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Regioselective and diastereoselective dimethyldioxirane epoxidation of substituted norbornenes and hexamethyl Dewar benzene

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Abstract

Various substituted norbornenes, such as *endo*-dicyclopentadiene **1**, *exo*-dicyclopentadiene **5**, 5-methylenebicyclo[2.2.1]hept-2-ene **8** and hexamethyl Dewar benzene **10** were transformed into the corresponding mono- and bis-epoxides by epoxidation with dimethyldioxirane (as an acetone solution). © 2000 Elsevier Science Ltd. All rights reserved.

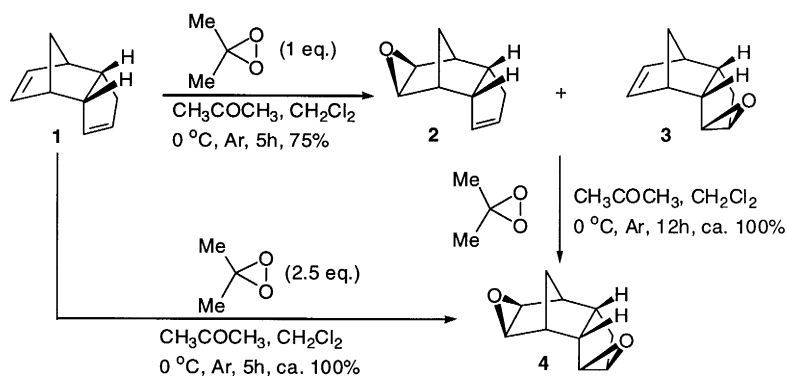
Keywords: dimethyldioxirane; epoxidation; diastereoselectivity; regioselectivity; substituted norbornenes.

Dimethyldioxirane, either as a solution in acetone or generated in situ, is a well known and powerful oxidizing agent.¹ The dimethyldioxirane reagent is advantaged by efficiency, convenience of preparation and isolation, and also on its performance under strictly neutral conditions. This reagent was further enhanced by achievements in diastereoselective and enantioselective oxidation by chiral dioxiranes,² generated in situ from a chiral ketone-catalyst and potassium monoperoxysulfate.³ Despite all its synthetic applications, little is known about the regioselectivity of dimethyldioxirane epoxidations, especially when two similar alkenes are present. To this end, some remarkable examples are the regioselective epoxidation⁴ of a disubstituted double bond over a trisubstituted enol ether moiety, and the exclusive epoxidation⁵ (at an endocyclic double bond) of the pentafulvenes.

A great number of studies⁶ have been devoted to epoxynorbornane derivatives due to the fact that these compounds are readily produced from cyclopentadiene, which is a large scale side-product of the coke and petroleum processing industries. In particular, dicyclopentadiene diepoxide has found application for the industrial manufacture of various polymeric materials with valuable properties. Since this oxidation is usually carried out with peracetic, peroxyphthalic and monoperoxymaleic acids, it was of interest to examine the behaviour of such substrates towards dimethyldioxirane. Herein we report preliminary results of the dimethyldioxirane epoxidation of substituted norbornenes and hexamethyl Dewar benzene.

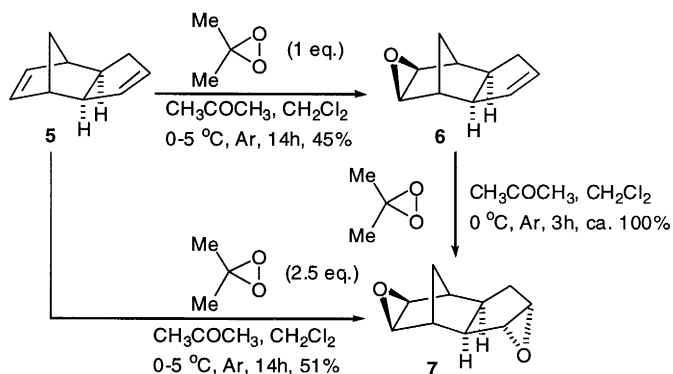
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Dimethyldioxirane epoxidation⁷ of *endo*-dicyclopentadiene **1** gave a mixture of epoxides **2**⁸ and **3**⁸ (Scheme 1), which were separated⁹ by flash column chromatography in 35% and 40% yield, respectively. In contrast, *m*CPBA epoxidation⁹ of **1** leads to a 1.5:1 mixture of epoxides **2** and **3**. Treatment of either epoxide **2** or **3** with another batch of dimethyldioxirane afforded bis-epoxide **4**, which was also isolated in 66% yield when *endo*-dicyclopentadiene **1** was treated with 2.5 equiv. of dimethyldioxirane. Of the four possible stereoisomers, only epoxide **4**, characterized by the *syn* arrangement of each epoxide function to the subsequent bridge, was produced.



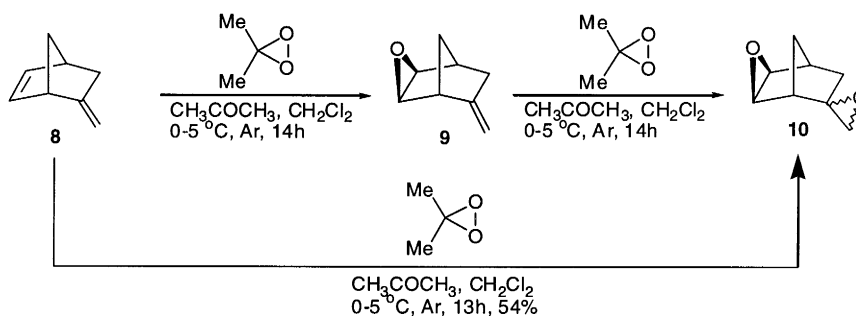
Scheme 1.

However, epoxidation of *exo*-dicyclopentadiene **5**¹⁰ with stoichiometric amounts of dimethyldioxirane gave only epoxide **6** in 45% yield (Scheme 2). The treatment of epoxide **6** with dimethyldioxirane or *exo*-dicyclopentadiene **5** with 2.5 equiv. of dimethyldioxirane gave bis-epoxide **7** in ca. 100% and 51% yield, respectively. Again, of the four possible stereoisomers, only epoxide **7** is produced.



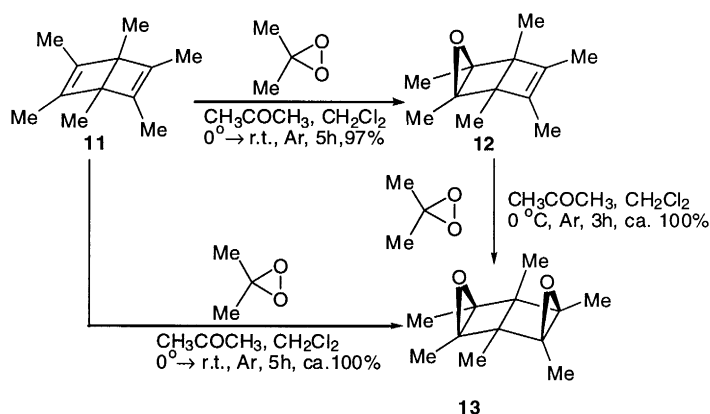
Scheme 2.

The reaction of 5-methylenebicyclo[2.2.1]hept-2-ene **8** with 1 equiv. of dimethyldioxirane afforded epoxide **9**¹¹ (Scheme 3). Further treatment of epoxide **9** with dimethyldioxirane or diene **8** with 2.5 equiv. of dimethyldioxirane yielded bis-epoxide **10**¹¹ as a 72:28 mixture of diastereomers. The typical *exo*-selectivity^{6,12} of the epoxidation of norbornene derivatives is also observed for the double bond which resides in the ring. However, as the second double bond moves away from the norbornene group, the influence of the methylene bridge becomes less significant, and attack at the double bond occurs from both sides. For dicyclopentadienes **1** and **5**, where the C4–C5 double bond is also moved away from the norbornene group, there is a second bridge between the C2 and C6 atoms which controls the face-selectivity of the epoxidation at the subsequent double bond.



Scheme 3.

Dimethyldioxirane epoxidation of hexamethyl Dewar benzene **11** yields a mixture of the mono-epoxide **12**⁸ and bis-epoxide **13**⁸ (Scheme 4), the ratio of which depends on the amount of dioxirane employed. Quite surprisingly, with 1 equiv. of dimethyldioxirane, epoxide **12** was isolated in 97% yield while, with excess of dimethyldioxirane, the bis-epoxide **13** was quantitatively isolated instead. Epoxide **12** had been previously postulated¹³ as the labile intermediate in the peracid epoxidation of **11**, which was not even detected due to rapid acid hydrolysis. The stereochemistry of the two oxygen atoms in bis-epoxide **13** is *syn* according to the observed symmetry of the NMR signals. No NOE effect was observed between the epoxide and the bridge's methyl groups.



Scheme 4.

In summary, we have demonstrated that dimethyldioxirane (as an acetone solution) serves as a convenient and diastereoselective oxidant for the preparation of various mono- and bis-epoxides of substituted norbornenes and hexamethyl Dewar benzene. We are presently examining the optimization of these reactions, employing various in situ techniques, and our results will be presented in due course.

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- General procedure for the preparation of epoxides **2** and **3**: A 0.075 M solution of dimethyldioxirane (80 mL, 6.0 mmol) was slowly added to a cooled (0°C) solution of *endo*-dicyclopentadiene **1** (2.0 mL, 14.8 mmol) in CH_2Cl_2 (20 mL) under an argon atmosphere. The stirring was continued at 0°C for 5 h. The solvents were evaporated under reduced pressure and the residue was chromatographed (flash silica gel: CH_2Cl_2 :pet. ether=2:1) to afford epoxide **2** (310 mg, 35% yield) and epoxide **3** (355 mg, 40% yield) as colorless oils.
- All new compounds were fully characterized. Selected spectroscopic data for representative compounds. Compound **2**: ^1H NMR (400 MHz, CDCl_3): δ =0.82 (d, J =9.6 Hz, 1H), 1.36 (d, J =9.6 Hz, 1H), 2.23–2.27 (m, 1H), 2.23 (dd, J =1.5, 3.9 Hz, 1H), 2.47 (d, J =3.3 Hz, 1H), 2.52 (dd, J =1.5, 3.0 Hz, 1H), 2.61–2.68 (m, 1H), 2.89 (d, J =3.6 Hz, 1H), 3.13–3.18 (m, 1H), 3.15 (dd, J =1.0, 3.9 Hz, 1H), 5.55 (ddd, J =2.2, 4.3, 8.0 Hz, 1H), 5.63 (ddd, J =2.2, 4.3, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ =29.0 (t), 31.3 (t), 38.4 (d), 40.0 (d), 41.8 (d), 49.2 (d), 50.9 (d), 53.2 (d), 129.5 (d), 132.1 (d). Compound **3**: ^1H NMR (400 MHz, CDCl_3): δ =1.33 (ddd, J =2.7, 3.3, 14.9 Hz, 1H), 1.33 (dd, J =7.8 Hz, 1H), 1.49 (dt, J =1.8, 8.2 Hz, 1H), 1.89 (dd, J =9.0, 14.9 Hz, 1H), 2.49–2.56 (m, 1H), 2.78 (br.s, 1H), 2.80 (dd, J =4.0, 8.0 Hz, 1H), 2.91 (br.s, 1H), 3.15 (d, J =2.5 Hz, 1H), 3.30 (t, J =2.5 Hz, 1H), 6.06 (dd, J =2.9, 5.7 Hz, 1H), 6.10 (dd, J =2.9, 5.7 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ =31.0 (t), 43.9 (d), 44.6 (d), 46.4 (d), 50.9 (d), 51.9 (t), 60.7 (d), 61.8 (d), 134.8 (d), 135.0 (d). Compound **12**: ^1H NMR (400 MHz, CDCl_3): δ =0.94 (s, 6H), 1.32 (s, 6H), 1.56 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ =8.1, 10.6, 11.1, 58.7, 75.1, 142.6. Compound **13**: ^1H NMR (400 MHz, CDCl_3): δ =0.86 (s, 6H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3): δ =6.7, 10.6, 64.6, 68.6.
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