Oxidations of Alkylbenzenes with Dimethyldioxirane

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The oxidation of various alkylbenzenes (1–17) with excess dimethyldioxirane (DMDO) in homogeneous acetone solutions has been studied. In general, the benzylic methylene and methine C–H bonds were oxidized to give the corresponding phenones and tertiary benzylic alcohols, respectively, in relatively low yields. Whereas a *tert*-butyl substituent at the reaction centre leads to very low conversion due to steric hindrance, the presence of additional phenyl groups appears to favour the oxidation in most, but not all cases. Di- and triphenylmethane (4 and 14) were found to be considerably less reactive than *cis*-decalin. By contrast, the intramolecular competetive oxidation of isobutylbenzene (19) and 1-methyl-4-phenylcyclohexanes (20) reveals that the benzylic C–H bonds are slightly more reactive than the tertiary ones at remote positions.

Introduction

Dioxiranes constitute a particular group of oxidizing reagents in organic chemistry. Different from transition metal oxo- and peroxo compounds, dioxirans react by insertion of oxygen atoms into aliphatic C–H bonds. A considerable knowledge on dioxirane oxidations has been worked out during the past decade and has been collected in recent review articles [1, 2].

The reactions of dimethyldioxirane (DMDO) with alkylbenzenes and related arylaliphatic hydrocarbons have been almost completely ignored, probably because of the relatively facile selective oxidation of benzylic C–H bonds by many other oxidation reagents. The only studies of alkylbenzenes reported so far were performed by Murray *et al.* [3], who studied the reactivity of DMDO toward toluene, ethylbenzene, and cumene, and by Curci *et al.* [4], who oxidized the same substrates with the related but more reactive (trifluormethyl)-methyldioxirane.

We became interested in using DMDO in acetone solution for the selective oxidation of complex polycyclic indan hydrocarbons ("centropolyindans" [5–8]) which contain several benzylic and/or benzhydrylic C–H bonds. Because of the low solubility of the centropolyindans, the utilization of acetone as the solvent, in contrast to more polar media often used with other oxidation re-

agents, appeared advantageous. Some results of these investigations will be reported in a separate paper [9].

In view of the scarce data available so far, we wish to report here on our study of DMDO oxidations of a larger variety of alkylbenzenes.

Results and Discussion

Oxidation of primary alkylbenzenes (α-methylene groups)

The reactions of excess DMDO in acetone solution with various primary alkylbenzenes, α,ω-diphenylalkanes, and some benzocycloalkanes (Table I) give the corresponding ketones (1a–10a), but the yields are low or moderate in most cases. The reaction is particularly slow for ethylbenzene (1) and diphenylmethane (4), in spite of the formally activated methylene C–H bonds in the latter substrate. The higher homologues 2 and, respectively, 5 and 6 give higher yields (16–28%), and the same holds for indan (8) and tetralin (9). Fluorene (10) reacts slightly better than 4, as in many other oxidation reactions, but the yield of fluorenone (10a) is surprisingly low as well. Neopentylbenzene (3) reacts very slowly, obviously because of steric reasons.

It is interesting to note that with α,ω-diphenylalkanes and benzocycloalkanes 5–9 no bis-oxidation product is observed along with the monoketones (5a–9a). By using a fivefold excess of DMDO in acetone, 1,3-diphenylpropane (6) gives dihydrochalcone (6a) in quantitative yield. More-

Table I. Oxidations of primary alkylbenzenes with DMDO in acetone.
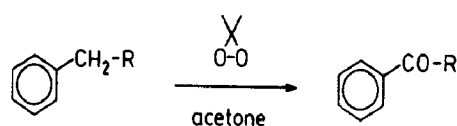
1 - 7   **1a - 7a**

Substrate	R	Product		Yield [%][a]
1	Me	1a		6.9
2	Et	2a		22
3	t-Bu	3a		2.7
4	Ph	4a		3.2
5	CH₂Ph	5a		22
6	(CH₂)₂Ph	6a		28[b]
7	(CH₂)₃Ph	7a		16
8	Indan	8a	1-Indanone	11[c]
9	Tetralin	9a	1-Tetralone	13
10	Fluorene	10a	9-Fluorenone	8.2

[a] Determined by GC-MS analysis (see Experimental); [b] use of a fivefold excess of DMDO gives a 99% yield of 6a; [c] at 4 °C, 49% of 8a and 11% of 1-indanol (8b) is formed.

Tab. II. Oxidations of secondary alkylbenzenes with DMDO in acetone.

11 - 14   **11a - 14a**

Substrate	R¹	R²	Product	Yield [%][a]
11	Me	Me	11a	13.4
12	Ph	Me	12a	1.0
13	Ph	t-Bu	13a	0.5
14	Ph	Ph	14a	17.5
15		Me	15a	4.2
16		t-Bu	16a	6.8[b]
17		Ph	17a	21

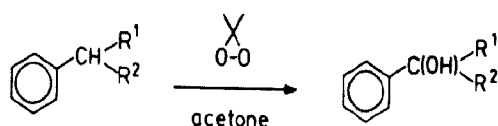[a] Determined by GC-MS analysis (see Experimental); [b] 9-fluorenone (10a, 11%) is formed as well.

over, working at low temperature (+4 °C) with the usual, one-molar excess of DMDO, indan (8) gives a considerable amount of 1-indanol (8b) along with 8a [10].

These data show that the oxygen insertion in the α-methylene C–H bonds of alkylbenzenes is particularly slow. The presence of bulky groups (cf. 3, and possibly 4) seems to hinder the reaction, whereas additional ω-phenylalkyl groups of a fused arene ring support the reaction. Consecutive oxidation processes appear to be even slower than the first oxidation step.

Oxidation of secondary alkylbenzenes (α-methine groups)

The reaction of one-molar excess of DMDO in acetone with secondary (α-substituted) alkylbenzenes 11–17 (Table II) are again slow and give the corresponding alcohols 11a–17a in only moderate yields. Taking into account the reduced number of benzylic C–H bonds, sec-propylbenzene (11) behaves similar to the normal isomer 2. In 11, some steric hindrance may prevail over C–H bond activation. Clearly, this trend is most pronounced in 1,1-diphenylethane (12) and 2,2-dimethyl-1,1-diphenylpropane (13), which are oxidized extremely slowly, even more so than the primary (mono-

phenyl) analogues 4 and 3, respectively. By contrast, triphenylmethane (14) does not exhibit steric hindrance; the relatively high yield of triphenylmethanol (14a) is attributed, in view of the other results, to the favourable influence of several adjacent π-systems rather than to a pronounced C–H bond activation.

The effect of steric hindrance is less clear for DMDO oxidations with the 9-alkylfluorenes 15 and 16. While a methyl group in 15 seems not to hinder the reaction as compared to 10, 9-(tert-butyl)-fluorene (16) is oxidized more efficiently than the parent hydrocarbon 10. As a surprising result, the oxidation of 16 leads to ca. 60% 9-fluorenone (10a), which has to be formed by oxidative C–C bond cleavage.

Finally, 9-phenylfluorene (17) is oxidized to 9-phenyl-9-fluorenol (17a) in relatively high yields, much like triphenylmethane (14). Again, the oxidation appears to be accelerated by the presence of an additional π-system. In this case, no oxidative fragmentation is observed.

Competitive oxidations

The results presented in the previous sections provide only rough information on the relative reactivity of benzylic C–H bonds with DMDO. In

order to get a more reliable comparison for typical alkylbenzene substrates, some inter- and intramolecular competition experiments have been performed. cis-Decalin (18) has been selected as the reference substrate for the intermolecular comparison.

Equimolar mixtures of diphenylmethane (4) and 18 were treated with subequivalent amounts of DMDO in acetone and allowed to react for several days. GC-MS analysis shows the formation of only 0.9% benzophenone (4a), but of 25% 4a-hydroxy-cis-decalin. In similar experiments, a mixture of triphenylmethane (14) and 18 gives 0.6% triphenylmethanol (14a) and 46% of the decalol. Assuming the primary oxidation of 4 to be the rate-limiting step, the tertiary, aliphatic C–H bonds of 18 appear to be ca. 28 times more reactive than a benzylic C–H bond of 4 and ca. 38 times more reactive than the C–H bond of 14. A direct competition experiment with 4 and 14, giving 13% 4a and 8.7% 14a, confirmed the similar reactivities (per C–H bond) of these two alkylbenzenes [13]. In comparison to tertiary C–H bonds of 18, however, the oxygen insertion reaction into benzyl and benzhydryl C–H bonds is considerably slower.

The greater reactivity of DMDO toward aliphatic as compared to benzylic C–H bonds is in accordance with previous results of Murray et al. [3]. However, the origin of the reluctance of the reaction of DMDO with alkylbenzenes is not obvious, and the considerable differences found for the substrates studied here do not reflect a clear trend. In order to independently compare the reactivities of benzylic and aliphatic C–H bonds, we performed two intramolecular competition experiments (Schemes 1 and 2).

The oxidation of isobutylbenzene (19, Scheme 1) with DMDO under standard conditions (r.t., 3 days) leads to a mixture of 15.6% butyrophenone (19a) and 4.0% 2-methyl-1-phenylpropan-2-ol (19b) as the only oxidation products.
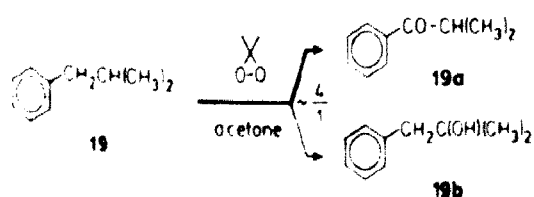
Scheme 1
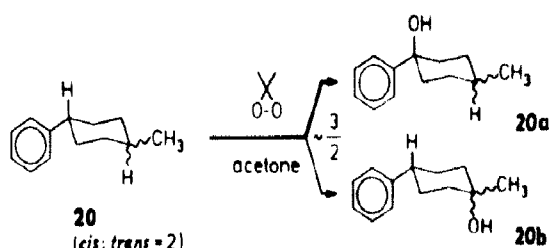
Surprisingly, in this case, the benzylic C–H bonds are about two times (per bond) more reactive than the tertiary one. In another experiment, the intramolecular competition was probed with a mixture of stereoisomeric 1-methyl-4-phenylcyclohexanes (ratio [cis-20]:[trans-20] = 2.0, Scheme 2). Again, after three days of reaction time, the benzylic C–H bonds are found to be more reactive than the tertiary aliphatic ones. GC-MS analysis of the product mixture reveals 33% of benzylic oxidation (cis- and trans-20a) and 19.5% of oxidation at the tertiary C(4)–H bond (20b). Thus, similar to 19, the benzylic C–H bonds in 20 react more readily than the non-benzylic, tertiary ones. The ratio of stereoisomeric tertiary alcohols 20b was found to be [trans-20b]:[cis-20b] = 2.0 [14], reflecting complete stereospecificity of the DMDO oxidation. Thus, in analogy to the stereospecific DMDO oxidation of the 1,2-dimethylcyclohexanes [3, 4], epimerization during the oxidation process can be excluded [15]. Hence, similar to isobutylbenzene (19), the benzylic C–H bonds of 1-methyl-4-phenylcyclohexane (20) are more reactive (ca. 1.7 times) than "normal", tertiary aliphatic C–H bonds.

Scheme 2

Experimental

solvent was evaporated under normal pressure and the oily residue was subjected to GC MS analysis: Finnigan 1020 B with SE-54 capillary column (25 m×0.25 mm), injector temperature 250 C, oven temperature programme (80 C 4 min, gradient 15 C/min, 250 C), MS 70 eV. The quantification of ratios of substrate and products was performed after calibration of the system with mixtures of the expected components with known molar ratios.

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[10] By applying the in-situ method (refs. 11, 12) to generate DMDO, 5 is oxidized to desoxybenzoin (7%) and 1,2-diphenylethanol (5%).

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[12] R. W. Murray and R. Jeyaraman, J. Org. Chem. 50, 2847 (1985).
[13] This result is contradictory to the yields obtained with separate DMDO oxidation of 4 and 14 (Tables I and II); certainly, the latter experiments have to be considered less reliable.
[14] Besides 20a and 20b, the isomeric 1,4-diols are formed in ca. 3% yield.
[15] The product ratio of cis- and trans-20a could not be determined.
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