)- or (−)-α-pinene (**1a**, X = H) has been of exceptional importance in syntheses of chiral compounds. Its hydroboration product, diisopinocampheylborane, has been developed by Brown's group as a crystalline, readily prepared reagent, which hydroborates some *cis*-alkenes with high enantiomeric excess.[2] Boronate esters of pinanediol, obtained from α-pinene, have been used by Matteson's group to form a wide variety of compounds having one or more chiral centers, often with high stereoselection.[3] We are investigating applications to asymmetric synthesis of other available bicyclo[3.1.1] compounds, including (1*R*)-myrtenol (**1b**, X = OH) and (1*S*,2*S*,5*S*)-myrtanol (**2**). The geometry of these compounds is of interest to us, as is that of isopinocampheol (**3**), which is a compound having the approximate geometry of diisopinocampheylborane and its projected analogues.[4]

Two bicyclo[3.1.1] compounds whose NMR spectra were examined in the course of our synthetic studies showed sufficient separation of NMR peaks at 300 or 500 MHz to permit a preliminary estimate of most of the chemical shifts and coupling constants. Our experience has been that in these systems spectra that have minimal overlap are not often available, even at 500 MHz. Accordingly, we utilized these opportune spectra in conjunction with NMR simulation to provide the first complete assignments of J values in bicyclo[3.1.1] systems, so far as we can determine. In the case of the phenylmyrtanols (to be described), the assignment of chemical shifts permitted an interesting assignment of the configuration of diastereomers without resort to X-ray data.

We were prompted to compare the above-mentioned NMR coupling constants with those calculated by the program PCMODEL.[5] This program utilizes the MM2 force field[6] (or an extended version of it) to calculate energy-minimized structures from structures drawn on an IBM pc screen. In PCMODEL coupling constants are calculated by a complex elaboration of the Karplus relationship developed by Altona et al.[7] Our study provides some indication of the reliability and usefulness of the calculated J values and dihedral angles.

Synthetic Studies

Previous studies from our group have involved the asymmetric hydroboration–oxidation of vinyl ethers with diisopinocampheylborane.[8] When benzyl or diphenylmethyl vinyl ethers were used, the resulting ether–alcohols were readily cleaved to partially resolved 1,2-diols. We wished to prepare analogues of the above-mentioned ethers in which the benzylic moiety is chiral. Preliminary studies[9] showed that addition of phenyllithium or naphthylmagnesium bromide to (1*R*)-(−)-myrtenal gave diastereomeric alcohols of the desired type, which were separable with some difficulty by high performance liquid chromatography (HPLC). Although these alcohols are potentially convertible to vinyl ethers by acylation followed by Tebbe

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. Acknowledgment is made to the National Science Foundation (grant no. CHE-8411172) and the National Institutes of Health (grant no. 10S10-RR02425-1) for support of the purchase of a Bruker 300-MHz NMR spectrometer and to the National Science Foundation (grant no. CHE-8904942) for support of the purchase of a Bruker 500-MHz NMR spectrometer.

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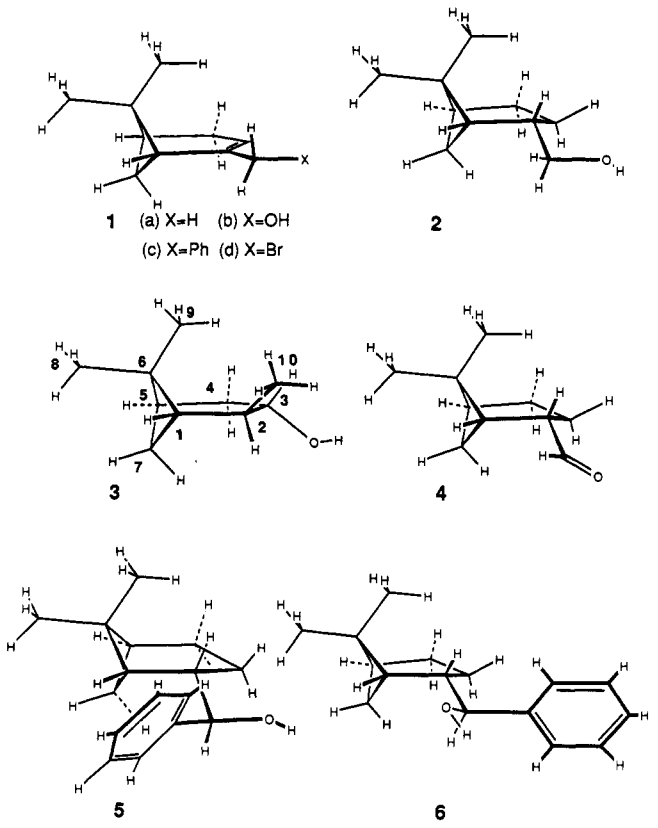
Chart I



methylenation, molecular mechanics studies using PCMODEL showed that several conformations of comparable energy resulted from rotation around the bond from the ring to the exocyclic carbon. We judged that this situation was not favorable for finding high enantiomeric excess values upon hydroboration of the vinyl ethers.

Comparable compounds derived from (1*S*,2*S*,5*S*)-myrtanol (**2**) appeared to be ideal for our purpose, however. Swern oxidation to the aldehyde **4** followed by reaction with phenyllithium or phenylmagnesium bromide gave an approximate 3:1 mixture of diastereomers **5** and **6** (Chart I). The aldehyde group in **4** is in the more stable configuration away from the bulky dimethyl group on the four-membered ring. Accordingly, potential problems with epimerization at the aldehyde stage are minimized. For our purposes we are especially interested that the alcohol diastereomers are "locked". The preferred conformer is that in which the hydrogens on C2 and C10 are anti in order to minimize steric repulsion of the bulky groups on C10. As we envisioned, chromatographic separation of the alcohols was exceptionally facile, since one of them, **6**, has the OH group in a more sterically congested environment, inhibiting its hydrogen bonding to silica during chromatography.

The geometries of the most favorable conformers of **5** and **6** calculated by PCMODEL are those depicted in Chart I. Other formulas in Chart I also are drawn from PCMODEL output. A few carbon–hydrogen bond lengths were altered to enhance the clarity of the structures. If shielding by the phenyl group in **5** and **6** should occur, the bridgehead hydrogen H1 (attached to C1, numbered as shown for formula **3**) should be the most affected in **5** whereas the H3 methylene hydrogens would be the most affected in **6**. Experimentally, the earlier eluting diastereomer, thought to be **6** did, in fact, show two shielded hydrogens at δ 1.12 and 0.99, a region in which only methyl groups are usually found. Decoupling experiments (500 MHz) showed these to be hydrogens on C3, as expected. Furthermore, the bridgehead hydrogen, H1 of the other diastereomer, **5**, appeared as an approximate triplet (J = 5.4 Hz) at δ 1.50, 0.71 ppm upfield from the chemical shift (δ 2.31) of H1 of **6**. The assignment appears to be unambiguous, obviating the need for further study, such as X-ray crystallography of a derivative.

In another study involving the use of compounds in Chart I in asymmetric syntheses, we noted that the preparation of hydroborating agents derived from the relatively unstudied substituted pinenes could be of interest.[10] Here we report the preparation of 10-phenyl-α-pinene (**1c**, X = Ph) from myrtenol (**1b**, X = OH). Previously 10-phenyl-α-pinene has been prepared in 32% yield from the ene reaction of β-pinene with benzyne derived from anthranilic acid.[11] It has been obtained in 30% yield from β-pinene by conversion to the myrtenyl derivative, **1**, X = $SONHSO_2Ph$, followed by a CuBr-catalyzed Grignard reaction.[12] In a third synthesis the palladium-catalyzed reaction of β-pinene with phenylmercuric acetate gave 10-phenyl-α-pinene in 29% yield.[13] In our route myrtenyl bromide (**1d**, X = Br) readily underwent reaction with phenylmagnesium bromide to give phenylpinene in 62% yield. Alternatively, the reaction of myrtenyl acetate with excess phenylmagnesium bromide and CuI gave phenylpinene in 70% yield, mixed with biphenyl whose separation by distillation was inconvenient. In some instances the presence of 3-phenyl-β-pinene, the product of γ attack, was discernable in our products.

We carried out some preliminary studies of 10-phenyl-α-pinene in order to find if it would give a useful hydroborating agent comparable to that obtained from α-pinene. We do not report these results, which have not been promising and which have been difficult to reproduce.

NMR Studies

Long range couplings and upfield chemical shifts of methylene hydrogens in bicyclo[2.1.1] systems have been noted by Meinwald and Lewis[14] and/or by Wiberg et al.[15] One detailed NMR study of 6,6-dimethylbicyclo[3.1.1]-hexane systems has appeared.[16] In this study a long range coupling (J = 6 Hz), between the bridgehead hydrogens, was reported. As in the bicyclo[2.1.1] system, one of the hydrogens on the four-membered ring of various bicyclo-[3.1.1] systems (assigned as H7-endo) appears upfield, sometimes in the methyl region of the NMR spectra. Other workers, e.g., those of the Matteson group,[3] also have reported the upfield doublet, attributable to geminal coupling. As in the bicyclo[2.1.1] system, the approximate zero coupling to the bridgehead hydrogens is attributed to the magnitude of the dihedral angle (approximately 90°).[17]

We have done decoupling studies of the bicyclo[3.1.1] systems **3** and **6**. We were able to assign the chemical shifts of all of the hydrogens except methyl hydrogens. In an approach that is general for these systems, decoupling of

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Table I. Coupling Constants (hertz) in Isopinocampheol (3)

hydrogen	J obsd	J from PCM (angle, deg)	J, PCM, fixed[a] (angle, deg)
1-2	2.1	2.0 (64)	1.5 (68)
1-5 (bridgeheads)	5.6		
1-7exo	6.0	7.7 (30)	7.9 (29)
1-7endo	0.5 ● 0.5	1.5 (99)	1.6 (100)
2-3 (trans)	4.7	3.5 (131)	4.2 (135)
2-10 (Me)	6.8		
3-4exo (cis)	9.4	9.7 (7)	9.7 (11)
3-4endo (trans)	4.7	3.7 (124)	4.7 (129)
4exo-5	3.4	3.2 (56)	4.1 (52)
4exo-4endo (gem)	13.97		
4exo-7 (W)	2.46		
4endo-5	2.6	3.3 (57)	2.2 (63)
5-7exo	6.0	7.7 (30)	7.9 (30)
5-7endo	0.5 ● 0.5	1.4 (97)	1.5 (98)
7exo-7endo (gem)	9.8		

[a] The C1-C7 distance was decreased by using "fix atom". Minimization of the energy was carried out on the "fixed" molecule.

Table II. Coupling Constants (hertz) in (10*S*)-*endo*-10-Phenylmyrtanol (6) and (10*R*)-*endo*-10-Phenylmyrtanol (5)

	J for 6	J_{calc}(6) (angle, deg)	J_{calc}(5) (angle, deg)
1-2	0.5 ± 0.5	1.0 (0)	
1-7exo	5.74	8.0 (28)	8.0 (28)
1-7endo	0.5 ± 0.5	1.6 (100)	1.7 (100)
1-5 (bridgeheads)	5.3		
2-3exo (cis)	8.6	7.8 (31)	7.9 (31)
2-3endo (trans)	9.6	9.1 (146)	9.0 (145)
2-7exo (W)	1.3		
2-10 (anti)	9.0	9.7 (171)	10.6 (178)
3exo-4exo (cis)	9.3	10.2 (26)	10.3 (25)
3exo-4endo (trans)	1.1	0.0 (89)	0.1 (92)
3exo-3endo (gem)	15.3		
3endo-4exo (trans)	9.3	9.0 (140)	89.9 (139)
3endo-4endo (cis)	9.3	10.6 (24)	10.6 (24)
4exo-5	1.6	1.7 (68)	1.7 (68)
4endo-5	4.5	5.2 (45)	5.2 (46)
4exo-4endo (gem)	14.3		
4exo-7exo (W)	1.3		
5-7 exo	5.7	7.7 (30)	7.7 (30)
5-7endo	0.5 ± 0.5	1.5 (90)	1.5 (98)
7exo-7endo	10.2		

the above-mentioned H7-endo upfield doublet located H7-exo. Decoupling of H7-exo in turn helped to locate the bridgehead hydrogens. Although W couplings of H7-exo to H2-exo and H4-exo hydrogens were a complicating factor, the W coupling was useful in assigning the exo configuration to one of the hydrogens on C4. Additional decoupling, including that of downfield hydrogens attached to carbon-bearing oxygen, provided additional assignments.

For isopinocampheol (**3**) and (10*S*)-10-phenylmyrtanol (**6**) most of the patterns of the NMR spectra could be tentatively understood on the basis of first-order splitting diagrams, allowing preliminary *J* values to be assigned. We were then able to simulate the spectra of these compounds using a seven-spin spectral simulation program, PANICCAL, supplied as part of the Bruker NMR software. Appropriately chosen partial structures were used, since our molecules have more than seven coupled hydrogens. The iterative procedure of PANICCAL was used to achieve the optimized *J* values reported in Tables I and II. Calculated and observed portions of spectra are compared in Figure 1. It is of considerable interest to compare the observed *J* values with the *J* values given by the above-mentioned PCMODEL program, also shown in Tables I and II and plotted in Figures 2 and 3.

The observed spectrum for the diastereomeric myrtanol **5** contains many overlapping peaks, making simulation impracticable. Accordingly, only the calculated *J* values are given for it. We note, however, that J_{2-10} was observed to be 8.1 Hz, which may be compared with 9.03 Hz observed for the diastereomer **6**. We have not assessed the possible small contribution of other conformers involving rotation around the C2-C10 bond of **5** and **6**, other than to note that the calculated J_{2-10} values fit approximately as well as the other ones.

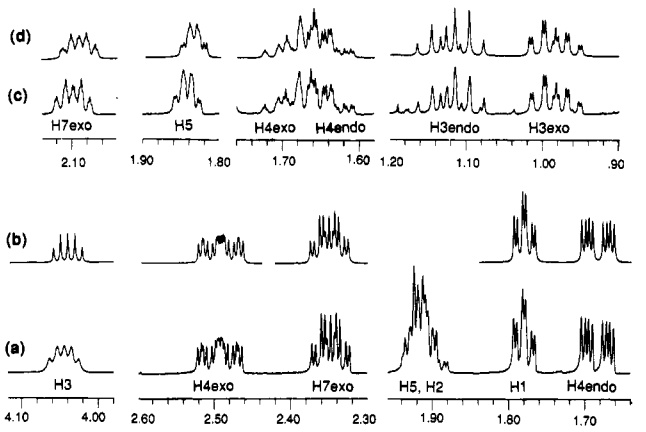

Figure 1. Observed and simulated NMR spectral regions. (a) Isopinocampheol (**3**), observed. (b) Isopinocampheol, simulated. (c) (10*S*)-10-Phenylmyrtanol (**6**), observed. (d) (10*S*)-10-Phenylmyrtanol, simulated.

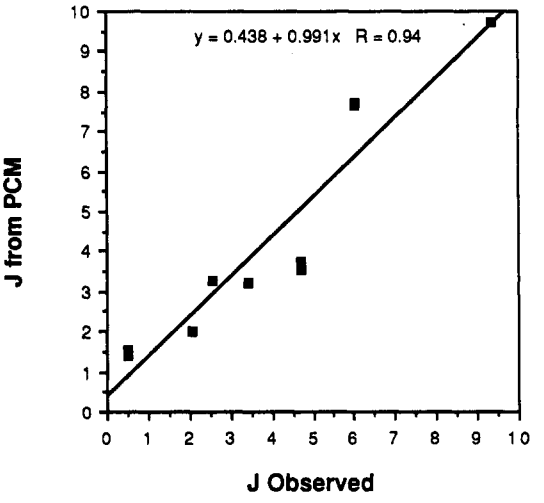

Figure 2. Calculated versus observed *J* values for isopinocampheol (**3**).

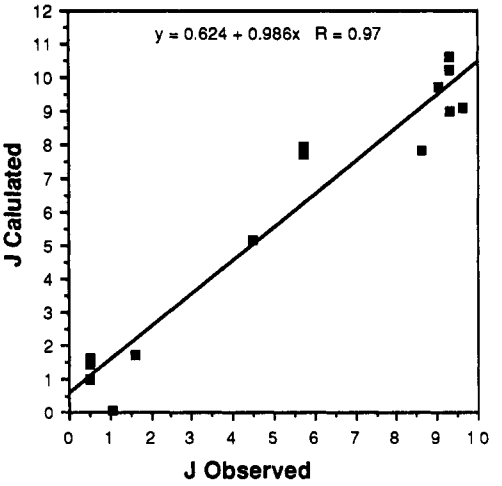

Figure 3. Calculated versus observed *J* values for (10*S*)-10-phenylmyrtanol (**6**).

It is of interest that the MM2-based structures **2**, **3**, **4**, **5**, and **6** have three-carbon bridges that are much flattened, compared to cyclohexane chairs. As expected, the exocyclic groups cause the flattened chair of isopinocampheol (**3**) to have a preferred "exo" conformation, and that of the myrtanols **2**, **5**, and **6** to have a preferred "endo" conformation.

As may be noted in Table I, cis couplings are of larger magnitude than trans couplings in the flattened ring of isopinocampheol (**3**) because the dihedral angles are in the range where the relative magnitude of the respective couplings has "crossed over" from that found in cyclohexanes. We used the "fix-distance" feature of PCMODEL (which incorporates a spring constant between the atoms) to move the carbon skeleton of isopinocampheol to a more chair-like conformation (Table I). After reminimization the resulting small changes in structure brought the couplings into better agreement with the observed J values. These results suggest that the MM2 structure of isopinocampheol is somewhat too flat owing to a small overestimation of the steric effect of the *gem*-dimethyl group. It will be noted in Table I that the dihedral angles of isopinocampheol as calculated for PCMODEL differ only by 4° to 6° from those (0° or 120°) in a planar ring.

In (10*S*)-10-phenylmyrtanol (**6**) the opposite chair-like conformation is present, compared to that in isopinocampheol, as a consequence of the tendency of the C10 side chain to have equatorial character. The dihedral angles are approximately 30° from those in a planar ring. Here the *gem*-dimethyl group does not interfere with chair formation, as it does in isopinocampheol. The degree of ring flattening found here is in the "cross-over" range where approximate 30° cis couplings and approximate 150° trans couplings are of equal magnitude.

In **6** a 30° rotation from hypothetical planar dihedral angles converts one 120° dihedral angle (H3exo–H4endo) of the planar ring to an approximate 90° angle. The resulting near zero trans coupling constant is strikingly revealed in the splitting pattern of the H3 upfield hydrogens (Figure 1). A small coupling (1.6 Hz) is found for only one of these, identifying it as H3exo.

A comparison of calculated and observed J values is shown in Tables I and II and in the plots of Figures 2 and 3. The agreement is good enough for the calculated values to be a useful aid in assigning experimental spectra. Examination of the literature reference,[7] which describes the origination of the Karplus-like relationship used by PCMODEL revealed that carbon skeletons based on MM1 molecular mechanics calculations (not MM2, used in PCMODEL) were used optimize the parameters. Refinement of the J value calculation using MM2 or MM3[18] is a possible avenue for further work.

Our NMR results provide a basis for the examination of configurations in bicyclo[3.1.1] compounds having substituents of unknown stereochemistry on the three-carbon bridge. The different degree of ring flattening for exo- or endo-substituted compounds results in the substantially different coupling patterns which have been described.

Experimental Section

Preparation of (1*S*,2*S*,5*S*)-6,6-Dimethylbicyclo[3.1.1]-heptane-2-carboxaldehyde (4) ((1*S*,2*S*,5*S*)-Myrtanal). According to the published procedure for Swern oxidation,[19] oxalyl chloride (4.86 mL, 9.72 mmol) was added to anhydrous methylene chloride (CH_2Cl_2) contained in a flame-dried nitrogen-flushed 100-mL flask. The stirred mixture was cooled with dry ice–acetone. Distilled dimethyl sulfoxide (DMSO) (1.52 mL, 17.66 mmol) was very slowly injected. After 5 min, (1*S*,2*S*,5*S*)-6,6-dimethylbicyclo[3.1.1]heptane-2-methanol (**2**) (also named (1*S*,2*S*,5*S*)-(−)-myrtanol, Aldrich, 1.00 g, 6.48 mmol in 6.5 mL of CH_2Cl_2) was injected. Triethylamine (5.00 mL, 32.4 mmol) was injected. After 5 min the flask was allowed to warm to room temperature. A white solid formed. After 20 min the solution was extracted (H_2O–CH_2Cl_2), dried ($MgSO_4$), and evaporated to give (1*S*,2*S*,5*S*)-myrtanal (0.82 g, 83%): ^{1}H NMR δ 9.55 (s, 1 H), 2.77 (t, 1 H), 2.64 (s, 1 H), 2.23 (m, 1 H), 2.08 (m, 2 H), 1.86 (m, 2 H), 1.56 (m,1 H), 1.24 (s, 3 H), 1.03 (d, 1 H), 0.87 (s, 3 H). The reported values are 9.7 (bs, 1 H), 1.27 (s, 3 H), 0.91 (s, 3 H) for material prepared[20] by oxidation of the alcohol on silica-pyridinium dichromate. Our aldehyde underwent aldol condensation upon standing at room temperature.

Preparation of (1*S*,2*S*,5*S*,10*R*)- and (1*S*,2*S*,5*S*,10*S*)-6,6-Dimethylbicyclo[3.1.1]heptane-2-phenylmethanol (10-Phenylmyrtanols). Freshly ground magnesium turnings (0.68 g, 0.0280 mol) and an iodine crystal were placed in a 50-mL round-bottomed flask equipped with a condenser and septum, stirrer, and nitrogen bubbler. Dry ethyl ether (30 mL) was injected. Bromobenzene (4.40 g, 0.0280 mol) was slowly injected. After refluxing ceased, myrtanal (1.42 g, 9.32 mmol) was added. After 2 h the mixture was added to a NH_4Cl–H_2O–ice mixture, extracted (hexanes), dried ($MgSO_4$), and evaporated to give the diastereomeric alcohols (2.03 g, 95%) **5** and **6** in a 3:1 ratio (NMR analysis). They were separated by using preparative HPLC (12-mm o.d. silica column) with 10% ethyl acetate/cyclohexane. The peaks eluted after approximately one column volume with base-line resolution.

The 10*R* (major) isomer **5** had mp 59–60 °C: ^{1}H NMR δ 7.21–7.34 (phenyl, 5 H), 4.42 (d, J = 8.1, H10), 2.26 (quartet, J = 0.9, H2), 2.0 (dt, H7-exo), 1.60–1.85 (multiplets), 1.51 (td, J = 5.4 and 0.9 H1), 1.38 (d, H7-endo), 1.08 (s, 3 H), 0.78 (s, 3 H); ^{13}C NMR 144.09, 128.73, 128.06, 127.54, 77.77, 43.43, 42.37, 40.95, 39.45, 27.21, 24.54, 23.71, 20.54, 18.80. ^{1}H NMR of (1*S*,2*S*,5*S*,10*S*)-phenylmyrtanol: decoupling experiments have been described (this paper). The 10*S* isomer **6**, mp 55–56 °C, was characterized by ^{1}H NMR, including simulation and J value determinations (this paper), δ 7.51 (m, phenyl), 4.33 (d, H10, sometimes showing further splitting by OH), 2.30 (overlapping t and quartet, H1 and H2), 2.10 (dt, H7-exo), 1.84 (quartet of d, H5), 1.60–1.74 (m, H4-exo and H4-endo), 1.37 (d, H7-endo), 1.24 (s, Me), 0.84 (s, Me), 1.12 (m, H3-endo), 0.99 (m, H3-exo). Anal. Calcd for $C_{16}H_{22}O$ (distilled mixed isomers): C, 83.43; H, 9.63. Found: C, 82.90, H, 9.51.

Preparation of (1*R*)-2-(Phenylmethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (1c) (10-Phenyl-α-pinene) from Myrtenyl Acetate. Earlier work in our group involved the preparation of 10-phenylpinene from myrtenyl acetate, phenylzinc chloride, and a Pd^0 catalyst.[21] We failed to reproduce our successful earlier preparation. Accordingly we turned to the use a cuprate procedure[22] for substitution of allylic acetates. Phenylmagnesium bromide was prepared as described in the preceding procedure from 0.102 mol of bromobenzene. The solution in 50 mL of ether was cooled to 0 °C. Cuprous iodide (9.80 g, 0.0515 mol), which had been Soxlet extracted with ethanol and dried was added. The mixture was stirred for 10 min. (1*R*)-(−)-Myrtenyl acetate (4.01 g, 0.0205 mol) was injected and the mixture was stirred for 3 h at 0 °C.

Quenching (NH_4Cl–water–ice), extraction (hexanes), and appropriate workup gave material that was distilled (1 mm, 126 °C) with the aid of heating tape on the distillation head to facilitate the removal of a forerun of biphenyl. A later fraction consisted of 10-phenylpinene and biphenyl (3.29 g) in a molar ratio of 10.6 to 1, based on NMR areas. The corrected yield of phenylpinene

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was 70%. ^{1}H NMR δ 7.25 (m, 6 H), 5.22 (m, 1 H), 3.27 (t, 2 H), 2.30 (m, 2 H), 2.21 (m, 1 H), 1.98 (t, 1 H), 1.27 (m, 1 H), 1.18 (s, 3 H), 1.14 (d, 1 H), 0.74 (s, 3 H). The reported δ values[8] are 7.2 (s, 5 H), 5.3 (bs, 1 H), 3.33 (s, 2 H), 1.2 (s, 3 H), 0.73 (s, 3 H). The amount of product from γ substitution was less than 3% in some reactions. The amount of γ substitution, as indicated by olefinic hydrogen multiplets at δ 4.82 and 4.53 in the NMR spectrum, appeared to be larger when the reaction temperature was below 0 °C or when less than a two to one ratio of cuprous iodide to myrtenyl acetate was used.

Preparation of (1*R*)-2-(Bromomethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (1d) (Myrtenyl Bromide). In a modification of the published procedure,[23] phosphorus tribromide (1.13 mL, 0.012 mol) was injected into dry ethyl ether in a flame-dried nitrogen-flushed 50-mL round-bottomed flask, and the mixture was cooled to 0 °C. A catalytic amount of pyridine was injected followed by myrtenol (5.00 g, 0.032 mol). Reaction for 45 min and isolation gave undistilled (1*R*)-myrtenyl bromide, showing a clean NMR spectrum (5.78 g, 82%). ^{1}H NMR δ 5.645 (s, 1 H), 3.92 (AB pattern, 2 H), 2.41 (m, 1 H), 2.23 (m, 3 H), 1.28 (s, 3 H), 1.15 (d, 1 H), 0.80 (s, 3 H). Reported[24] ^{1}H NMR (100 MHz): δ 5.61 (m, 1 H), 3.85 (m, 2 H), 2.44 (dt, 1 H), 2.30 (m, 2 H), 1.31 (s, 3 H), 1.18 (d, 1 H), 0.83 (s, 3 H).

Preparation of 10-Phenyl-α-pinene from Myrtenyl Bromide. This procedure was based one used previously to couple allylic compounds.[25] Undistilled (1*R*)-myrtenyl bromide (5.92 g, 0.0275 mol) in ether (50 mL) was allowed to react under nitrogen with phenyllithium in cyclohehexane–ethyl ether (28 mL, 0.056 mol, injected slowly). As in the above preparation, distillation (1 mm, 126 °C) gave of a mixture of phenylpinene and biphenyl (3.97 g total) having a molar ratio of 1 to 0.096. The corrected yield of phenylpinene was 62%. ^{1}H NMR δ 7.245 (m, phenyl), 5.22 (m, vinyl H), 3.27 (AB pattern, 2 H), 2.30 (m, 2 H), 2.21 (m, 1 H), 1.98 (t, 1 H), 1.27 (m, 1 H), 1.183 (s, 3 H), 1.143 (d, 1 H), 0.742 (s, 3 H). The reported ^{1}H NMR values[8] are 7.2 (s, 5 H), 5.3 (bs, 1 H), 3.33 (s, 2 H), 1.2 (s, 3), and 0.73 (s, 3 H).

Registry No. **1b**, 19894-97-4; **1b** (X = OAc), 36203-31-3; **1c**, 91200-45-2; **1d**, 55527-89-4; **2**, 53369-17-8; **3**, 24041-60-9; **4**, 128301-02-0; **5**, 128244-23-5; **6**, 128244-24-6.

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Covalent Nucleoside Adducts of Benzo[*a*]pyrene 7,8-Diol 9,10-Epoxides: Structural Reinvestigation and Characterization of a Novel Adenosine Adduct on the Ribose Moiety

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The diastereomeric 7,8-diol 9,10-epoxides metabolically derived from the carcinogenic hydrocarbon benzo[*a*]pyrene react with the purine bases in nucleic acids to alkylate their exocyclic amino groups. *The major adducts formed from polyguanylic acid and the enantiomers of diol epoxide-1 (the diastereomer in which the benzylic 7-hydroxyl group and the epoxide oxygen are cis) have been shown to result from cis opening of the epoxide by the N-2 amino group of guanine, rather than trans opening as had been previously reported.* Four adducts resulting from alkylation of the exocyclic N-6 amino group of adenosine 5′-monophosphate by racemic diol epoxide-1 have been prepared and characterized. In addition, a major adduct formed from adenosine 5′-monophosphate and (−)-(7*R*,8*S*)-diol (9*R*,10*S*)-epoxide-1, but not from its (+) enantiomer, has been identified as a product of alkylation of the 2′-hydroxyl group of the sugar. We also report a quantitative reevaluation of the extent and distribution of covalent adduct formation from calf thymus DNA and both diastereomeric benzo[*a*]pyrene diol epoxides, as well as the identification of the principal DNA adducts formed from the enantiomers of diol epoxide-1. Tentative identification of several new minor adducts formed upon reaction of diol epoxide-2 with *denatured* DNA is described. The present results provide additional support for our previously proposed correlation between the signs of the circular dichroism bands of these adducts and their absolute configurations at the N-substituted benzylic carbon atom.

Introduction

Bay-region diol epoxides that are metabolically formed by the combined action of cytochrome P-450 and epoxide hydrolase have been shown or implicated as ultimate carcinogens from a large number of tumorigenic polycyclic aromatic hydrocarbons.[1] For a given hydrocarbon, two diastereomeric diol epoxides can be formed from the trans dihydrodiol metabolite by epoxidation of the benzo ring double bond from either face of the dihydrodiol; namely, diol epoxide-1, in which the epoxide oxygen and the benzylic hydroxyl group are cis, and diol epoxide-2, in which these groups are trans. Since the trans dihydrodiol can exist in two enantiomeric forms, four optically active isomeric diol epoxides are metabolically possible. These diol epoxides are reactive electrophiles whose cytotoxic, mutagenic, and tumorigenic activities presumably result from their ability to alkylate nucleic acids and/or other biological macromolecules. Covalent addition of these diol epoxides to DNA is well documented.[2-9] The major iso-

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