Allylic oxidation in annulated bicyclo[2.2.2]octenones: Effect of conformational flexibility of the annulated Rings

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Allylic oxidation of annulated bicyclo[2.2.2]octenones with PDC-BuOOH has been reported. While the oxidation of 10,11 gives the usual products, the compounds 1-4 afford the enones 5-8 involving migration of the double bond.

In context of a synthetic endeavour we were interested in the allylic oxidation of tricyclo[7.2.2.02.8]trideca-3,12-dien-11-one 1 to the dien-dione 9. Though there are several reagents for allylic oxidation,1,3 oxidation of 1 with PDC-BuOOH 2a was attempted. However, the enone 5 was obtained instead of 9. This type of migration of the double bond is rather unusual. In order to test the generality and scope, we investigated the oxidation of several tricyclic systems of type 2-4 and 10,11 and wish to report the results herein.

Thus, the treatment of the ketone 1(0.46mmole) with PDC (5 equivalent) and 'BuOOH (70%, excess) at ambient temperature, furnished the dien-dione 5 as a major product (50%) whose structure was deduced from its spectral and analytical data. The IR spectrum of 5 showed characteristic absorption bands at 1725 and 1656 cm<sup>-1</sup> clearly indicating the presence of a conjugated enone. The <sup>1</sup>H NMR spectrum showed signals at δ 6.57 (superimposed dd, J<sub>1</sub> = J<sub>2</sub> = -7Hz, 1H), 6.17 (superimposed dd, J<sub>1</sub> = J<sub>2</sub> = -7Hz, 1H) and 6.00 (br s, 1H) corresponding to only three olefinic protons in addition to other methine and methylene protons. <sup>13</sup>C NMR spectrum of 5 also corroborated with its structure since it exhibited signals at δ 210.82 and 203.44 for both the carbonyl groups. It also showed signals for four olefinic carbons at δ 155.66, 137.82, 127.81 and 124.00 in addition to other resonances for methine, methylenes, methyl and quaternary carbons.

Similarly, oxidation of the ketones 2, 3 and 4 having eight- and six-membered rings annulated to bicyclo[2.2.2]octane framework, also gave the enones 6,7 and 8 (Scheme I) respectively, in moderate yields.

Interestingly, the oxidation of ketones 10,11 having a five-membered ring annulated to bicyclic [2.2.2]octenone moiety gave a mixture of isomeric enones 12-13 (Scheme II) without migration of the double-bond to the ring junction.

Though the detailed mechanism of oxidation with PDC-BuOOH is not known, the difference in the mode of oxidation between 1-4 and 10, 11 is apparently due to the conformational flexibility of the annulated rings which may control the formation of

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1Dedicated to Prof. U R Ghatak on his 70<sup>th</sup> birthday
the initial allylic radical during the oxidation\(^3\) and migration of the double bond. The enones \(5-8\) are obtained during the oxidation of \(1-4\) presumably because the seven-, eight- and six-membered rings can stabilize the allylic radical of type \(14\) (Figure 1) at the ring junction in a better fashion than the five membered ring fused to bicyclo[2.2.2]octenone framework.

In summary, a highly unusual migration of the double bond during the oxidation of annulated at the ring junction in a better fashion than the five-membered ring fused to bicyclo[2.2.2]octenone framework.

Experimental Section

IR spectra were recorded on a Nicolet Impact 400 FF-IR Instrument. UV spectra were recorded on a Shimadzu 260 instrument. \(^1\)H NMR (300 MHz) and \(^13\)C NMR (75 MHz) were recorded on a Varian VXR 300 instrument. Most of the samples were dilute solutions in \(\text{CDCl}_3\) with \(\text{SiMe}_4\) as internal standard. Mass spectra were recorded on a HP GCD 1800A mass spectrometer. Microanalyses were conducted on a CEST 1106 instrument. Melting points were determined on a vegoe apparatus and are uncorrected. All the organic extracts were dried over anhydrous sodium sulphate. Column chromatography was performed using Acme/SRL silica gel (60-120 and 100-200 mesh). Elution was done with petr. ether (60-80 °C) and ethyl acetate mixtures.

Compounds \(1^{5\text{a}}, 4^{6\text{b}}, 10^{5\text{c}}\) and \(11^{5\text{a}}\) were synthesized by a method developed in our laboratory. The compounds \(2\) and \(3\) were prepared from cycloocta-1,3-diene and 6-chloromethyl-6-hydroxy cyclohexa-2,4-diene following analogous procedure.\(^5\text{a}\)

General procedure for allylic oxidation of the ketones

A suspension of the appropriate ketone and celite in benzene were cooled to \(~15\) °C followed by the addition of PDC (5 equivalent) and \(3\)BuOOH (70%, excess). The reaction was maintained at the above temperature for 15 minutes after which the reaction medium was brought to ambient temperature and stirred for 24 hr. The reaction medium was diluted with ether and was filtered through a celite bed. The celite bed was washed with a little ethyl acetate. The filtrate was concentrated under reduced pressure and the residue was chromatographed over silica gel. Elution with petroleum ether-ethyl acetate gave the desired enones as solids which were recrystallized from petroleum ether-ethylacetate. Yields are based on recovered starting materials.

\[10,10\text{-Dimethyl-endo-tricyclo[7.2.2.0^{2,8}]trideca-2,12-dien-4,11-dione 5.}\] Dienone \(1\) (0.1 g, 0.4629 mmole) in benzene (15 mL) was treated with PDC (0.87 g, 2.31 mmole) and \(3\)BuOOH (excess) according to the general procedure described above to give 5 (0.05 g, 50%). IR (neat) \(v_{\text{max}}\): 1725 and 1656 cm\(^{-1}\); \(^1\)H NMR (300MHz, \(\text{CDCl}_3\)): \(\delta\) 6.54-6.59 (superimposed dd, \(J_1=J_2=7\) Hz, \(1H\)), \(\gamma\) H of \(\beta\)-\(\gamma\)-enone moiety), 6.13-6.19 (superimposed dd, \(J_1=J_2=7\) Hz, \(1H\), \(\beta\) H of \(\beta\)-\(\gamma\)-enone moiety), 6.0 (broad s, \(1H\), \(\alpha\) H of \(\alpha,\beta\)-enone group), 3.76-3.79 (d, \(J=6\) Hz, \(1H\), bridged H \(\alpha\) to carbonyl), 3.14-3.19 (m of d, \(1H\), methine H), 2.44-2.47 (complex m, \(3H\), methylene H merged with methine H), 1.90-1.91 (complex m, \(2H\), methylene H), 1.41-1.66 (complex m partly merged with \(H_2O\) in \(\text{CDCl}_3\)), 1.71 (s, \(3H\), \(\text{CH}_3\)), 1.10 (s, \(3H\), \(\text{CH}_3\)).

\(^13\)C NMR (63 MHz, \(\text{CDCl}_3\)): 210.82, 203.44 (carbonyl), 155.66, 152.87, 152.17, 151.08, 137.77, 131.95, 125.16 (olefinic carbons), 63.13, 43.37, 40.69, 40.64, 38.1, 32.47, 23.66, 22.69, 14.98 (other methylene, methine, quarternary and methyl carbon atoms); Mass (m/z): 230(M+). Anal. Found: C,77.69; H, 7.82%.

**Endo-tricyclo[8.2.2.0^{2,8}]tetradeca-2,13-dien-4,12-dione 6.** Dienone 2 (0.12 g, 0.594 mmole) in benzene (15 mL) was treated with PDC (1.1 g, 2.95 mmole) and \(3\)BuOOH (excess) according to the general procedure described above to give 6 as a solid (0.019 g, 17%), mp 105-07 °C; IR (neat): 1736 and 1645 cm\(^{-1}\); \(^1\)H NMR (300MHz, \(\text{CDCl}_3\)): \(\delta\) 6.54-6.49 (superimposed dd, \(J_1=J_2=7\) Hz, \(1H\), olefinic H), 6.29-6.23 (m, \(2H\), olefinic H), 3.79 (d, \(J=1H\) Hz, \(1H\)), 3.47-3.41 (m, \(1H\)), 3.14-2.92 (m, \(2H\)), 2.46-2.56 (m, \(1H\)), 2.08-2.22 (cluster of m, \(2H\)), 1.96-1.76 (cluster of m, \(4H\)), 1.28-1.3 (m, \(2H\)).

\(^13\)C NMR (63 MHz, \(\text{CDCl}_3\)): 208.8, 201.78 (CO), 151.08, 137.77, 131.95, 125.16 (olefinic carbons), 63.13, 43.37, 40.69, 40.64, 38.1, 32.47, 23.66, 22.69, 14.98 (for other methylene, methine, quarternary and methyl carbon atoms); Mass (m/z): 230(M+). Anal. Found: C,77.82; H, 7.82%.

\[11\text{-Methyl-endo-tricyclo[8.2.2.0^{2,8}]tetradeca-2,13-dien-4,12-dione 7.}\] Dienone 3 (0.2 g, 0.925 mmole) in benzene (15 mL) was treated with PDC (1.04 g, 2.76 mmole) and \(3\)BuOOH (excess) according to the general procedure described above to give 7 as a solid (0.059 g, 36%), mp 95-96 °C; IR (neat): 1727
and 1652 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) : \(\delta\) 6.60-6.55 (superimposed dd, \(J_1=J_2=7\) Hz, 1H, olefinic H), 6.20-6.25 (2H, olefinic H), 3.75-3.72 (dd, \(J_1=1\) Hz, \(J_2=7\) Hz, 1H, methine H), 3.64-3.56 (m, methine H, 1H), 2.88-3.02 (2H, 2.48-2.58 (1H), 2.32-2.22 (1H), 1.90-1.72 (2H), 1.72-1.58 (3H), 1.5-1.32 (1H, merged with H\(_2\)O in CDCl\(_3\)), 1.14-1.16 (d, \(J=7.5\) Hz, 3H, CH\(_3\)). \(^{13}\)C NMR (63 MHz, CDCl\(_3\)): 208.8, 201.78, 151.08, 137.77, 131.95, 125.16 (olefinic carbons), 63.13, 43.37, 40.69, 40.64, 38.1, 32.47, 23.66, 22.69, 14.98 (for other methylene, methine, quartenary and methyl carbon atoms); Mass (m/z): 230(M+). Anal. Found: C, 78.71; H, 7.99. Caled for C\(_{15}\)H\(_{18}\)O\(_3\) : C, 78.26; H, 7.82%.

9-Hydroxy-1,9,11-trimethyl-endo-tricyclo[6.2.2.0\(^{2,7}\)]dodeca-2,11-dien-4,10-dione 8. Dienone 4 (0.15 g, 0.721 mmole) in benzene (15 mL) was treated with PDC (0.813 g, 2.16 mmole) and BuOOH (excess) according to the general procedure described above to give 8 as a solid (0.060 g, 46%), mp 136-38°C; IR (neat): 1729 and 1650 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 5.8-5.76 (d, \(J_1=3\) Hz, 1H, olefinic H), 5.45-5.40 (broad s, 1H, olefinic H), 3.34-3.24 (m of d, \(J_2=7.5\) Hz, 3H, CH\(_3\)), 1.32 (s, 3H, CH\(_3\)). \(^{13}\)C NMR (62 MHz, CDCl\(_3\)): \(\delta\) 1729 and 1703 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.49-7.45 (dd, \(J_1=6\) Hz, \(J_2=3\) Hz, 1H, \(\beta\) H of \(\alpha,\beta\)-ene moiety), 6.30-6.26 (dd, \(J_1=3\) Hz, \(J_2=6\) Hz, 1H, \(\alpha\) H of \(\alpha,\beta\)-ene moiety), 6.15-6.09 (dd, \(J_1=9\) Hz, \(J_2=6\) Hz, 1H, olefinic H), 5.95-5.87 (d, \(J=9\) Hz, 1H, olefinic H), 3.72 (s, 3H, OCH\(_3\)), 3.62-3.67 (m, 1H, methine H), 2.95-2.88 (dd, \(J_1=1.2\) Hz, \(J_2=6\) Hz, 1H, methine H), 2.80-2.75 (q of d, 1H, methine H), 1.18-1.16 (s, 3H, CH\(_3\)), 1.24-1.2 (s, 3H, CH\(_3\)). Mass (m/z): 232 (M+); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 211.61, 204.90 (CO), 164.5, 138.21, 132.75, 127.55 (olefinic carbons), 86.57, 53.91, 45.49, 43.99, 40.7, 42.64, 28.21, 23.71 (for other methylene, methine, quartenary and methyl carbon atoms). Anal. Found: C, 72.63; H, 7.01. Caled for C\(_{15}\)H\(_{18}\)O\(_3\) : C, 72.41; H, 6.89%.

**Endo-tricyclo[5.2.2.0\(^{2,6}\)]undeca-3,10-dien-5,9-diene 13a and endo tricyclo[5.2.2.0\(^{2,6}\)]undeca-4,10-dien-3,9-diene 13b**. Dienone 11 (0.25 g, 1.56 mmole) in benzene (15 mL) was treated with PDC (1.76 g, 4.68 mmole) and BuOOH (excess) according to the general procedure described above to give 13a (0.050 g, 23%), mp 120-21°C and 13b (0.046 g, 21%), mp 101-02°C. 13a : IR (neat): 1718 and 1696 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.38-7.36 (dd, \(J_1=6\) Hz, \(J_2=3.4\) Hz, 1H, \(\beta\)-H of \(\alpha,\beta\)-ene moiety), 6.29-6.22 (m, 2H, olefin H), 5.89-5.85 (superimposed dd, \(J=7\) Hz, 1H, olefinic H), 3.43-3.27 (complex m, 3H, methine H), 2.61-2.57 (dd, \(J_1=6\) Hz, \(J_2=3\) Hz, 1H, methine H), 2.18-2.09 (superimposed dd, \(J_1=4.2\) Hz, \(J_2=3\) Hz, 2H, methylene H \(\alpha\) to carbonyl); \(^{13}\)C NMR (63 MHz, CDCl\(_3\)): \(\delta\) 209.18, 207.93 (CO) 164.04, 137.8, 134.4, 125.61, (olefinic carbons) 51.65, 48.65, 42.99, 37.84, 34.42; Mass (m/z): 174 (M+). Anal. Found: C, 76.17; H, 5.36. Caled for C\(_{15}\)H\(_{18}\)O\(_3\): C, 75.86; H, 5.74%. 13b : IR (neat): 1718.3, 1697 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.44-7.38 (dd, \(J_1=6\) Hz, \(J_2=H\) of \(\alpha,\beta\)-ene moiety), 6.32-6.24 (m, 2H, olefinic H), 5.94-5.86 (dd, \(J_1=6\) Hz, \(J_2=3\) Hz, 1H, olefinic H), 3.46-3.30 (m, 3H, methine H), 2.66-2.61 (dd, \(J_1=15\) Hz, \(J_2=6\) Hz, 1H, methine H), 2.19-2.11 (dd, \(J_1=12\) Hz, \(J_2=6\) Hz, 2H, methylene H \(\alpha\) to...
Notes

1147

Carbonyl; $^{13}$C NMR (63 MHz, CCl$_4$ +CDCl$_3$) : δ 208.0, 206.9 (CO), 164.4, 137.9, 133.3, 126.5, (olefinic carbons) 51.0, 46.6, 44.8, 38.9, 35.27; Mass (m/z): 174 (M$^+$). Anal. Found: C, 75.91; H, 5.83.
Calcd for C$_{11}$H$_{10}$O$_2$: C, 75.86; H, 5.74%.

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References