Concerning the Metal–Ammonia Reduction of Biphenyl-4-carboxylic Acid

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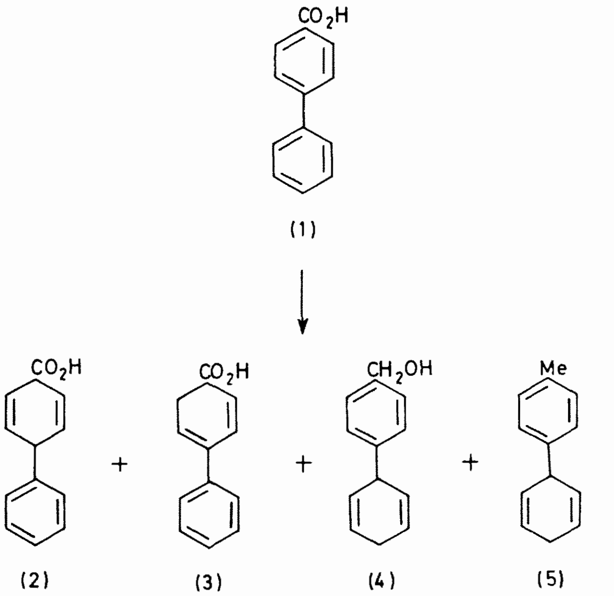
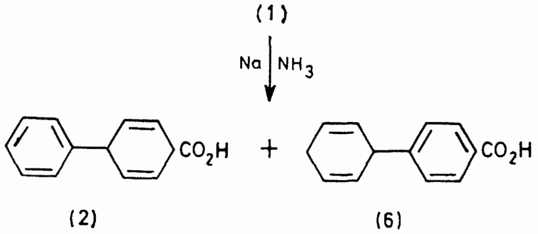
Summary In contrast with a previous report, biphenyl-4-carboxylic acid is reduced by Na–NH_3 to provide only the 1,4- and 1′,4′-dihydrobiphenyl-4-carboxylic acids, by using rapid quenching techniques.

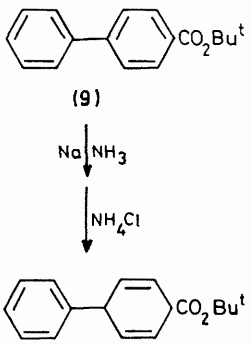
A RECENT communication reports[1] that significant yields of alcohol and hydrocarbon products are obtained in the metal–ammonia reduction of 4-phenylbenzoic acid, and that this is a result of increased conjugation in the reaction intermediates. This is contrasted with the behaviour of 2-phenylbenzoic acid which provides high yields of 2-phenyl-1,4-dihydrobenzoic acid. Thus, Grossel *et al.*[1] report that the reduction of (**1**) with Li or Na (4 mol. equiv.) provides the isomeric reduced acids (**2**) and (**3**), a non-acidic component (**4**) and (**5**) constituting 25% of the yield, and unchanged (**1**).



They suggested that carboxy-function reduction may be related to a variation in protonation sites owing to extended conjugation in this system. Since both the mechanistic and synthetic implications of the above results are rather substantial, we felt it would be important to communicate our own results with the sodium–ammonia reduction of this system which differ considerably from those mentioned above.

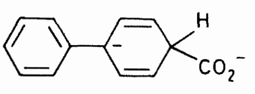
Thus, by using the rapid quenching techniques[2] that we have recently described,† we obtained a complete conversion of (**1**) into only two isomeric products (**2**) and (**6**)‡ in a ratio of *ca.* 3 : 1, respectively, without any detectable amounts of non-acidic products. Hence (**2**) and (**6**) must be regarded as the primary reduction products of (**1**), and compounds (**3**), (**4**), and (**5**) must be the result of secondary reactions.





Compound (**3**) can be dealt with easily as an isomerization product of (**2**) since identical problems have been documented for the reduction of biphenyl itself.[3] It was suggested that (**4**) and (**5**) were produced by a hydride shift in (**7**) which was postulated as an intermediate. However, we would suggest, on the basis of the pK_a values[4] for PhMe *vs.* $MeCO_2^-$, that (**8**) would be more likely than (**7**) as a probable intermediate. Furthermore, the fact that Grossel *et al.*[1] did not observe any (**6**) [which, like (**4**) and (**5**), is reduced in the unsubstituted ring], together with the observation that the 25% yield of (**4**) plus (**5**) is almost identical to the yield reported herein for (**6**), suggests that (**6**) is, in fact, a more likely source of (**4**) and (**5**).§

In addition to the mechanistic importance of these results, we need also to note that the complete conversion of (**1**) into only two products provides a substantial synthetic advantage. These preliminary results[5] also suggest that even



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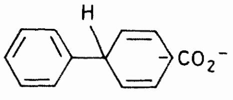

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† As an alternative to the inverse quenching techniques (ref. 2), good results may be obtained with normal quenching provided a large excess of sodium is avoided.

‡ Compound (**6**) was clearly identified by ^1H- and ^{13}C- n.m.r. (2*sp*^{3}, 6*sp*^{2} and 1 C=O carbons, 25·9, 42·2, 124·6, 127·7, 128·2, 130·6, 151·4, and 170·9 p.p.m.); separation by h.p.l.c. followed by recrystallization from cyclohexane gave colourless crystals, m.p. 150—152 °C.

§ This hypothesis will be tested if adequate amounts of (**6**) can be isolated.

greater regioselectivity may be possible in the reduction of the corresponding t-butyl ester (**9**) In this case it appears that reduction in the substituted ring only occurs

Thus, a wide range of results may be possible for this system depending on reaction conditions, and this may explain the contrast of our findings with those of Grossel *et al*[1] For example, it has been noted that substantial amounts of non-acidic products result when alkylbenzoic acids are reduced with ammonium chloride present before the addition of alkali metal[6] Once again we urge that the rapid quenching technique be used to avoid these problems

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