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Selective Oxidation of Nitrocompounds by Dimethyldioxirane

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Abstract: An efficient monooxidation of nitrodiols was performed by dimethyldioxirane, exploiting the inhibiting effect of the nitro group on reaction at adjacent centers. The reaction appears of general value when an alcoholic moiety is in α or β to the nitro group.
A double bond was similarly deactivated towards epoxidation, and other functional groups reacted preferentially. Copyright © 1996 Published by Elsevier Science Ltd

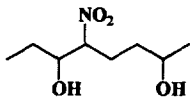
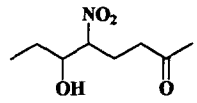
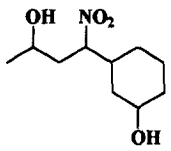
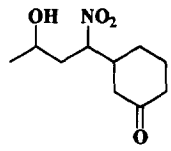
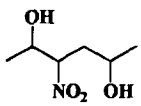
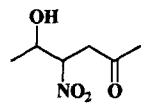
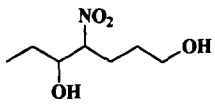
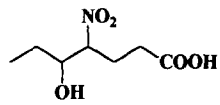
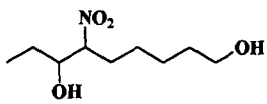
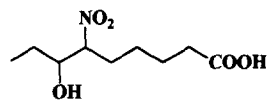
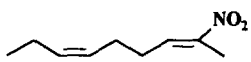
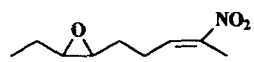
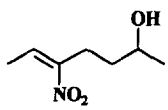
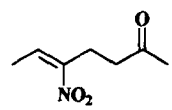
In the last few years dimethyldioxirane (DMD) has become an important reagent for its high efficiency and selectivity in a variety of oxidation reactions.[1] It has shown to be extremely sensitive to stereoelectronic effects and a dipole group close to the reactive center may influence the reaction, favouring a chemo and stereospecific attack[2] or preventing, in other cases, the oxidation.[3]

In 1,2 and 1,3 diol systems we noted a strong inhibiting effect of the formed carbonyl group on the oxidation of the second function, allowing us to selectively oxidize these compounds to keto-alcohols.[4]

In the light of these observations we considered it useful to investigate the reactivity of DMD on polyfunctionalized substrates with strong dipole groups lying close to reactive centers. Polyfunctionalized nitroalkanes[5] and conjugated nitroalkenes[6] are of particular interest in complex organic synthesis because of the many possible transformations of the nitro functionality.

For oxidation by DMD, Murray and coworkers proposed a mechanism in which an electrophilic attack of the reagent generates a small positive charge on the carbon atom.[7] Then we may assume that a dipole close to the reactive center such as the nitro group, destabilizes the transition state inhibiting the attack of the reagent.

Table 1. Selective oxidation of nitrocompounds by DMD

Entry	Substrate	Product	yield% (isolated)
1	 **1**	 **2**	90[a] (55[c])
2	 **3**	 **4**	>96[a] (85[c])
3	 **5**	 **6**	low conversion
4	 **7**	 **8**	80[a]
5	 **9**	 **10**	>96[c,d]
6	 **11**	 **12**	>96[b]
7	 **13**	 **14**	90[b] (75[c])

a) GC yield b) yield by NMR analysis c) yield of isolated products d) characterized as methyl ester

Taking advantage of this property, we were able to perform the selective oxidation of nitrodiols to nitroketols, meanwhile other reagents fail to discriminate between the two hydroxyl groups.[8]

The behavior of **1**, **3** and **5** (Table 1 entries 1,2,3) showed that the deactivating effect of the nitro group is extended to α and β positions.

The most interesting transformation apears the oxidation of a primary hydroxyl group in the presence of a secondary alcohol close to a nitro group. Thus, **7** and **9** were oxidized to the corresponding carboxylic acids with a selectivity hitherto never observed.

The deactivating effect was emphasized on the olefin mojety. We found it possible to selectively oxidize a double bond in a diene which carries a nitro group. Thus, **11** was converted to **12** in exceptionally high yield. Moreover the nitroolefin moiety was shown to be much less reactive than a hydroxyl one; i.e. **13** was oxidized to **14**. Only with an excess of reagent and prolonged reaction times was some of epoxiderivative produced. Usually an olefin is much more reactive then an alcohol. In this case there is a clear inversion of selectivity in agreement with the withdrawing effect of the nitro group which makes the double bond electron-deficient.

All reactions were performed, in a typical procedure, by adding rapidly 1.5 equivalents of DMD solution[9] (0.09M in acetone) to a stirred solution of substrate (100 mg) in acetone (1 ml) at room temperature (ca. 25°C). If necessary, further amount of reagent was added until complete conversion of the substrate. **11** was reacted at -20°C for 2 hr. All other substrates were stirred overnight at room temperature. Reactions were monitored by TLC and GC, and products characterized by ^{1}H-NMR and ^{13}C-NMR spectroscopy.[10] When necessary, the reaction products were purified by flash chromatography eluting with a mixture of petroleum ether and ethyl acetate, but sometimes yields decreased owing to partial decomposition of nitroalcohols on silica gel. All starting materials were prepared by methods reported in the literature as mixtures of diastereoisomers,[11] but no difference in reactivity for each steroisomer was observed.

The reactions reported here, together with the previous observations, lead us to consider of general value the influence of a dipole group on DMD behavior and encourage us to further investigate the synthetic potential of this method.

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10. Selected data for reaction products. **2**: oil, mixture of *syn* and *anti* diastereoisomers. ^{1}H-NMR of the main isomer, δ = 1.0 (d, J=7 Hz, 3H, CH_3), 1.4-1.65 (m, 4H, CH_2), 2.1 (s, 3H, CH_3CO), 2.5 (dt, J=7 Hz, J=3 Hz, 2H, CH_2CO), 3.8 (ddd, J=8.5 Hz, J=7 Hz, J=4 Hz, 1H, C<u>H</u>OH), 4.4-4.5 (m, 1H, C<u>H</u>NO_2). ^{13}C-NMR, δ = 9.5, 24.1, 26.5, 30, 38.8, 73.3, 91.4, 206.5. **4**: oil, mix. of ds., ^{1}H-NMR, δ = 1.2 (d, J=2 Hz, 3H, CH_3), 1.5-2 (m, 11H), 3.6-3.8 (m, 1H, C<u>H</u>OH), 4.7-4.9 (m, 1H, C<u>H</u>NO_2). ^{13}C-NMR, δ = 63.9 + 65.6 + 65.65 (C-OH), 89.0 + 89.1 + 89.2 (C-NO_2), 200.1 (C=O). **8**: mixture of *syn* and *anti* ds. ^{1}H-NMR, δ = 0.98, 1.0 (2t, J=7 Hz, 3H, CH_3), 3.7-4.0 (m, 1H, C<u>H</u>OH), 4.3-4.6 (m, 1H, $CHNO_2$). ^{13}C-NMR, isomer (a) δ= 9.4, 24.9, 26.2, 29.6, 73.2, 91.2, 176.5; isomer (b) δ= 9.9, 22.0, 22.7, 30.1, 73.7, 90.3, 177.0. **10**: oil, mixture of *syn* and *anti* ds, characterized as methylester derivative. ^{1}H-NMR, δ = 1.18, 1.2 (2t, 3H, J=6 Hz, CH_3), 1.2-1.7 (m, 8H, CH_2), 2.2 (t, 2H, J=8 Hz, $C\underline{H}_2COOCH_3$), 3.6 (s, 3H, $COOCH_3$), 4.0-4.1 (m, 1H, C<u>H</u>OH), 4.25-4.4 (m, 1H, $CHNO_2$). ^{13}C-NMR, isomer (a) δ=19.5, 24.2, 25.1, 28.1, 29.8, 33.5, 51.4, 68.3, 94.1, 175.3; isomer (b) δ=18.9, 24.1, 25.3, 28.0, 29.8, 33.5, 51.4, 68.3, 92.9, 174.4. **12**: Oil. ^{1}H-NMR, δ = 0.9 (t, 3H, J=7 Hz, CH_3), 1.4-1.7 (m, 2H, CH_2), 2.1 (d, 3H, J=1 Hz, CH_3C=C), 2.4 (m, 2H, CH_2), 2.9 (m, 2H, CH_2C=C), 7.1 (tq, 1H, J=8 Hz, J=1 Hz, CH=C). ^{13}C-NMR, δ = 10.2, 12.2, 20.9, 25.1, 26.4, 56.0, 58.4, 134.7, 148.4. **14**: Oil, ^{1}H-NMR, δ = 1.87 (d, 3H, J=7.4 Hz, CH_3C=C), 2.1 (s, 3H, CH_3CO), 2.6-2.8 (m, 4H, CH_2), 7.16 (q, 1H, J=7.4 Hz, CH=C). ^{13}C-NMR, δ=13.3, 19.9, 29.6, 40.6, 133.2, 151.3, 206.8.

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