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Synthesis of functionalized tricyclo[5.3.1.$0^{2,6}$]undecadienones

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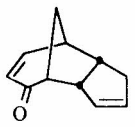
Synthesis of 8-bromo-1-hydroxytricyclo[5.3.1.$0^{2,6}$]undecadienones **7** and **8** from *endo* annulated bicyclo[2.2.2]octenones **5** and **6**via acid-catalyzed rearrangement has been described.

Tricyclo[5.3.1.$0^{2,6}$]undecadienones of type **1** have been used as models for light energy storage and provided an easy access to *cis, syn, cis*-triquinanes[1]. The tricyclo[5.3.1.$0^{2,6}$]undecane framework of type **2** also forms the carbocyclic core of many natural products mainly those of gymnomitrol type[2]. However, only a few methods have been reported for the synthesis of tricyclo[5.3.1.$0^{2,6}$]undecadienones[3,4]. The methods reported are tedious and involve multistep synthesis. Ogino and Awano have prepared substituted tricyclo[5.3.1.$0^{2,6}$]undecadienones starting from *endo*-dicyclopentadiene[3]. Other method for the preparation of 3-substituted tricyclo[5.3.1.$0^{2,6}$]undecadienones involves flash vacuum pyrolysis of 1,2,4-trishomocubanes which also gives *cis, syn, cis*-triquinane along with tricyclo[5.3.1.$0^{2,6}$]undecadienones[4].

In connection with the synthesis of functionalized *cis, syn, cis*-triquinanes, we have recently synthesized the functionalized tricyclo[5.3.1.$0^{2,6}$]undecadienones from the readily available annulated bicyclo[2.2.2]octenones involving an acid-catalyzed rearrangement[5]. In continuation of our efforts in this area we explored the possibility of acid-catalyzed rearrangement in the substrates **5** and **6** which contain acid sensitive vinyl bromide moiety, and wish to report the synthesis of more functionalized 8-bromo-11-methyl-1-hydroxy-and 8-bromo-11, 11-dimethyl-1-hydroxy-tricyclo [5.3.1.$0^{2,6}$] undecadienones **7** and **8**.

The required annulated bicyclo[2.2.2]octenones **5** and **6** were prepared starting from 5-bromovanilyl alcohol **3**[6]. Thus, **3** was oxidized with sodium metaperiodate and the spiroepoxy cyclohexa-2,4-dienone[7], generated *in situ*, was trapped with freshly cracked cyclopentadiene to give the ketoepoxide **4** (Scheme I). The ketoepoxide **4** was reduced with zinc in dry dioxane to the methyl ketone **5** which was further alkylated with methyl iodide in the presence of sodium hydride to give the dimethyl ketone **6**.



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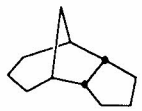

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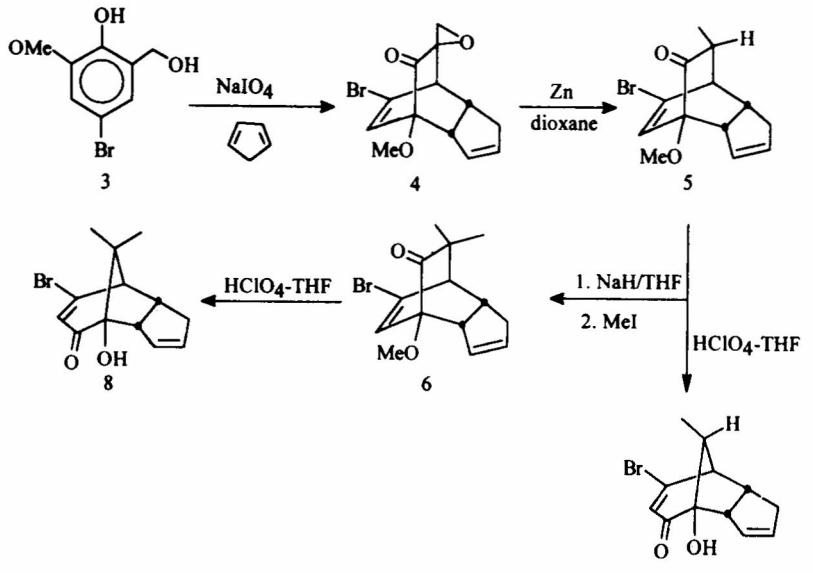
Towards the rearrangement we first treated the bromoketone **6** with perchloric acid (70%) in tetrahydrofuran at room temperature for 12 hr. It was indeed surprising to observe the formation of single product in excellent yield (85%) to which we assigned the structure **8** (SchemeI) on the basis of spectral data as described below. The IR spectrum showed absorption bands at 1684 and 3473 cm^{-1} corresponding to α,β-unsaturated carbonyl and hydroxyl groups, respectively. Its high field ^1H NMR (300 MHz) spectrum displayed a signal at δ 6.48 (1H, d, J=~1 Hz) corresponding to the α-proton of α,β-enone moiety. The signals of other olefinic protons were observed at δ 5.64 and 5.51 as multiplets. A signal was observed at δ3.95 for OH proton. Resonances also appeared at δ1.22(3H, s, CH_3) and 0.94 (3H, s, CH_3) due to *anti* and *syn* methyl groups. Other resonances for methine and methylene protons appeared at δ 3.56 (1H, m of d, J= 9 Hz), 3.44 (1H, m), 3.08 (1H, d, J= 6 Hz) and 2.46 (2H, m). The ^{13}C NMR spectrum of **8** showed a signal at δ 200.1 for a conjugated carbonyl carbon besides the signals at 152.7, 133.6, 130.5 and 128.8 for four olefinic carbon atoms[8]. It displayed resonances at δ 89.3 and 62.6 for quaternary carbons –C–O– and C–C–. It also gave signals at δ 58.5, 54.9, 39.8, 33.4, 22.1 and 18.9 corresponding to methine, methylene and methyl carbons.

Similarly, **5** was treated with perchloric acid (70%) to give the rearranged ketone **7** whose structure is consistent with spectral data.



Scheme I

In summary, we have shown that the acid-catalyzed rearrangement is general and can be extended to a variety of functional groups.

Experimental Section

General. Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 681 infrared spectrophotometer. NMR spectra were recorded on a Varian VXR 300S spectrometer using $CDCl_3$ as solvent containing TMS as internal standard (chemical shifts in δ, ppm downfield from TMS).

Preparation of 11-bromo-1-methoxytricyclo-[5.2.2.0^{2,6}]undeca-3, 10-dien-8-spirooxiran-9-one 4. To a solution of **3** (2 g, 8.58 mmoles) in acetonitrile (50 mL), freshly cracked cyclopentadiene (8 mL, excess) was added at ~10°C. A solution of $NaIO_4$ (6 g in 60 mL of water) was added to it dropwise while stirring. Stirring was continued for 6-8 hr after which the organic layer was separated. The aqueous layer was saturated with NaCl and extracted with ether (4×30 mL). The combined organic extract was washed with brine and dried over anhydrous sodium sulphate. The solvent was removed and the residue chromatographed over silica gel to give the adduct **4** (0.69g, 27.3%), m.p. 110°; IR: 1740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.32 (1H, dd of d long range couplings, J_1 = 2Hz, J_2 = 1 Hz, β-H of β,γ-enone), 5.86 (1H, dd of d J_1 = 6 Hz, J_2 = 4.5 Hz, J_3 = 2Hz, olefinic H), 5.61 (1H, dd of d, J_1 = 6 Hz, J_2 = 4.5 Hz, J_3 = 2 Hz, olefinic H), 3.58 (3H, s, OCH_3), 3.40 (1H, m of d, J = 7.5 Hz, methine H), 3.18 (1H, part of AB system, J = 6 Hz, OCH_2), 3.16 (1H, methine H), 3.04 (part of AB system, J = 6 Hz. OCH_2), 2.74 (1H, m merged with another m, methine H), 2.72 (1H, m of dd, J_1 = 18 Hz, J_2 = 9 Hz, methylene H), 2.34 (1H, m of d,, J = 18 Hz, methylene H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.7, 135.0, 129.2, 127.4, 118.3, 89.5, 57.2, 54.1, 52.3, 37.8, 37.7.

Preparation of 11-bromo-1-methoxy-8-methyltricyclo[5.2.2.0^{2,6}]undeca-3, 10-diene-9-one 5. To a suspension of zinc (12 g) in dry dioxane (50 mL) was added NH_4Cl (3 g) followed by **4** (3 g, 0.01 mmole) and the mixture heated under reflux for 2 hr. Zinc was filtered on a Celite bed and the filtrate concentrated under reduced pressure. Water (10 mL) was added to the residue and the whole mixture extracted with ether (4×10 mL). The combined organic extract was washed with brine and dried over anhydrous sodium sulphate.The solvent was removed *in vacuo* and the residue chromatographed over silica gel to give **5** (1.88 g, 66%); IR: 1740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ6.26 (1H, dd, J_1 = 3.5 Hz, J_2 = 1 Hz, β-H of β,γ-enone), 5.82 (1H, d of dd, J_1 = 6 Hz, J_2 = 5 Hz, J_3 = 3 Hz, olefinic H), 5.58 (1H, d of dd, J_1 = 6 Hz, J_2 = 5 Hz, J_3 = 3 Hz, olefinic H), 3.53 (3H, s, OCH_3), 3.10-2.92 (3H, cluster of m, methine H), 2.65 (1H, dd of d, J_1 = 16 Hz, J_2 = 9 Hz, J_3 = 5 Hz, methylene H), 2.37, 2.26 (2H, two merged m, methine H), 1.17 (3H, d, J = 7 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ210.5, 134.4, 128.0, 127.7, 121.8, 89.3, 54.0, 53.0, 52.8, 42.4, 37.9, 35.7, 13.8.

Preparation of 11-bromo-8, 8-dimethyl-1-methoxytricyclo[5.2.2.0^{2,6}]undeca-3,10-dien-3, 10-dien-9-one 6. To a suspension of NaH (1.0 g, excess) in

freshly dried THF (35 mL) was added a solution of **5** (2.0 g, 7 mmoles) in THF (5 mL) and the mixture heated to reflux for 1 hr. After cooling the mixture to room temperature (~30°C), methyl iodide (6 mL) was added dropwise and the reaction mixture stirred for another 8 hr. The solvent was removed under reduced pressure and water (20 mL) added dropwise to the residue.The aqueous layer was extracted with ether (4×20 mL). The organic extract was washed with brine and dried over sodium sulphate. The solvent was removed *in vacuo* and the residue chromatographed over silica gel to give **6** (1.87 g, 89.25%), m.p. 68°; IR: 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.22 (1H, $J_1=3$ Hz, $J_2=\sim 1$ Hz, β-H of β,γ-enone), 5.82 (1H, dd of d, $J=6$ Hz, olefinic H), 5.58 (1H, m of d, $J=6$ Hz, olefinic H), 3.53 (3H, s, OCH_3), 3.13-3.08 (2H, cluster of m, methine H), 2.82 (1H, dd, $J_1=J_2=3$ Hz, methine H), 2.62 (1H, d of dd, $J_1=17$ Hz, $J_2=9$ Hz, $J_3=5$Hz, methylene H), 2.32 (1H, m of d, $J=17$ Hz, methylene H), 1.21 (3H, s, CH_3), 1.14 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.4, 134.5, 128.1, 126.7, 122.0, 89.1, 58.1, 54.0, 51.5, 44.6, 37.9, 36.9, 27.0, 23.7; MS: m/z 298 ($M^+ + 1$).

Preparation of 8-bromo-1-hydroxy-11-methyltricyclo[5.3.1.$0^{2,6}$]undeca-3,8-dien-10-one 7. A solution of **5** (0.2 g, 0.7 mmole) in THF (5 mL) was treated with $HClO_4$ (70%, 1.5 mL) and the mixture stirred at room temperature (~30°C) for 15 min. THF was removed under reduced pressure. To the residue was added a saturated solution of $NaHCO_3$ until the effervesence had ceased. The aqueous layer was extracted with ether (3×20 mL), washed with brine and dried over sodium sulphate. Removal of the solvent followed by chromatography over silica gel gave the rearranged ketone **7** (0.16 g, 85.54%); IR: 3466, 1677 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.38 (1H, d, $J=\sim 1.5$ Hz, α-H of α,β-enone), 5.63 (1H, dd of d, $J_1=6$ Hz, $J_2=4.3$ Hz, $J_3=3$ Hz, olefinic H), 5.54 (1H, dd of d, $J_1=6$ Hz, $J_2=4.5$ Hz, $J_3=3$ Hz, olefinic H), 3.95 (1H, br s, OH), 3.52 (1H, m of d, $J=9$ Hz, methine H), 3.44 (1H, m), 3.19 (d, $J=9$ Hz, methine H), 2.48 (2H, m, methine and methylene H), 2.38 (1H, q, $J=7$ Hz, methine H), 1.18 (3H, d, $J=7$ Hz, CH_3);^{13}C NMR (75 MHz, $CDCl_3$): δ 200.5, 155.8, 133.2, 130.0, 128.7, 88.8, 58.2, 57.3, 53.2, 40.4, 3.3, 13.0; m/z: 270 ($M^+ + 1$).

Preparation of 8-bromo-11,11-dimethyl-1-hydroxytricyclo[5.3.1.$0^{2,6}$]undeca-3,8-dien-10-one 8. The bromoketone **6** (0.45 g, 1.5 mmoles) was dissolved in THF (10 mL), treated with $HClO_4$ (70%, 2 mL) and the mixture stirred at room temperature for 12 hr. Usual workup as described above followed by chromatography over silica gel furnished **8** (0.365 g, 85.14%); IR: 3473, 1684 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.48 (1H, d, $J=\sim 1$ Hz, α-H of α,β-enone), 5.64 (1H, dd of d, $J_1=6$ Hz, $J_2=4.5$ Hz, $J_3=\sim 2$ Hz,olefinic H), 5.51 (1H, merged m of d, $J=6$ Hz, olefinic H), 3.95 (1H, s, OH), 3.56 (1H, m of d, $J=9$ Hz, methine H), 3.44 (1H, complex m, methine H), 3.08 (1H, d,$J=6$ Hz, methine H), 2.46 (2H, merged m), 1.22 (3H, s, CH_3), 0.94 (3H, s, CH_3), ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.1, 152.7, 133.6, 130.5, 128.8, 89.3, 62.6, 58.5, 54.9, 39.8, 33.4, 22.1, 18.9; m/z: 284 ($M^+ + 1$).

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