Coupling of phenoxy and alkyl radicals derived from the photolysis of phenol/ketone pairs: an intermolecular approach to the photo-Claisen rearrangement

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Abstract

Photolysis of phenol/di-t-butylketone mixtures in cyclohexane afforded phenoxy/t-butyl radical coupling products. t-Butyl phenyl ethers were the major products, except for 4-methoxyphenol which underwent considerable methoxy substitution. Mechanistically, coupling of phenoxy and alkyl radicals generated in such way could be considered as the intermolecular counterpart of the photo-Claisen rearrangement. © 1998 Elsevier Science S.A. All rights reserved.

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1. Introduction

The photo-Claisen rearrangement (PCR) of phenyl ethers [1–5] to *ortho* and *para*-alkylphenols has attracted much attention because it is a simple model for the study of a number of basic chemical problems, such as recombination vs. escape of radical pairs from a solvent cage or the effect of solvent viscosity on the course of the reaction. The mechanism of this photochemical process is depicted, in a simplified way, in Scheme 1; it has been proved to be valid to explain the photorearrangement of aryl amides [6], phenoxyacetic acids [7], aryloxyacetophenones [8], benzyl enol ethers [9] as well as phenyl esters (photo-Fries rearrangement) [10].

There are many reports dealing with its mechanism. Chemically Induced Dynamic Nuclear Polarization (CIDNP) [11–13] and other techniques like Electron Spin Resonance (ESR) [14] and Laser Flash Photolysis (LFP) [15] have clearly demonstrated that PCR takes place from the first excited singlet state of phenyl ethers and that a radical pair is involved. Also, the participation of 2,4 and 2,5-cyclohexadienones is well documented [14]. Although it is assumed that PCR is an intramolecular reaction which occurs inside the solvent cage, there is some evidence (crossover experi-
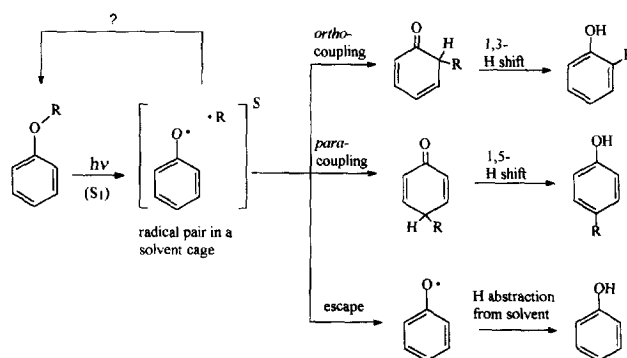
Scheme 1.

ments with different ethers) which point out that, as a minor route, radicals escape from the solvent cage and recombine as free radicals.

In the course of our investigations related to the PCR [16–20] we have developed a novel approach to this reaction. It consists of the photochemical generation of the phenoxy and alkyl radicals involved in the unimolecular rearrangement by means of a bimolecular reaction [21]. Norrish type I fragmentation of di-t-butylketone (DTBK) in the presence of phenols leads to t-butyl phenyl ethers plus their expected products in the intramolecular PCR: *ortho* and *para-t*-butylphenols.

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2. Experimental details

2.1. General irradiation procedures

Pyrex test tubes containing solutions of phenols 1 a–d (10^{-2} M) (from Merck) and di-t-butylketone (3×10^{-2} M) (from Aldrich) in cyclohexane, under Ar atmosphere, were irradiated for 5 h, with a 125 W medium pressure mercury lamp. The photomixtures were concentrated under reduced pressure and the reaction products isolated by column chromatography using hexane–dichloromethane mixtures as eluants.

2.2. Identification of the reaction products

The isolated photoproducts were identified by proton nuclear magnetic resonance (^{1}H NMR) spectroscopy and gas chromatography/mass spectrometry (GC/MS). Also, when it was necessary, comparison with spectral data of authentic samples was made. Alternative synthesis of ethers was carried out according to the method described by Vowinkel [22]. The synthesis of t-butylated phenols was also achieved by conventional Friedel–Crafts reactions [23].

t-Butyl 2,4-di-t-butylphenyl ether (4) was synthesized from 2,4-di-t-butylphenol and t-butanol catalyzed by N,N-dicyclohexylcarbodiimide [22]. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.32 (d, $J = 2.6$ Hz, 1H, 3-ArH), 7.08 (dd, $J = 8.8$, 2.6 Hz, 1H, 5-ArH), 6.96 (d, $J = 8.8$ Hz, 1H, 6-ArH), 1.55 (s, 9H, CH$_3$), 1.38 (s, 9H, CH$_3$), 1.29 (s, 9H, CH$_3$); FT-IR (cm^{-1}): 2966, 1601, 1489, 1397, 1234, 1176, 1088, 930, 815; HRMS (m/z): calc. 262.2300, found 262.2302; MS (EI, m/z): 262 (1), 206 (15), 191 (100), 175 (3), 147 (1), 107 (2), 91 (2), 57 (6).

3. Results and discussion

DTBK was a very suitable ketone for our purposes since its overall decomposition quantum yield is 0.71 ($\phi_{singlet} = 0.31$ and $\phi_{triplet} = 0.40$) the rate constant for this reaction from the triplet excited state is quite high: $7–9 \times 10^9$ s^{-1} [24]. In fact, attempts to perform the same reaction using acetone (where α-cleavage is less favoured) as a source of methyl radicals were unsatisfactory. Moreover, DTBK did not react by abstracting H from phenols since no pinacol products were detected in the photomixtures. Absorption of light by the ketone and not by the phenols was assured because the former absorbs above the Pyrex filter cutoff while the latter do not.

When a mixture of DTBK and phenol (1a–d) in cyclohexane was irradiated, variable amounts of t-butyl phenyl ethers (2a–d, 4) and t-butylphenols (3a–d, 1c) were obtained. Table 1 shows the percentages of products, the phenol conversions and the mass balance of each reaction.

From the mechanistic point of view the above results could be rationalized according to Scheme 2: Norrish type I photofragmentation of DTBK produces t-butyl radicals which

Table 1
Product distribution from irradiation of di-t-butylketone in the presence of phenols

Phenol	Conversion (%)	Mass balance (%)	Product distribution (%)				
			2	3	4	1c	Others
1a	10	92	77	–	–	10	13 [a]
1b	75	83	83	17	–	–	–
1c	52	75	75	–	25	–	–
1d	100	34	34	–	–	57	9 [a]

[a] 2c.
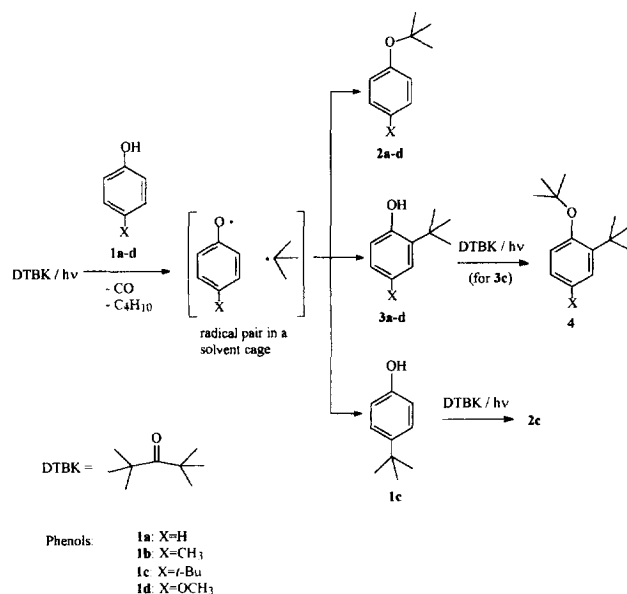
Scheme 2.

abstract H from the phenol present in the medium. Once formed, the phenoxy radical would undergo coupling with another t-butyl radical at *ortho* and *para* ring positions, as well as at the oxygen atom leading to the final products. No cyclohexadienone was isolated from the photomixtures. Due to the Pyrex filter, a secondary PCR of the product is prevented. As a matter of fact, a solution of t-butyl phenyl ether was irradiated under the same conditions but without DTBK and the ether remained unchanged. On the other hand, the possibility of a PCR caused by energy transfer sensitization from the ketone to the ethers is completely ruled out, since it is well established that PCR is a singlet reaction.[1]

The complete absence of *meta*-coupling products confirms the involvement of phenoxy radicals in the process and the formation of ethers constitutes a direct evidence for the reversibility of the PCR from the radical pair stage. Up to

[1] Besides, the triplet energy of DTBK must be ca. 6 kcal/mol lower than that of acetone (79 kcal/mol) and thus energy transfer to t-butyl phenyl ether would be endothermic (E_T of the model compound methyl phenyl ether is 81 kcal/mol). On the other hand, singlet–singlet energy transfer would be even more disfavoured (E_S of acetone = 88 kcal/mol; E_S of methyl phenyl ether = 103 kcal/mol). These data can be found in Refs. [25,26].

date, this feature has been suggested only by indirect proofs such as CIDNP measurements.

4-Methoxyphenol (1d) showed a different behaviour from that of the rest of the studied phenols. In this case methoxy substitution by t-butyl radicals (66%) took place to yield 4-t-butylphenol (1c), which reacted further with t-butyl radicals as indicated by the presence of t-butyl 4-t-butylphenyl ether (2c). In order to rule out a possible direct attack of the phenolic ring by t-butyl radicals, DTBK was irradiated in the presence of 1,4-dimethoxybenzene; no products at all were obtained in this experiment.

Finally, the solvent influence is worth mentioning. While in a non polar solvent like cyclohexane the phenol conversion was significant, in polar solvents (acetonitrile and methanol) there was no apparent reaction. This could be explained if previous association between phenol and ketone (for instance, by means of a hydrogen bond) is a pre-requisite for product formation. In this way, acetonitrile or methanol could be disrupting such hydrogen bonds, keeping the phenol apart from ketone. On the other hand, cyclohexane would not interfere, making it possible for the two molecules to be in close proximity. In order to check this hypothesis the ^{1}H NMR chemical shifts of the 1c and 1d phenolic protons were measured in deuterated cyclohexane, both in the presence and in the absence of DTBK. A remarkable deshielding of the signal occurred upon addition of the ketone: for 1c the δ value increased from 4.8 ppm to 5.3 ppm and for 1d an analogous variation was found between 4.2 ppm and 5.0 ppm. This fact clearly supports a strong preassociation between the reactants in cyclohexane. A parallel deshielding, although not so drastic, was observed in ^{13}C NMR for the ketone carbonyl. Thus, while in deuterated methanol the δ value was 221 ppm, and did not depend on the phenol presence, in deuterated cyclohexane it changed from 215 ppm (ketone alone) to 216 ppm (with 1d) and 217 ppm (with 1c).

4. Conclusions

In summary, photochemical α-cleavage of DTBK in the presence of phenols leads to *ortho, para-t*-butylphenols, and t-butyl phenyl ethers. This constitutes a new approach to PCR, which allows a consideration from an intermolecular perspective. The ketone/phenol system constitutes an interesting model for the study of interactions between alkyl and phenoxy radicals in solution, which simulates the situation of alkyl and phenoxy radicals generated in the PCR.

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