Unprecedented 1,3-Acyl Shift from Alkyl to Aryl Carbon *via* a Phenyl Anion

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Summary A 1,3-shift of an acyl group from sp^3 to sp^2 carbon is exhibited by 2-methyl- and 2,4-dimethyl-2,4-diphenylpentan-3-one under strongly basic conditions ($\mathrm{Bu^tO^-}$–$\mathrm{Bu^tOH}$, 185 °C) in competition with rearrangement through *β*-enolizable methyl groups and Haller–Bauer type cleavage.

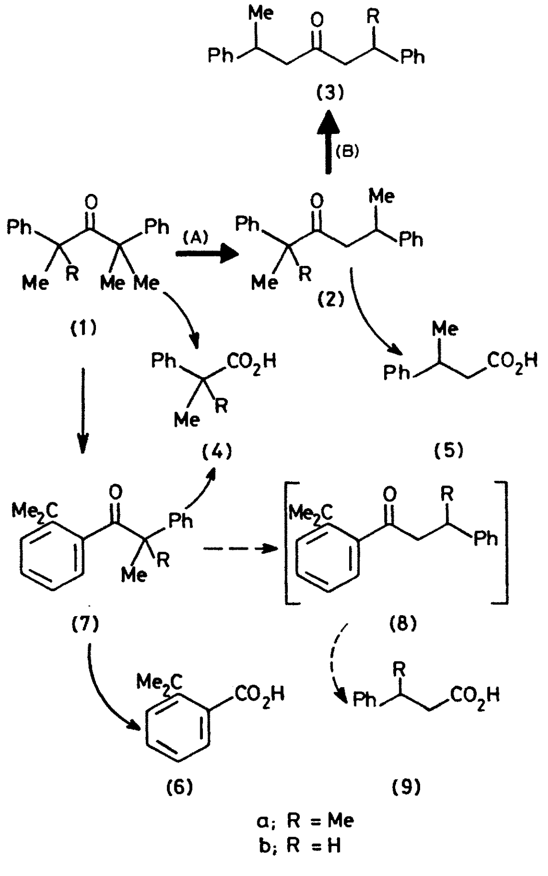
SKELETAL rearrangement *via* *β*-enolizable methyl groups had been observed for di-t-butyl ketone and 5,5,7,7-tetramethylundecan-6-one in our earlier studies[1] and hydrogen–deuterium exchange was found to occur only at the methyl sites. In addition, there was no evidence of any other products. In an extension of this study, we have examined the behaviour of 2,4-dimethyl-2,4-diphenylpentan-3-one (**1a**) and its 2-methyl analogue (**1b**) under similar conditions ($\mathrm{Bu^tO^-}$–$\mathrm{Bu^tOH}$, 185 °C) to find that these compounds are more reactive (two types of rearrangement and cleavage) than the initial aliphatic systems examined. Thus only 10—20% of (**1a**) and (**1b**) was recovered after reaction times which gave only 20% rearrangement in the initial aliphatic examples. A significant portion of the product is acidic, in contrast to the earlier cases, and contains a number of components including 2-isopropylbenzoic acid. The generation of this acid requires an acyl shift from alkyl to aryl carbon.

To a solution of $\mathrm{KOBu^t}$ in $\mathrm{Bu^tOH}$, prepared by dissolving potassium metal in the anhydrous alcohol, was added (**1a**) to give a solution 0·35 M in ketone and 1 M in base. Aliquots were transferred to dried Pyrex tubes under argon and, after degassing and sealing, the tubes were heated for various times in an oil bath at 185 °C. The neutral products were extracted with pentane and the mixture analysed by g.l.c. (3% SE 30). After 192 h, the pentane extract (67% recovery) contained (**1a**) (33%), (**2a**) (30%), (**3**) (30%), and an unidentified component (7%) shown to be isomeric with (**1**)—(**3**) by g.l.c.–mass spectroscopy. Ketones (**2a**) and (**3**) were isolated as oils by t.l.c. and characterized by ^{13}C and ^{1}H n.m.r., i.r., and high resolution mass spectrometry; (**2a**) was also synthesized independently. After longer reaction times, the neutral fraction was almost exclusively (**3**) which in all cases was a 1:1 mixture of diastereoisomers. The aqueous layer after pentane extraction was acidified and the products were extracted with ether. The total acidic product (28% yield) was converted into a mixture of methyl esters by treatment with CH_2N_2. G.l.c. analysis revealed three components: (**4a**) (25%), (**5**) (40%), and (**6**) (35%); the structures of these esters were confirmed by independent syntheses.

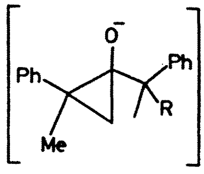
Similar treatment of (**1b**) led, after 223 h, to a neutral fraction (55% recovery) containing (**1b**) (21%), (**2b**) (57%), and (**7b**) (17%) as well as small amounts (*ca.* 5%) of unidentified material. The ketone (**2b**), isolated as an oil, was a 1:1 mixture of diastereoisomers; this mixture was also obtained by independent synthesis. The ketone (**7b**) could only be isolated as a 1:1 mixture with (**2b**) but its structure was deduced from ^{13}C and ^1H n.m.r. spectra. The acidic fraction (40% yield) after conversion into a mixture of methyl esters was found to contain (**4a**) (15%), (**4b**) (24%), (**5**) (53%), and (**6**) (8%). After much longer reaction times, an additional component was visible by g.l.c. having the same retention time as the methyl ester of (**9b**). This indicates that (**7b**) rearranges to (**8b**) in a minor process. From experiments at shorter times, it was apparent that (**4b**) was generated twice as fast as (**4a**).

To examine ^1H–^2H exchange accompanying rearrangement and cleavage of (**1a**), experiments were conducted with Bu^{t}OD (99% deuteriated) as solvent and deuterium assays by mass spectrometry on recovered $[^2H_x]$-(**1a**) samples showed an uptake of 3·5 and 5·3 atoms of ^2H per molecule after 16 and 88 h, respectively. The ^2H n.m.r. spectra† of these samples established that exchange occurred only at aryl sites, with no detectable signals for methyl deuterons.

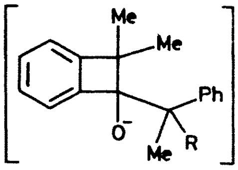
These results provide additional examples of skeletal rearrangement through β-enolizable methyl groups. The corresponding reactions are indicated by steps (A) and (B) in the Scheme,‡ presumably involving intermediates such as (**10**) in the conversion (**1**) → (**2**). The experiments in deuteriated media reveal that the cleavage of (**10**) is highly regioselective such that a tertiary carbanion is generated by ring opening in preference to a primary centre which would regenerate (**1**). The fact that the tertiary anion is benzylic probably governs the course of the cleavage. The experiments also illustrated the relative ease of aryl exchange which is not unexpected since aryl protons are more acidic than alkyl protons.[2] However, isolation of (**6**) suggests the intermediacy of (**11**) from which (**7**) is produced by ring opening. Proton abstraction would be expected to occur at each position on the aryl rings[3] and the formation of an *ortho* phenyl anion could lead to the cyclobutoxide (**11**). Generation of similar species has been observed in a few saturated polycyclic systems under comparable conditions.[4]



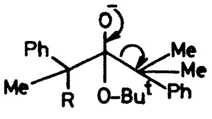
SCHEME



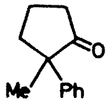
(**10**)



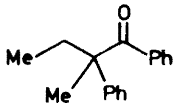
(**11**)



(**12**)



(**13**)



(**14**)

The mixture of acids, isolated as their methyl esters, shows that the ketones with the exception of (**3**) undergo Haller–Bauer type cleavage *via* species such as (**12**) formed by attack of Bu^{t}O$^-$ at the carbonyl group. It has been found that t-butyl esters from ketonic cleavage in other systems do not survive the reaction conditions.[5] It is interesting that (**13**)[6] and (**14**)[7] undergo cleavage exclusively under similar reaction conditions. The driving force for cleavage of (**13**) and (**14**) as well as of (**1**), (**2**), and (**7**) must be the generation of a benzylic anion. This feature is common to the ring opening of (**10**) and (**11**) as well and the fact that rearrangements of (**1**) and (**2**) are competitive with Haller–Bauer cleavage suggests that attack at their carbonyl groups is hindered relative to (**13**) and (**14**). The fact that (**4**) forms more readily from (**1b**) than from (**1a**) supports this notion. In any event, the isolation of (**6**) reveals an unprecedented 1,3-acyl shift from alkyl to aryl carbon.

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† ^2H N.m.r. spectra were obtained at 15·4 MHz with a Varian XL-100-15 system operating in Fourier transform mode with complete proton decoupling.

‡ The hydrocarbon products from Haller–Bauer cleavage have been omitted from the Scheme for simplicity.

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