Equilibria in Cyanohydrin Formation from, and the Kinetics of Reduction by Sodium Borohydride of, Substituted Acetylbiphenyls

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Equilibria in cyanohydrin formation from 4'-substituted-4-acetylbiphenyls in 80% v/v dioxan–water at 30 °C and their rates of reduction by sodium borohydride in propan-2-ol at 30, 35, and 40 °C have been studied. The Hammett equation is obeyed by both these reactions. The ρ values are found to be 0.52 and 0.66 at 30 °C for cyanohydrin formation and for borohydride reduction, respectively. These results agree with the earlier conclusion that the transmission of electronic effects of substituents is less in the biphenyl than in the benzene system.

ALTHOUGH the influence of *meta*- and *para*-substituents has been analysed for a large number of reactions of benzene derivatives,[1] relatively few similar investigations have been reported for biphenyl derivatives.[2-8] This prompted us to prepare a number of 4'-substituted-4-acetylbiphenyls and determine their equilibrium constants for cyanohydrin formation, and also to investigate their kinetics of reduction by sodium borohydride with a view to testing the applicability of the Hammett equation to these reactions, and to estimate the extent of transmission of electronic effects of substituents across the biphenyl system relative to that for the benzene system.

EXPERIMENTAL

Materials and Methods.—All the 4'-substituted-4-acetylbiphenyls and 2-acetylfluorene were prepared and purified by known methods.[2,4,9] Acetophenone was purified through its semicarbazone and fractionated under reduced pressure. Their physical constants agreed with the literature values.[2,4,9] Dioxan [10] and propan-2-ol [11] were purified by the methods reported earlier.

The method of Lapworth and Manske [12] was followed to determine the formation constants of the cyanohydrins. The formation constants were calculated by using the equation [13] $K_f = x/(a - x)(b - x)$, where K_f is the formation constant, x is the equilibrium concentration of cyanohydrin, and a and b are the initial concentrations of ketone and hydrogen cyanide respectively.

The kinetics of reduction by sodium borohydride were followed by estimating the concentration of borohydride as a function of time by a standard iodometric method.[14] The experimental procedure was similar to that of Ananthakrishnanadar *et al.*[15] The second-order rate constants k were calculated from the equation $k = \ln[b(a - 4x)/a(b - x)]/(a - 4b)t$, where a and b are the initial concentrations of ketone and sodium borohydride respectively and x is the concentration of sodium borohydride consumed in t seconds.

RESULTS AND DISCUSSION

The experimental results are given in Tables 1 and 2. The results indicate that electron-withdrawing groups increase the reactivity while the reverse is the case for electron-donating groups, in cyanohydrin formation as well as in borohydride reduction. The Hammett equation [16] was applied in these two cases. The Hammett σ_p values [17] were used and an excellent correlation was obtained both for cyanohydrin formation with ρ 0.52 (r 0.999) and for borohydride reduction with ρ 0.66 (r 0.992) at 30 °C. This reveals that a linear free-energy relationship is obeyed by these two reactions. This is illustrated in the Figure.

The ρ value of 0.66 for the reduction by sodium borohydride of 4'-substituted 4-acetylbiphenyls is very low compared with the value of 3.06 obtained by Bowden and Hardy [18] for the reduction of substituted acetophenones and the value of 3.32 obtained by Ananthakrishnanadar

TABLE 1

Formation constants of the cyanohydrins of 4'-substituted-4-acetylbiphenyls in 80% v/v dioxan–water at 30 °C

Substituent	K_f*/l mol^{-1}
H	24.2
F	26.2
Cl	31.7
Br	32.1
NO_2	61.4
CH_3	19.4
Acetophenone	28.2
2-Acetylfluorene	16.7

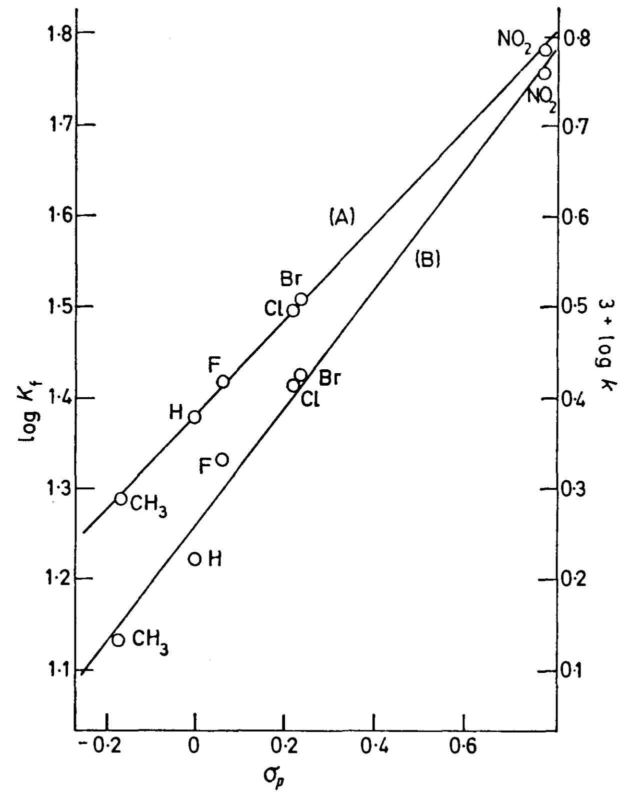
* Formation constants are accurate to ±1.5%.

TABLE 2

Rate constants for the borohydride reduction of 4'-substituted-4-acetylbiphenyls in propan-2-ol

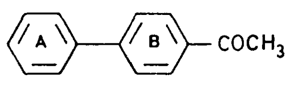
	$10^3 k$/l mol^{-1} s^{-1}		
Substituent	30 °C	35 °C	40 °C
H	1.65 ± 0.01	2.20 ± 0.01	3.11 ± 0.03
F	2.16 ± 0.02	2.55 ± 0.03	3.45 ± 0.01
Cl	2.60 ± 0.02	3.00 ± 0.01	4.05 ± 0.01
Br	2.62 ± 0.01	3.17 ± 0.03	4.15 ± 0.04
NO_2	5.70 ± 0.02	6.50 ± 0.02	7.71 ± 0.03
CH_3	1.34 ± 0.01	1.81 ± 0.01	2.58 ± 0.02
Acetophenone	2.07 ± 0.04	2.60 ± 0.01	3.40 ± 0.01
2-Acetylfluorene	0.90 ± 0.01	1.40 ± 0.01	2.15 ± 0.02

et al.[15] in the reduction of 6-substituted-2-acetonaphthones by sodium borohydride under identical conditions. If biphenyl acts similarly to benzene or naphthalene in transmitting the substituent effects, the ρ value obtained in the present case would be as high as 3.0. The low value may, therefore, be due to the long distance between the substituents and the reaction centre, which will damp the electrostatic effects appreciably and may also be due to the lack of complete coplanarity of the two rings in biphenyl as a result of restricted rotation about the 1,1′-bond,[19] resulting in an interplanar angle of 30—45° between the two rings.[20]

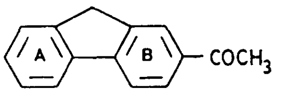


Hammett plots for (A) cyanohydrin formation, (B) borohydride reduction

The ratio of the ρ value for the borohydride reduction of 4′-substituted-4-acetylbiphenyls to that for substituted acetophenones[18] in propan-2-ol at 30 °C is 0.22. This means that approximately one-fifth of the electronic effect of a substituent in the *meta*- or *para*-position of acetophenone is transmitted to the carbonyl group by a 4′-substituent in 4-acetylbiphenyl and may be compared to the value of one-quarter found for the alkaline hydrolysis of ethyl 4′-substituted-biphenylcarboxylates.[3] In view of the similar nature of the rate-determining step (involving nucleophilic attack) in borohydride reduction[21] and in ester hydrolysis,[22] the extent of transmission of electronic effects across the biphenyl system found from the present study is quite reasonable.



(I)



(II)

The data in Table 1 indicate that the formation constant for the cyanohydrin from 4-acetylbiphenyl (I) is lower than that of the cyanohydrin of acetophenone. In 4-acetylbiphenyl the $-M$ effect of the acetyl group may induce a $+M$ response from ring A in opposition to its $-I$ effect. The overall effect of ring A seems to be, therefore, electron releasing and this explains the low formation constant of the cyanohydrin of 4-acetylbiphenyl compared with that of the cyanohydrin of acetophenone. However, the formation constant of the cyanohydrin of 2-acetylfluorene(II) is lower than that of the cyanohydrin of 4-acetylbiphenyl. This may be due to the combined effect of greater conjugation between the acetyl group and ring A in 2-acetylfluorene resulting from the attainment of planarity of the two rings and also the electron-releasing hyperconjugative effect of the methylene bridge. A similar conclusion can also be arrived at from the rate constants presented in Table 2 for the borohydride reduction of 4-acetylbiphenyl, acetophenone, and 2-acetylfluorene.

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