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ELECTRON-TRANSFER PROCESSES

NEW SYNTHESIS OF γ-LACTONES BY PEROXYDISULFATE OXIDATION OF ISOPROPYLBENZENES AND ALIPHATIC CARBOXYLIC ACIDS

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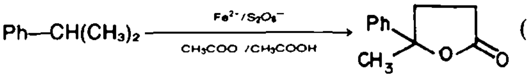
Abstract—A new synthesis of γ-lactones by peroxydisulfate oxidation of isopropylbenzenes is described. Evidence concerning the free-radical mechanism is reported; the intermediate formation of alkyl and benzyl radicals is evidenced by trapping them with quinoxaline. The role of the iron catalyst is discussed.

Increasing evidence[1] for the intermediate formation of aromatic radical cations in the oxidation of aromatics by peroxydisulfate has recently been reported.

We now report on a new synthesis of γ-lactones by simultaneous oxidation of isopropylbenzene and aliphatic carboxylic acids by peroxydisulfate. The reaction is of synthetic interest and, at the same time, provides new contributions concerning the oxidation of aromatic compounds by peroxydisulfate.

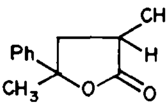
Thus, when isopropylbenzene is oxidized by peroxydisulfate in acetic acid in the presence of potassium acetate and of catalytic amounts of basic ferric acetate, a high yield of the γ-lactone **1** is obtained (eqn 1)



(1)

1 (81%)

Similarly the γ-lactones **2** (as a diastereoisomeric mixture) and **3**, contaminated by **1**, are obtained with propionic acid and with an isobutyric-acetic acid mixture, respectively.



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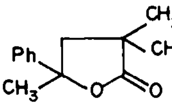
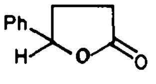


3

The compound **3** is not formed in the absence of acetic acid. Only a very small yield (~1%) of the γ-lactone **4** is obtained when ethylbenzene is used instead of cumene, the main reaction products being the benzylacteate **5** and the diphenylbutane **6** as a mixture of the two diastercoisomers. We explain the new γ-lactones formation according to the sequence of Scheme 1.



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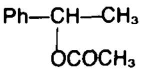
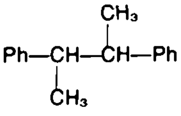


$$Ph-\underset{OCOCH_3}{CH}-CH_3$$

5



$$Ph-\underset{CH_3}{CH}-\overset{CH_3}{CH}-Ph$$

6

It is striking that such a complex scheme leads to the high yield of the lactone **1**, especially considering that the reaction is initiated by two independent oxidation processes (aromatic ring (eqn 2) and acetate anion (eqn 4)). The steps reported in the scheme are substantiated by the results reported below.

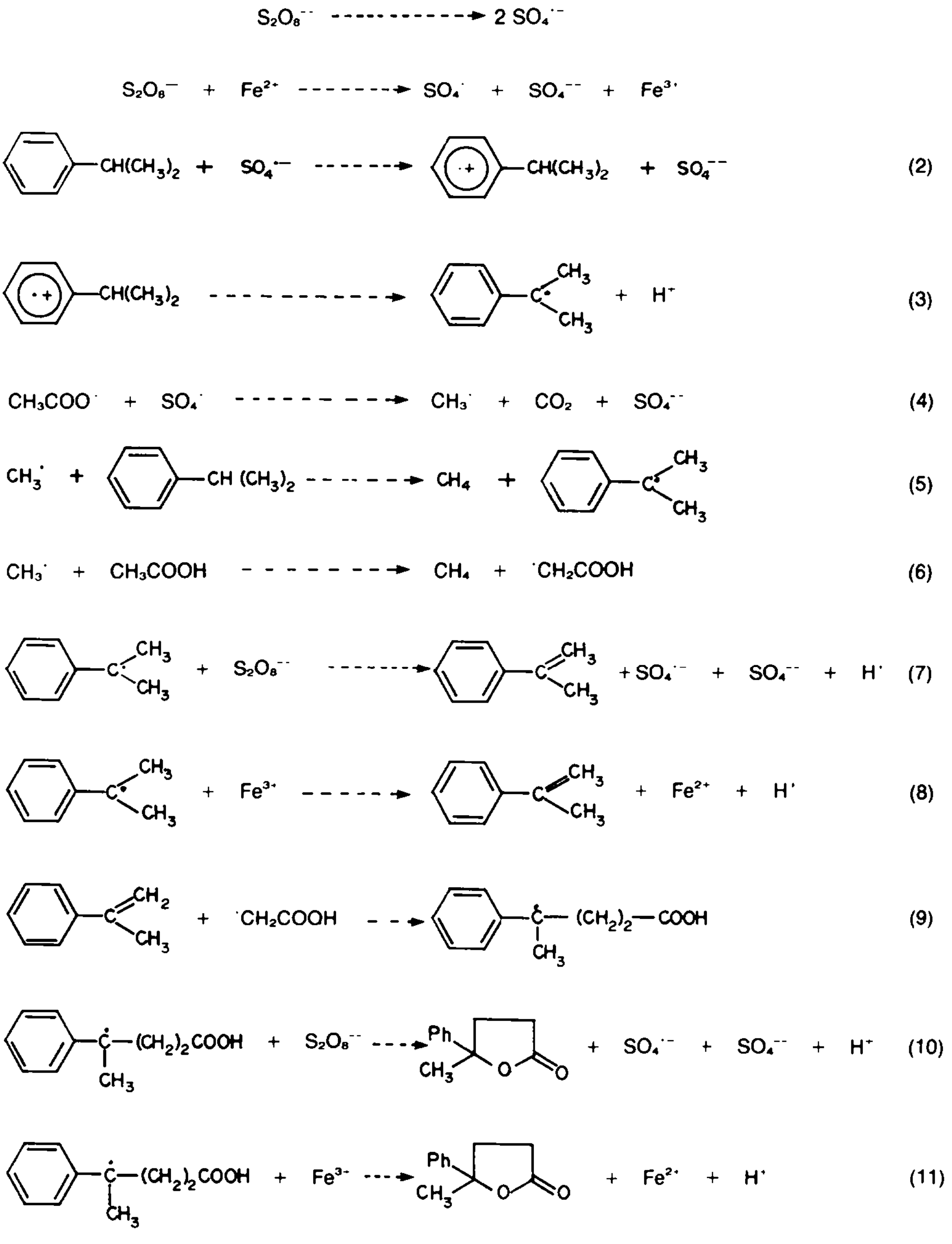
The basis of this successful synthetic combination is just the comparable rate of electron-transfer of the interactions (2) and (4) and the hydrogen transfer of the interactions (5) and (6) in agreement with our recent results[2] and in contrast with previous reports[3].

Lactone **1** is synthesized from α-methylstyrene under similar conditions,[4] but only if the olefin is slowly added to the reaction mixture, whereas very poor results are obtained if α-methylstyrene is suddendly introduced in the reaction mixture.

This means that, in the reaction leading to **1**, cumene acts as a source of α-methylstyrene while carboxymethyl radicals are generated from acetic acid (eqn 6). The fast reaction between the latter species (eqn 9) keeps a low stationary concentration of α-methylstyrene favouring high yield of **1**.

The fact that the lactone **3** is not formed from cumene in the absence of acetic acid, and that with α-methylstyrene the formation of **3** takes place also in the absence of acetic acid,[4] indicates that the role of the methyl radical is determinant in generating the α-methylstyrene. This is consistent with the lower capacity of $^{\cdot}CHMe_2$, generated via oxidative decarboxylation of isobutyric acid, in abstracting hydrogens than $MeCH_2^{\cdot}$ and $Me^{\cdot}$ radicals. Moreover these findings suggest that isobutyric acid, present in large excess, in oxidized at a faster rate than the aromatic ring (eqns 2 and 3).

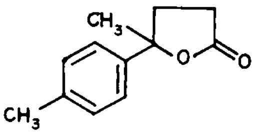
Evidence for the above suggestion is given by the reaction of *p*-cymene with potassium peroxydisulfate in the presence of Cu(II) acetate in isobutyric acid, which does not give rise to the formation of the isobutyrate function at the Me position; on the contrary, the acetate



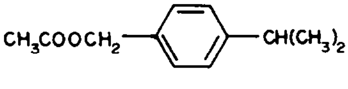
at the Me position is formed by carring out the reaction in acetic acid[1], owing to intermediate formation of the aromatic radical cation.

The different behaviour of ethylbenzene is related to the fact that the secondary benzylic radical is oxidized at slower rate than the tertiary benzylic radical so that it partially dimerizes to **6**; moreover the oxidation of the secondary benzylic radical mainly leads to the acetate **5** and in minor amounts of styrene, explaining in this way the low yield in the lactone **4**.

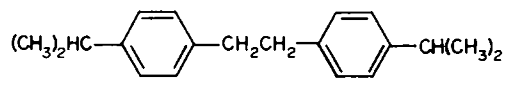
In order to obtain further evidence concerning the different steps and radicals involved in scheme 1, we have investigated the behaviour of *p*-cymene with peroxydisulfate in the absence of catalyst, and in the presence of basic ferric acetate and quinoxaline. The main product in the oxidation of *p*-cymene by peroxydisulfate and basic ferric acetate is the lactone **7**, but significant amounts of the acetate **8** and of the diarylethane **9** are also obtained. Since the oxidation of *p*-cymene[1] by $SO_4^{\cdot-}$ through a radical cation only involves the methyl group (eqn 12), whereas the hydrogen abstraction preferentially involves the isopropyl group (eqn 13), it can be deduced that the lactone **7** if formed by hydrogen abstraction (eqn 13), and **8** and **9** according to eqn (12).



7 (30%)

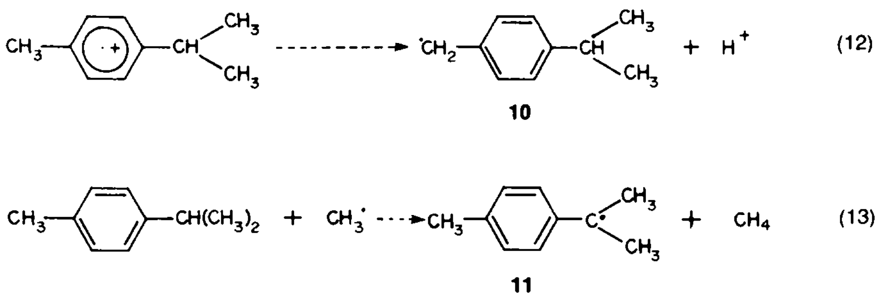


8 (12%)



9 (8%)

With cumene both mechanisms of eqns (3) and (5) operate in the same direction with the formation of the lactone **1**. The amounts of the CO_2 and CH_4 formed agree with this interpretation.

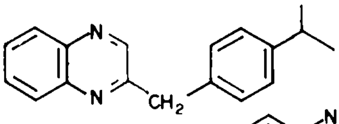


In the absence of the ferric salt the overall yield of **7**, **8** and **9** decreases because considerable amounts of resinous material is formed.

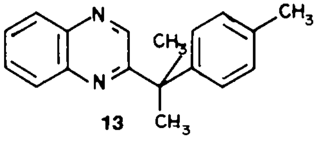
The ratio **7** to **8** is higher than that obtained in the presence of Fe(III). Three benzylic dimers, arising from self- and cross-dimerization of **10** and **11** are formed, whereas only the isomer **9** is formed in the presence of the ferric salt.

This means that peroxydisulfate is able to oxidize significantly the tertiary benzyl radical according to eqns (7) and (10), and much less the primary benzyl radical X; in any case the ferric salt is more effective in oxidizing benzylic radicals minimizing the formation of resinous products. The lactones formation can arise by intramolecular cyclization of the benzyl cation or directly by cyclization of the radical adduct of eqn (9) according to the mechanism previously discussed.[4]

When the oxidation of *p*-cymene is carried out under the same reaction conditions, but in the presence of quinoxaline (a good trap for nucleophilic alkyl and benzyl radicals[5]), yields of **7** and **8** dramatically decrease, **9** is not formed and the main reaction products are the 2-methyl and 2, 3-dimethylquinoxaline and the benzylquinoxalines **12** and **13**.



12



13

These findings clearly indicate that Me radicals and the benzyl radicals **10** and **11** are formed in the reaction. Compounds **12** and **13** are both obtained without the ferric salts, whereas in their presence only **12** is formed indicating that the oxidation rate of the tertiary benzylic radical by Fe(III) is higher than the addition rate to quinoxaline. In any case **12** considerably prevails over **13** supporting the suggestion that **12** arises from the radical cation of *p*-cymene (eqn 12); quinoxaline, trapping most of the Me radicals, dramatically reduces the attack on the i-Pr group (eqn 13).

EXPERIMENTAL

Potassium peroxydisulfate and basic ferric acetate were obtained from Fluka. Alkylbenzenes were commercially available. They were purified by distillation. NMR data were determined in $CDCl_3$ with a TMS internal standard on Jeol C-60 HL spectrometer. IR (nujol) spectra of compounds **1**, **2**, **3**, **4** and **7** showed $-\overset{|}{C}=O$ bond stretching at 1760 – 1770 cm^{-1} (Perkin Elmer 137). Mass data were determined with a GC-Mass system (Varian MAT 112 S) operating at an ionizing potential of 70 eV and an accelerating potential of 816 V.

General procedure. A mixture of potassium peroxydisulfate (0.02 mol), potassium aliphatic carboxylate (0.16 mol), alkylbenzene (0.02 mol), basic ferric acetate (0.005 mol) in aliphatic carboxylic acid (50 ml) was heated at reflux. After 3 hr potassium peroxydisulfate was completely decomposed and generation of CO_2 and CH_4 ceased. CO_2 and CH_4 were determined by trapping on KOH pellets and by GLC molecular sieves (5 Å, 3 m, T = 100°), respectively. The mixture was cooled, diluited with water and extracted with diethylether. The organic extracts were combined together, washed with 0.2 N HCl soln (4 × 100 ml) and with a sat Na_2CO_3aq soln (4 × 100 ml). The organic soln after addition of methyl benzoate, as internal standard, was analysed by GLC on a glass column (2 m) of 10% UCC W 982 on chromosorb (80–100 mesh) with a GLC "Hewlett-Packards" mod. 575. Yields, based on GLC analysis, were calculated on converted alkylbenzenes. In parallel experiments reaction crudes were chromatographed on silica gel (70–230 mesh) using *n*-pentane/diethylether mixture as eluent in order to isolate reaction products, which were purified by distillation. Known products were identified by comparison with authentic samples, the others on the basis of their IR, ^{1}H-NMR, mass spectral data.

5-Methyl-5-phenyl-dihydro-2(3H)-furanone (**1**) *from cumene and acetic acid*

Conversion of cumene. 49% (the theoretical conversion is 50%, assuming 2 mol of $K_2S_2O_8$ for mole of lactone) 81% yield CO_2 (616 mg), CH_4 (192 mg). I[6] (b.p. 116–117/1.8 mmHg; ^{1}H-NMR (δ) 1.70 (s, 3H), 2.47 (m, 4H); mass data (*m*/*e*): 161 (100%), 43 (81%), 105 (49%), 121 (47%), 77 (34%), 51 (26%), 56 (25%), 176 (M^{+}, 7%).

3,5-Dimethyl-5-phenyl-dihydro-2 (3H)-furanone (**2**) *from cumene and propionic acid*

Conversion of cumene. 33% II (mixture of the two diastereoisomers in ratio ~ 1 : 1) 95% yield. Pure diastereoisomers were separated from the mixture via chromatography on silica gel (70–230 mesh) using n-pentane/diethylether 85 : 15 as eluent.

First eluted diastereoisomer. b.p. 101–102/1.4 mmHg; ^{1}H-NMR

(δ) 1.25 (d, 3H, J = 7.5 Hz); 1.74 (s, 3H), 2–3(m, 3H); mass data: 105 (100%), 175 (69%), 43 (66%), 77 (37%), 42 (35%), 131 (23%) 121 (19%), 190 (M$^{\cdot+}$, 5%).

Second eluted diastereoisomer. b.p. 104–106/1.4 mmHg; ^{1}H-NMR (δ): 1.25 (d, 3H, J = 7.5 Hz), 1.67 (s, 3H), 2–3.2 (m, 3H); mass data (*m/e*): 105 (100%), 175 (54%), 43 (38%), 77 (27%), 42 (21%), 131 (11%), 121 (10%), 190 (M$^{\cdot+}$, 3%).

3, 3, 5 - *Trimethyl - 5 - phenyl - dihydro* - 2 (3H) - *furanone* (**3**) *from cumene and isobutyric-acetic acid mixture* (*ratio* 1:1 *v/v*)

Conversion of cumene. 12%. **3** (contaminated by the presence of I, ratio 3/1 = 92:8) 70% yield. ^{1}H-NMR (δ): 1.00 (s, 3H), 1.35 (s, 3H), 1.72 (s, 3H), 2.25–2.67 (ABq, 1H + 1H, J = 14.2 Hz). Mass data (*m/e*): 105 (100%), 43 (54%), 189 (32%), 145 (29%), 77 (27%), 56 (21%), 121 (19%), 204 (M$^{\cdot+}$, 3%).

Compounds **4**, **5** *and* **6** *from ethylbenzene and acetic acid*

Conversion of ethylbenzene. 72%; **4**[6], **5** and **6** were formed in 1%, 48% and 10% yield respectively. **4**, **5** and **6** were identified on the basis of their mass spectra data. Compound **4**, mass data (*m/e*): 56 (100%), 107 (68%), 162 (M$^{\cdot+}$, 56%), 105 (45%), 77 (28%), 51 (23%).

Compounds **7**, **8** *and* **9** *from* p-*cymene and acetic acid*

Conversion of p-*cymene*, 58%. **7** (b.p. 129/1.2 mmHg; ^{1}H-NMR (δ): 1.70 (s, 3H), 2.30 (s, 3H), 2.60 (m, 4H); mass data (*m/e*): 43 (100%), 175 (64%), 135 (33%), 119 (29%), 91 (20%), 65 (12%), 56 (11%), 190 (M$^{\cdot+}$, 10%)), **8** and **9** were formed in 30%, 12% and 8% yield, respectively.

A parallel experiment carried out in the absence of basic ferric acetate gave the following results

Conversion of p-*cymene*: 77%. **7** and **8** were formed in 11.5% and 1% yield, respectively. In addition a mixture of **9**, 1 - (4' - isopropyl - phenyl) - 2 - (4 - methylphenyl) - 2 - methylpropane and 2, 3 - dimethyl - 2, 3 - (4' - methylphenyl) - butane were obtained in 12% yield.

Oxidation of p-*cymene in the presence of quinoxaline*

The general procedure was used in the presence of quinoxaline (0.05 mol). The organic extracts were washed with water and not with 0.2 N hydrochloric acid.

(a) *In the presence of basic ferric acetate.* The conversion of *p*-cymene and quinoxaline were 41.5 and 33%, respectively.

The following substituted quinoxaline were obtained: 2-methylquinoxaline (27%), 2, 3-dimethylquinoxaline (2%) and **12** (^{1}H-NMR (δ) 1.22 (d, 6H, J = 6.8 Hz), 2.85 (m, 1H, J = 6.8 Hz), 4.37 (s, 2H), 7.80 (m, 8H), 8.80 (s, 1H); mass data (*m/e*): **262** (M$^{\cdot+}$), 261, 247, 219, 143) (4.2%). Yields are based on the converted quinoxaline. **7** and **8** were obtained in 4.4% and 1% yield, respectively.

(b) *In the absence of basic ferric acetate.* The conversion of *p*-cymene and quinoxaline were 41% and 43%, respectively.

2-Methyl-quinoxaline (21%), 2, 3-dimethylquinoxaline (2%), **12** (10.2%) and **13** (^{1}H-NMR (δ): 1.86 (s, 6H), 2.3(s, 3H), 7.70 (m, 8H), 8.65 (s, 1H); mass data (*m/e*): 262 (M$^{\cdot+}$), 261, 247, 133; **119**, 105, 91) (2.7%), yields are based on converted quinoxaline. **7** and **8** were presented in 4.7% and 1% (if any) yield, respectively.

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