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Full Paper

New, Homochiral Synthons Obtained through Simple Manipulations of Enzymatically Derived 3-Halo-*cis*-1,2-dihydrocatechols

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The bromoepoxide **5a**, which is obtained from the homochiral and enzymatically derived *cis*-1,2-dihydrocatechol **1a**, is readily and efficiently transformed into either isomer **8a** or the corresponding methoxymethyl-ether **2a**. Though both of these products can be fully characterized, they are somewhat unstable, with the former being converted into the crystalline enone **3a** on standing and the latter readily participating in a Diels–Alder cycloaddition reaction with the potent dienophile *N*-phenyl-1,2,4-triazoline-3,5-dione to give adduct **7a**. The single-crystal X-ray structures of compounds **3a** and **7a** are reported. Using the related chemistry the chloro-analogue, **3b**, of enone **3a** can be obtained.

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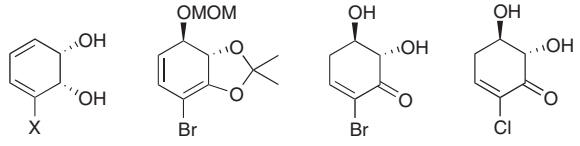
Introduction

A range of substituted arenes can be converted into the corresponding *cis*-1,2-dihydrocatechols using certain mutant forms of bacteria that express dioxygenase enzymes.[1] Hence, for example, using *Escherichia coli* JM109 (pDTG601), bromobenzene and chlorobenzene are both bio-transformed, under whole-cell conditions, into the metabolites **1a** and **1b**, respectively.[1,2] These types of conversions proceed in essentially quantitative yield, deliver the *cis*-1,2-dihydrocatechols in >99.8 % ee, and can be carried out on the kilogram if not the tonne scale. Furthermore, compounds such as **1a** and **1b** have proven to be extraordinarily versatile starting materials in chemical synthesis as evidenced by their conversion into a wide range of natural products including carbohydrates, terpenoids, and alkaloids.[1] A series of reviews that detail much of this type of work is available.[1] Based on this background, we herein report simple methods by which the *cis*-1,2-dihydrocatechol **1a** can be converted into the related diene **2a** or the enone **3a**, compounds that are likely to serve as useful new chirons in a range of settings. The synthesis of the chlorinated analogue, **3b**, of the latter product is also described (Fig. 1).



1 (**a**: X = Br, **b**: X = Cl) **2a** **3a** **3b**

Fig. 1. Structures of the starting diols **1a** and **1b** and the derived synthons **2a**, **3a** and **3b**.

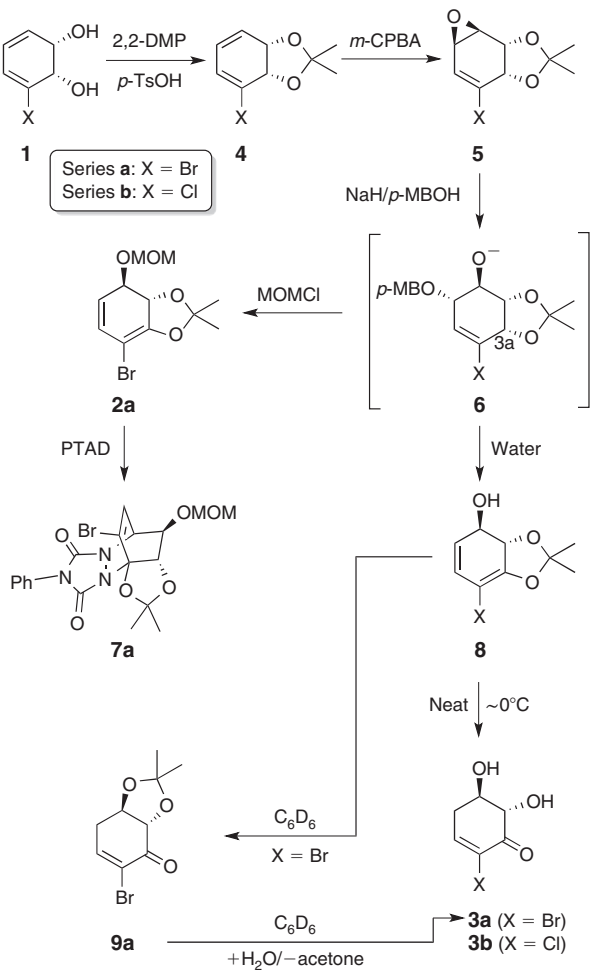
Results and Discussion

During the course of another project, we had occasion to convert the *cis*-1,2-dihydrocatechol **1a**, via the corresponding acetonide **4a**[3] (Scheme 1), into the previously reported and well-known epoxide **5a**.[3] A 'streamlined' procedure for doing so is described in the Experimental section and this allowed us to acquire compound **5a** in 93 % yield on a multi-gram scale. This epoxide was treated with the anion derived from *p*-methoxybenzyl alcohol (*p*-MBOH) under the expectation[4] that the nucleophilic ring-opening product **6a** would form and then, from it, the corresponding ether upon quenching with methoxymethyl chloride (MOMCl). However, when seemingly relevant conditions were employed for this purpose, the novel diene **2a** was obtained in 74 % yield. All of the spectral data acquired on this compound were fully consistent with the assigned structure and this result was confirmed upon single-crystal X-ray analysis of the Diels–Alder adduct **7a** (quantitative.) arising from reaction with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD).[5] The derived *ORTEP* is shown in Fig. 2.

When the reaction mixture, presumed to contain anion **6a**, was quenched with water rather than MOMCl and then worked up in the usual manner, a light yellow oil was obtained and on standing, slowly crystallized to give the enone **3a** (Scheme 1). This was obtained in 60 % yield as a white, crystalline solid, and its structure was confirmed by single-crystal X-ray analysis. When the above-mentioned oil was dissolved in C_6D_6, and the resulting solution allowed to stand at ambient temperatures for extended periods, diene **8a** rearranged to isomer **9a**, the associated *trans*-acetonide moiety of which was slowly cleaved to give enone **3a**. Although rather unstable, compound **9a** could be spectroscopically characterized after partial purification by flash chromatography. Interestingly, while diene **4a** engages in a

Diels–Alder dimerization reaction,[6] no equivalent process was observed in the case of congener **8a**.

The chloro-analogue, **3b**, of compound **3a** could be obtained by analogous means. Thus, the known acetonide derivative, **4b**,[7] of diol **1b** was treated with *m*-chloroperoxybenzoic acid (*m*-CPBA), thereby generating the epoxide **5b**[8] (87 % from **1b**). Epoxide **5b** was, in turn, treated successively with the anion derived from *p*-MBOH and then water. As a result, the chloroenone **3b** was obtained in 63 % yield. No efforts were made to isolate diene **8b** that is presumed to be the late-stage precursor to product **3b**.



Scheme 1.

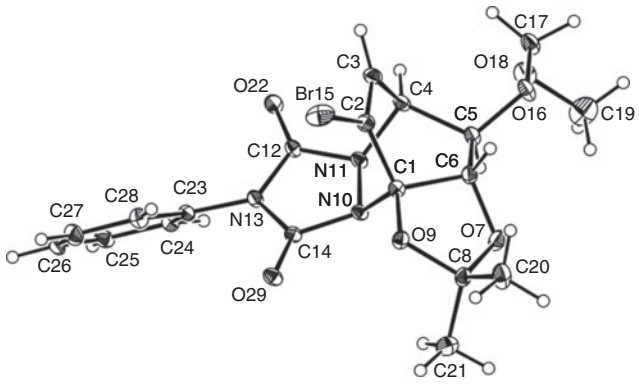
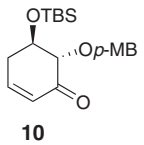


Fig. 2. *ORTEP* derived from the single-crystal X-ray analysis of compound **7a** (CCDC No. 1045883). Anisotropic displacement ellipsoids display 30 % probability levels. Hydrogen atoms are drawn as circles with small radii.

The detailed mechanism by which epoxides **5a** and **5b** are respectively converted into dienes **8a** and **8b** remains to be investigated. Nevertheless, some important observations can be made in this regard. Thus, when the first steps of the reaction sequence were attempted in the absence of *p*-MBOH (i.e. substrate **5a**, for example, was treated with NaH alone and the reaction mixture quenched with MOMCl), then only the starting materials were recovered. This outcome could suggest that the oxyanion **6** is an intermediate in the original process, but precisely how this would then lose the elements of the added alcohol (and in a seemingly regioselective manner) is unclear. A so-called E′ process appears unlikely since a *syn*-relationship is normally required between the departing groups (in this case the C3a hydrogen and the *p*-MBO anion; Scheme 1).[9,10] Another possibility is that *p*-MBO anion simply acts as a base (rather than a nucleophile) and thereby affects, after quenching of the resulting anion, the direct conversion of epoxide **5** into isomer **8**. This would involve a stereochemically favoured E′ process. Prompted by such considerations and the studies of Hill and Bock and Rickborn et al.,[10] a sample of the starting material **5a** was treated with lithium di-isopropylamide in THF at 0°C for 1 h and then quenched with MOMBr (MOMCl was not available when this experiment was conducted). As a result, compound **8a** could be obtained after rapid chromatographic purification in ~50 % yield. This was accompanied by traces of MOM-ether **2a**. Curiously, when the reaction was quenched with aqueous sodium bicarbonate (rather than MOMBr), then the starting epoxide **5a** was recovered. All of the spectroscopic data derived from diene **8a** were in complete accord with the assigned structure. It is appropriate to note that Hudlicky and Trant have observed[11] a closely related, but less efficient rearrangement.

Conclusion

We are currently exploring the synthetic utility of the new and readily accessible homochiral synthons **2a**, **3a**, **3b**, and **8a**. As an indication of their potential, we note that the related and enantiomerically pure cyclohexenone **10** (Fig. 3), which has been prepared by Chida et al. in about 12 steps from D-glucose,[12] has served as a key intermediate in that group's recently reported total synthesis of (−)-morphine.[13]



10

Fig. 3. Structure of synthon **10** prepared from D-glucose. TBS = tert-butyldimethylsilyl

Experimental

General Experimental Procedures

Unless otherwise specified, proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded at 18°C in base-filtered $CDCl_3$ on a Varian spectrometer operating at 400 MHz for proton and

100 MHz for carbon nuclei. For ^{1}H NMR spectra, signals arising from the residual protio forms of the solvent were used as the internal standards. ^{1}H NMR data are recorded as follows: chemical shift (δ) (multiplicity, coupling constant(s) *J* (Hz), relative integral). Multiplicity is defined as: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet or combinations of the above. The signal due to residual $CHCl_3$ appearing at δ_H 7.26 ppm and the central resonance of the $CDCl_3$ 'triplet' appearing at δ_C 77.0 ppm were used to reference ^{1}H and ^{13}C NMR spectra, respectively. Infrared spectra (ν_{max}) were recorded on a Perkin–Elmer 1800 Series Fourier transform infrared spectrometer. Samples were analyzed as thin films on KBr plates. Low-resolution electrospray ionization (ESI) mass spectra were recorded on a Micromass LC-ZMD single quadrupole liquid chromatograph–mass spectrometer, whereas high-resolution measurements were conducted on an LCT Premier time-of-flight instrument. Low- and high-resolution electron impact (EI) mass spectra were recorded on an Autospec Premier Micromass magnetic sector machine. Optical rotations were recorded in $CHCl_3$ at 20°C on a Perkin–Elmer 343 polarimeter. Melting points were measured on an Optimelt automated melting point system and are uncorrected. Analytical thin layer chromatography (TLC) was performed on aluminium-backed 0.2 mm thick silica gel 60 F_{254} plates as supplied by Merck. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid/ceric sulfate/concentrated sulfuric acid/water (37.5 g : 7.5 g : 37.5 g : 720 mL) or potassium permanganate/potassium carbonate/5 % sodium hydroxide aqueous solution/water (3 g : 20 g : 5 mL : 300 mL). Flash chromatographic separations were carried out following protocols defined by Still et al.[13] with silica gel 60 (40–63 μm) as the stationary phase and using the analytical reagent (AR)- or HPLC-grade solvents indicated. Starting materials and reagents were generally available from the Sigma-Aldrich, Merck, Tokyo Chemical Industry Co., Ltd (TCI), Strem Chemicals Inc., or Lancaster, and were used as supplied. Drying agents and other inorganic salts were purchased from the AJAX, BDH, or Unilab chemical companies. Diethyl ether (Et_2O), *N*,*N*-dimethylformamide (DMF), dichloromethane (CH_2Cl_2), and ethyl acetate (EtOAc) were dried using a Glass Contour solvent purification system that is based on a technology originally described by Grubbs et al.[14] Where necessary, reactions were performed under an inert atmosphere.

Specific Synthetic Transformations

Compound 5a: A magnetically stirred suspension of compound **1a** (15.0 g, 78.5 mmol) in Et_2O/2,2-dimethoxypropane (2,2-DMP) (200 mL of a 1 : 1 v/v mixture) maintained at room temperature was treated with *p*-toluenesulfonic acid (*p*-TsOH) monohydrate (500 mg, 2.6 mmol, 0.03 molar equiv.). After 1 h, the reaction mixture was quenched with $NaHCO_3$ (200 mL of a saturated aqueous solution), and the separated aqueous phase extracted with Et_2O (3 × 200 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated under reduced pressure, and the ensuing brown oil dissolved in CH_2Cl_2 (200 mL). The solution thus obtained, and presumed to contain acetonide **4a**,[3] was cooled to ~0°C then treated, in one portion, with *m*-CPBA (22.9 g, 102.1 mmol, 1.3 molar equiv.). The reaction mixture was then shaken vigorously for ~10 s before being left to stand at 0°C for 48 h with occasional shaking during this period. The suspension thus obtained was filtered through a pad of Celite™ while still cold, and the filter pad was washed with cold CH_2Cl_2 (2 × 50 mL). The combined filtrates were washed with Na_2SO_3 (150 mL of a saturated aqueous solution) before being dried (Na_2SO_4), filtered, and concentrated under reduced pressure to yield epoxide **5a**[3] (18.1 g, 93 % over two steps) as a waxy, white solid. This material, which was spectroscopically identical to an authentic sample, was of sufficient purity to be used directly in the reaction sequences described below.

Compound 2a: A magnetically stirred suspension of NaH (60 % dispersion in mineral oil, 2.41 g, 60.3 mmol, 1.5 molar equiv.) in DMF (300 mL) was cooled to 0°C while being maintained under an atmosphere of nitrogen, then treated over 0.08 h with a solution of *p*-MBOH (8.33 g, 60.3 mmol, 1.5 molar equiv.) in DMF (50 mL). After 1 h, the temperature of the reaction mixture was lowered to −10°C (ice–salt bath), and a solution of epoxide **5a** (9.93 g, 40.2 mmol) in DMF (50 mL) was added to it over 0.08 h. The ensuing mixture was maintained at −10°C for 1 h, and resulting the dark green solution was treated, in one portion, with a chilled (~0°C) solution of MOMCl (13.7 mL) in DMF (25 mL). After a further 0.25 h, the reaction mixture was quenched by slow addition of $NaHCO_3$ (100 mL of a half-saturated aqueous solution), then diluted with Et_2O (300 mL). The separated aqueous phase was washed with Et_2O (2 × 300 mL), and the combined organic phases were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1 : 5 v/v EtOAc/petroleum spirit elution), and concentration of the relevant fractions (R_F 0.3 in 1 : 3 v/v EtOAc/petroleum spirit) afforded *diene* ***2a*** (8.66 g, 74 %) as a clear, colourless oil. $[\alpha]_D$ −8.0° (*c* 0.5 in $CHCl_3$). ν_{max} (KBr)/cm^{-1} 2991, 2940, 2848, 1687, 1558, 1386, 1298, 1217, 1149, 1133, 1047, 1006, 855, 831, 791, 719. δ_H (C_6D_6, 400 MHz) 5.76 (ddd, *J* 10.0, 2.9, 0.5, 1H), 5.31 (dm, *J* 10.0, 1H), 4.95 (dm, *J* 12.0, 1H), 4.77 (dm, *J* 12.0, 1H), 4.71 (d, *J* 6.6, 1H), 4.51 (d, *J* 6.6, 1H), 3.14 (s, 3H), 1.28 (s, 3H), 0.99 (s, 3H). δ_C (C_6D_6, 101 MHz) 151.2, 129.0, 123.9, 115.8, 95.6, 82.6, 79.8, 77.7, 55.2, 26.5, 24.1. *m/z* (EI, 70 eV) 292 and 290 (28 % and 33 %, $M^{+\bullet}$), 230 and 228 (44 and 42), 210 (81), 190 and 188 (98 and 100). *m/z* (EI) 290.0150; $M^{+\bullet}$ requires 290.0154.

Compound 7a: A magnetically stirred solution of diene **2a** (100 mg, 0.34 mmol) in benzene (5 mL) maintained at ~18°C was treated, in small portions, with PTAD until a red colour persisted. The reaction mixture was concentrated under reduced pressure and the residue so obtained was subjected to flash chromatography (silica, 1 : 3 v/v EtOAc/petroleum spirit elution). Concentration of the relevant fractions (R_F 0.25) afforded a white foam that crystallized from CH_2Cl_2/hexane to give the *PTAD-adduct* ***7a*** (158 mg, quantitative) as a white, crystalline solid, mp 119°C (dec.). $[\alpha]_D$ +97.2° (*c* 0.5 in $CHCl_3$). ν_{max} (KBr)/cm^{-1} 2937, 1784, 1727, 1575, 1501, 1398, 1225, 1164, 1040, 845, 763, 690. δ_H (C_6D_6, 400 MHz) 7.48 (m, 2H), 7.01 (m, 2H), 6.93 (m, 1H), 5.93 (d, *J* 5.6, 1H), 4.97 (dd, *J* 5.6, 2.5, 1H), 4.26 (d, *J* 4.0, 1H), 4.22 (m, 1H), 4.20 (d, *J* 4.0, 1H), 3.92 (m, 1H), 2.95 (s, 3H), 1.77 (s, 3H), 1.25 (s, 3H). δ_C (C_6D_6, 101 MHz) 156.4, 156.1, 132.0, 129.1, 127.0, 125.8, 118.6, 117.7, 95.9, 95.3, 87.8, 72.4, 56.4, 55.4, 27.6, 25.6 (one signal obscured or overlapping). *m/z* (EI, 70 eV) 469 and 467 (both 16 %, $M^{+\bullet}$), 328 (22), 221 (23), 119 (100). *m/z* (EI) 467.0511; $M^{+\bullet}$ requires 467.0515.

Compound 3a: A magnetically stirred suspension of NaH (60 % dispersion in mineral oil, 12 mg, 0.30 mmol, 1.5 molar equiv.) in DMF (3 mL) maintained under a nitrogen atmosphere was cooled to 0°C, then treated dropwise with a solution of

p-MBOH (42 mg, 0.30 mmol, 1.5 molar equiv.) in DMF (1 mL). After stirring at 0°C for 1 h, the reaction mixture was cooled to −10°C (ice–salt bath), and a solution of epoxide **5a** (50 mg, 0.20 mmol) in DMF (1 mL) was then added dropwise. After a further 1 h (at −10°C), the resulting dark green reaction mixture was treated, in one portion, with a chilled solution of H_2O (1 mL) in DMF (1 mL). After stirring for a further 0.25 h, the reaction mixture was quenched by slow addition of $NaHCO_3$ (10 mL of a half-saturated aqueous solution). The ensuing mixture was diluted with Et_2O (20 mL), and the separated aqueous phase extracted with Et_2O (2 × 20 mL). The combined organic phases were then dried (Na_2SO_4) before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1 : 3 → 1 : 1 v/v EtOAc/petroleum spirit gradient elution), and concentration of the relevant fractions (R_F 0.25 in 1 : 1 v/v EtOAc/petroleum spirit) afforded a clear, light yellow and rather unstable oil presumed to contain *compound **8a***. On standing in the fridge, crystals began to form from this oil and after 48 h, the material was triturated with hexane (2 × 5 mL), and the solids retained after removal of the solvent were dried under reduced pressure to afford *bromoenone **3a*** (25 mg, 60 %) as a white, crystalline solid, mp 79.5°C (dec.). $[\alpha]_D$ −29.2° (*c* 0.5 in CH_3CN). ν_{max} (KBr)/cm^{-1} 3372, 1698, 1601, 1383, 1297, 1110, 1072, 991, 848, 767, 614. δ_H ($CDCl_3$, 400 MHz) 7.37 (dd, *J* 6.8, 2.5, 1H), 4.18 (d, *J* 10.9, 1H), 3.99 (m, 1H), 3.73 (br s, 1H), 2.96 (br s, 1H), 2.87 (dt, *J* 18.7, 4.0, 1H), 2.56 (dddd, *J* 18.7, 10.0, 2.6, 0.6, 1H). δ_C ($CDCl_3$, 101 MHz) 192.0, 148.4, 120.6, 79.1, 71.4, 34.3. *m/z* (EI, 70 eV) 208 and 206 (both 8 %, $M^{+\bullet}$), 190 and 188 (both 18), 161 and 159 (both 22), 148 and 146 (47 and 49), 109 (100), 81 (96), 60 (86). *m/z* (EI) 205.9582; $M^{+\bullet}$ requires 205.9579.

Compound 8a: A magnetically stirred solution of diisopropylamine (252 µL, 1.82 mmol) in dry THF (5 mL) maintained at 0°C was treated with *n*-BuLi (1.14 mL of a 1.6 M solution in hexane, 1.82 mmol). The resulting solution was stirred at 0°C for 0.5 h then cooled at −10°C and treated, dropwise, with a solution of epoxide **5a** (300 mg, 1.20 mmol) in THF (5 mL). After 1 h, the yellow reaction mixture was treated, in one portion, with a chilled solution of MOMBr (390 µL, 4.80 mmol) in THF (5 mL). After a further 0.25 h, the reaction mixture was quenched by slow addition of $NaHCO_3$ (20 mL of a half-saturated aqueous solution). The resulting mixture was diluted with Et_2O (40 mL) and the separated aqueous phase extracted with Et_2O (1 × 40 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure, and the ensuing yellow oil was subjected to chromatography (silica, 1 : 4 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_F 0.6), *compound **8a*** (150 mg, 50 %) as a clear, colourless oil. $[\alpha]_D$ −45.0° (*c* 1.0 in $CHCl_3$). ν_{max} (KBr)/cm^{-1} 3400, 2990, 2848, 1686, 1586, 1454, 1385, 1299, 1217, 1133, 1067, 979, 951, 854, 828, 792, 719, 691. δ_H (C_6D_6, 400 MHz) 5.70 (dd, *J* 10.0, 2.9, 1H), 5.17 (dm, *J* 10.0, 1H), 4.72 (d, *J* 12.9, 1H), 4.51 (br d, *J* 12.9, 1H), 1.81 (br s, 1H), 1.31 (s, 3H), 1.01 (s, 3H). δ_C ($CDCl_3$, 101 MHz) 151.4, 128.6, 125.7, 115.9, 83.7, 79.9, 73.8, 26.5, 24.2. *m/z* (EI, 70 eV) 248 and 246 (both 30 %, $M^{+\bullet}$), 190 and 188 (both 33), 109 (34), 81 (100). *m/z* (EI) 245.9894; $M^{+\bullet}$ requires 245.9892.

Compound 9a: A solution of diene **8a** (10 mg, 0.04 mmol) in C_6D_6 (750 µL) was allowed to stand in an NMR tube for 48 h then concentrated under reduced pressure. The resulting white solid was subjected to flash chromatography (silica, 1 : 1 v/v EtOAc/petroleum spirit → EtOAc gradient elution), thus affording two fractions, A and B.

Concentration of fraction A (R_F 0.6 in 1 : 1 v/v EtOAc/petroleum spirit) afforded *compound **9a*** (3.3 mg, 33 %) as a clear, colourless oil. $[\alpha]_D$ −168.5° (*c* 0.17 in $CHCl_3$). ν_{max} (KBr)/cm^{-1} 3048, 2984, 1711, 1578, 1382, 1371, 1226, 1138, 1090, 1047, 864, 835, 791, 640. δ_H (C_6D_6, 400 MHz) 6.15 (dd, *J* 6.3, 2.4, 1H), 3.39 (d, *J* 10.8, 1H), 3.27 (app. td, *J* 10.8, 4.7, 1H), 1.86 (ddd, *J* 17.3, 6.3, 4.7, 1H), 1.57 (ddd, *J* 17.3, 9.9, 2.4, 1H), 1.24 (s, 6H). δ_C (C_6D_6, 101 MHz) 185.4, 144.1, 124.0, 112.2, 82.1, 74.7, 33.1, 27.0, 26.5. *m/z* (ESI^+) 271 and 269 (98 % and 100 %, $(M + Na)^+$). *m/z* (ESI) 268.9788; calcd for $C_9H_{11}{}^{79}BrNaO_3$ 268.9784.

Concentration of fraction B (R_F 0.1 in 1 : 1 v/v EtOAc/petroleum spirit) afforded compound **3a** (4.5 mg, 54 %) as a white, crystalline solid that was identical, in all respects, to the material obtained as described above.

Compound 5b: The commercially available *cis*-1,2-dihydrocatechol **1b** was converted into the previously reported[8] epoxide **5b** using essentially the same procedure as described above for the conversion of **1a** into **5a**. By such means the title compound was obtained in 87 % yield as a white, crystalline solid, mp 59–60°C. This material was identical, in all respects, to an authentic sample.

Compound 3b: The transformation of epoxide **5b** into chloroenone **3b** was conducted on a 50-mg scale under exactly the same conditions as those used for the conversion of **5a** into **3a**. *Compound **3b*** (25 mg, 63 %) was thereby obtained as a white, crystalline solid, mp 84.6°C (dec.). $[\alpha]_D$ −42.2° (*c* 0.4 in $CHCl_3$). ν_{max} (KBr)/cm^{-1} 3389, 1700, 1610, 1424, 1329, 1117, 1074, 999, 922, 856, 785, 626. δ_H ($CDCl_3$, 400 MHz) 7.12 (m, 1H), 4.17 (d, *J* 10.8, 1H), 4.02–3.95 (complex m, 1H), 3.68 (br s, 1H), 2.90 (ddd, *J* 18.7, 6.8, 5.5, 1H), 2.90 (br s, 1H), 2.60 (ddd, *J* 18.7, 10.0, 2.5, 1H). δ_C ($CDCl_3$, 101 MHz) 191.8, 144.1, 130.1, 79.2, 71.5, 32.6. *m/z* (EI, 70 eV) 164 and 162 (8 % and 25 %, $M^{+\bullet}$), 144 (29), 133 (45), 116 (75), 115 (68), 81 (63), 60 (100). *m/z* (EI) 164.0055; $M^{+\bullet}$ requires 164.0054.

X-Ray Crystallographic Studies

Crystallographic Data

Compound 3a: $C_6H_7BrO_3$, *M* 207.02, monoclinic, space group *C*2, *a* 30.3600(15), *b* 5.0235(1), *c* 22.5219(11) Å, *β* 124.000(8)°, *V* 2847.7(3) Å^3, *Z* 16, D_c 1.931 g cm^{-3}, *T* 150 K, $2\theta_{max}$ 144°, 4536 unique data, *R* 0.019 (for 4469 reflections with $I > 2.0\sigma(I)$), *wR* 0.049 (all data), *S* 1.00.

Compound 7a: $C_{19}H_{20}BrN_3O_6$, *M* 466.29, orthorhombic, space group $P2_12_12_1$, *a* 8.8590(1), *b* 10.8990(1), *c* 20.9314(1) Å, *V* 2021.02(3) Å^3, *Z* 4, D_c 1.532 g cm^{-3}, *T* 150 K, $2\theta_{max}$ 144°, 3965 unique data, *R* 0.022 (for 3911 reflections with $I > 2.0\sigma(I)$), *wR* 0.057 (all data), *S* 1.00.

Structure Determinations

Images were measured on an Agilent SuperNova CCD diffractometer (CuKα, mirror monochromator, *λ* 1.54184 Å) and data were extracted using the *CrysAlis* package.[15] Structure solution was by direct methods (SIR92).[16] The structures of compounds **3a** and **7a** were refined using the *CRYSTALS* program package.[17] Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC nos 1045882 and 1045883 for compounds **3a** and **7a**, respectively). These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif (or from the Cambridge Crystallographic Data

Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; email: data_request@ccdc.cam.ac.uk).

Supplementary Material

The anisotropic displacement ellipsoid plot derived from the single-crystal X-ray structure of compound **3a** together with the ^{1}H and ^{13}C NMR spectra of compounds **2a**, **3a**, **3b**, **7a**, **8a**, and **9a** are available on the Journal's website.

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