Regio- and Stereo-selectivity Correlation of the Wittig Rearrangement

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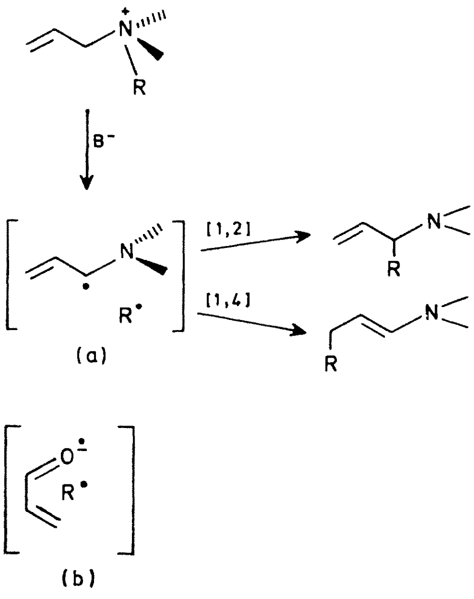
Summary The [1,2]- and [1,6]-rearrangements of s-octyl benzhydryl ether gave products in equal amounts whose formation occurred with 20% retention of configuration, and with complete racemization, for the [1,2]- and the [1,6]-products respectively; these results can be rationalized either by the formation of different non-equilibrating singlet radical pair intermediates, or by an important product formation after diffusion of the intermediate radical pairs.

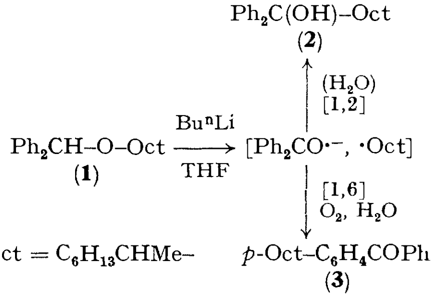
SIMPLE regio- and stereo-selectivity correlation was reported for the Stevens rearrangement, which occurs with partial retention of configuration;[1] on going from [1,2]- to [1,3]- or [1,4]-rearrangements, the amount of racemization increases. This trend is in excellent agreement with the widely accepted intermediacy of a radical pair[1,2] depicted in Scheme 1, pair (a), for the rearrangement of allylammonium species. Translational motion of the radical R• occurs with rotation, and so is responsible for the increased racemization.[3,4]



SCHEME 1

In spite of the quite similar mechanism of the Wittig rearrangement,[3,5] such a correlation was not observed in the Wittig rearrangement of allyl ethers, and in this case, results were rationalized in terms of the *cisoid* conformation of the radical anion intermediate imposing similar motions of the radical R• in the [1,2]- and [1,4]- rearrangements[3] [(b) in Scheme 1].

We report here the abovementioned motion–racemization correlation in the [1,2]- and [1,6]-rearrangements of s-octyl (1-methylheptyl) benzhydryl ether (**1**) (Scheme 2). The two main products of this reaction in tetrahydrofuran (THF) were s-octylbenzhydrol (**2**) and *p*-s-octylbenzophenone (**3**), obtained in a 1 : 1 ratio.† The absolute configurations and optical purities of the ether (**1**)[6] and the benzhydrol (**2**)[7] are known,‡ enabling us to determine that the [1,2]- rearrangement occurred with 20% retention of configuration, and that ketone (**3**) was formed with complete racemization.



$$\begin{tikzcd} & \mathrm{Ph_2C(OH){-}Oct}\ (\mathbf{2}) \\ \mathrm{Ph_2CH{-}O{-}Oct}\ (\mathbf{1}) \arrow[r, "\mathrm{Bu^nLi}", "\mathrm{THF}"'] & {[\mathrm{Ph_2CO^{\cdot -}},\ \cdot\mathrm{Oct}]} \arrow[u, "{(\mathrm{H_2O})\ [1,2]}"'] \arrow[d, "{[1,6]\ \mathrm{O_2, H_2O}}"] \\ \mathrm{Oct = C_6H_{13}CHMe{-}} & p\text{-}\mathrm{Oct{-}C_6H_4COPh}\ (\mathbf{3}) \end{tikzcd}$$

SCHEME 2.

These results are in agreement with the previous findings[3,4] and demonstrate that in the Wittig rearrangement too, larger translational motion of radical intermediates increases the racemization.

Scheme 2 suggests also a quantitative regio- and stereo-selectivity correlation. According to this Scheme, $k_{1,2}/k_{1,6}$ determines the products ratio, and $k_{1,2}/k_r$ and $k_{1,6}/k_r$ (k_r being the average rate constant of rotation and tumbling of the octyl radical) determine the ratios of retention of configuration over racemization[5] observed in the formation of the two products.

Comparison of the product ratio ([(**2**)] : [(**3**)] = 1) and the different retentions of configuration (20 and 0%) shows, however, that our results do not fit such a prediction.

Two modifications of Scheme 2 allowed us to rationalize this lack of quantitative regio- and stereo-selectivity correlation. (i) Primary and secondary geminate recombinations are involved respectively in the [1,2]- and [1,6]- rearrangement of alkyl benzhydryl ethers.[9] Assuming that two non-equilibrating singlet radicals (A) and (B) (Scheme 3),§ having definite but different geometries, are the actual ones

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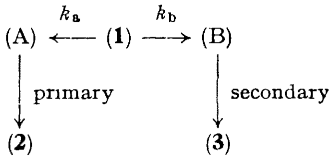
† A very small amount of optically active *o*-s-octyl benzophenone was also isolated.

‡ The previously reported highest optical rotations of the ether (**1**) (ref 6) and the benzhydrol (**2**) (ref. 7) correspond to partially racemized products; chemical correlation of these compounds with octan-2-ol {$[\alpha]_D^{20}$ 8·15°; optical purity 100% (ref. 8)} gives the following highest rotations: compound (**1**): $[\alpha]_D^{20}$ 43·3°; compound (**2**): $[\alpha]_{579}^{20}$ 27·1°.

§ Non-equilibrating radical pairs, generated from the same precursor [as are (A) and (B)], have already been postulated as intermediates of allowed and forbidden rearrangements (ref. 10).

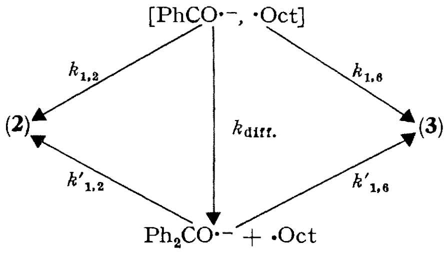
responsible for the formation of these two kinds of product, the regioselectivity (or product ratio) is determined by k_a/k_b, but the stereoselectivities depend on k_{prim}/k_r and k_{sec}/k_r



Scheme 3

Obviously, there is no reason why a simple correlation between these different rate constants should exist (ii) Products are formed not only by recombination of the radical and radical anion inside the cage (rate constants $k_{1,2}$ and $k_{1,6}$), but also after diffusion (rate constants $k_{1,2}$ and $k_{1,6}$), (Scheme 4) ¶

Only cage recombination occurs with partial retention of configuration, diffused radicals give completely racemized products



Scheme 4 Oct = $C_6H_{13}CHMe$–

If diffusion is relatively more important than cage recombination, the product ratio is dependent also on $k'_{1,2}/k_{1,6}$ These rate constants are not related to the retention of configuration, so again independent rate ratios determine the stereo- and the regio-selectivities of the rearrangement

Diffusion was estimated to be less than 20% in the rearrangement of benzyl[5] and benzhydryl[9] alkyl ethers Such a contribution is obviously not important enough to rationalize our results, but further experiments are necessary to corroborate either the first or second explanations

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¶ One of the referees suggested we should discuss the contribution of products of intermolecular origin, we acknowledge the constructive criticism of both referees

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