Anal. Calcd. for $C_{12}H_{15}N_3O_6$: C, 48.45; H, 5.08. Found: C, 48.48; H, 5.46.

Preparation of Authentic 1,3-Dimethyl-5-*sec*-butylbenzene (IV).—The 3,5-dimethylpropiophenone was synthesized from 3,5-dimethylbenzoyl chloride and diethylcadmium as described for the preparation of 3,5-dimethyl-*n*-butyrophenone. The yield of ketone was 48%, b.p. 110° (15 mm.), n^{25}D 1.5143.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.54; H, 8.64. Found: C, 81.18; H, 9.12.

The ketone formed a semicarbazone, m.p. 167°.

Anal. Calcd. for $C_{12}H_{17}N_3O$: C, 65.72; H, 7.81. Found: C, 65.64; H, 7.89.

Methylethyl-(3,5-dimethylphenyl)-carbinol was prepared from 45 g. of 3,5-dimethyl-*n*-propiophenone and methylmagnesium iodide in the usual manner, b.p. 109–111° (15 mm.), yield 24 g. (48%), n^{24}D 1.5148. This carbinol was reduced with hydrogen and copper chromium oxide catalyst to yield 21 g. of 1,3-dimethyl-5-*sec*-butylbenzene (IV), b.p. 95–96° (16 mm.), n^{24}D 1.4929.

Anal. Calcd. for $C_{12}H_{18}$: C, 88.81; H, 11.19. Found: C, 88.96; H, 11.50.

The trinitro derivative crystallized from alcohol in granules, m.p. 91°.

Anal. Calcd. for $C_{12}H_{15}N_3O_6$: C, 48.45; H, 5.08. Found: C, 48.18; H, 5.07.

Rearrangements with Aluminum Chloride.—The aluminum chloride was added to the hydrocarbon and the mixture warmed with stirring on a steam-bath. After heating for 3.5 hours, the complex was decomposed with iced hydrochloric acid and the hydrocarbon isolated in the usual manner.

1,3-Dimethyl-4-*n*-butylbenzene (I).—The product from 102 g. of hydrocarbon and 23 g. of aluminum chloride was fractionated at 16 mm.: (a) 17 g., 30–70°; (b) 8.5 g., 70–100°; (c) 1 g., 100–103°; (d) 31 g., 103–105°. Fraction (a) was identified by its trinitro derivative as containing mainly *m*-xylene. The trinitro derivative of (c) and (d) crystallized from alcohol in fibers, m.p. 94°, and it did not depress the melting point of the trinitro derivative, m.p. 95° of authentic II. The tribromo derivative of (d) melted at 53° and did not depress the melting point (53°) of the same derivative of authentic II.

Anal. Calcd. for $C_{12}H_{15}Br_3$: C, 36.10; H, 3.79. Found: C, 35.73; H, 3.80.

The principal trialkylbenzene formed by rearrangement of I is therefore 1,3-dimethyl-5-*n*-butylbenzene (II). The infrared spectrum of a center cut from redistillation of (d) through a Podbielniak column indicated the presence of a small amount of unchanged I.

1,3-Dimethyl-4-*sec*-butylbenzene (III).—The product from 133 g. of hydrocarbon and 29 g. of aluminum chloride was fractionated at 16 mm.: (a) 12 g., 45–50°; (b) 7 g., 50–91°; (c) 18 g., 91–95°; 63 g., 95–96°. Fraction (a) was mainly *m*-xylene. The trinitro derivative of (c) and (d) crystallized from alcohol in granules, m.p. 91°, mixed m.p. with the same derivative (m.p. 91°) of authentic IV, 90–91°. This rearrangement product was therefore 1,3-dimethyl-5-*sec*-butylbenzene. The infrared spectrum of a center cut of (d) indicated the presence of a small amount of unchanged III.

1,3-Dimethyl-4-isobutylbenzene (V).—The product from 100 g. of hydrocarbon and 20 g. of aluminum chloride was fractionated at 17 mm.: (a) 12 g., 50–65°; (b) 6 g., 80–91°; (c) 5 g., 91–98°; (d) 20 g., 98–101°.

Fraction (a) was mainly *m*-xylene. Carbon and hydrogen analyses of (d) agreed with the values of a dimethylbutylbenzene, and the infrared spectrum indicated a mixture of unchanged V and VI.

Anal. Calcd. for $C_{12}H_{18}$: C, 88.81; H, 11.19. Found: C, 88.66; H, 11.46.

The trinitro derivative of fraction (d) melted at 85–86°, and may be either the derivative of VI or a eutectic mixture.

Anal. Calcd. for $C_{12}H_{15}N_3O_6$: C, 48.45; H, 5.08. Found: C, 48.50; H, 5.37.

Nitrations.—The trinitro derivatives of the hydrocarbons were prepared by adding 2 ml. of the hydrocarbon slowly with shaking to an ice-cold mixture of 10 ml. of concd. sulfuric acid and 5 ml. of fuming nitric acid. After all of the hydrocarbon had been added, the mixture was warmed on a water-bath at 60–80° and then poured onto ice. The nitro compound was separated, washed with water and recrystallized from alcohol.

The trinitro derivative of 1,3-dimethyl-4-isobutylbenzene, not previously reported, melted at 115–116°. A mixture of this derivative and trinitro-1,3-dimethyl-5-*t*-butylbenzene (m.p. 112°) softened at 80–85° and melted at 86°.

Anal. Calcd. for $C_{12}H_{15}N_3O_6$: C, 48.45; H, 5.08. Found: C, 48.76; H, 5.22.

Brominations.—The brominations were all carried out with liquid bromine in the presence of iron powder as described by Hennion and Anderson.[4]

Infrared Absorption Spectra.—The absorption spectra were determined by Dr. E. E. Pickett of the spectrographic laboratory of the University of Missouri and by J. M. Shackelford, on a Beckman Infrared Spectrophotometer, Model IR-2, cell length 0.025 mm. The samples for spectroscopic analysis were center cuts obtained by redistillation of the trialkylbenzene fractions through a Podbielniak column.

COLUMBIA, MO.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

Conjugation in the Biphenyl System

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The dissociation constants of 3-hydroxybiphenyl, 4-hydroxybiphenyl, 3′-nitro-4-hydroxybiphenyl, 4′-nitro-4-hydroxybiphenyl, 2-hydroxyfluorene and 2-hydroxy-7-nitrofluorene have been measured by a spectrophotometric method in aqueous borate–boric acid buffers. The data are interpreted as indicating a lack of significant contribution by contributing structures involving conjugation between the two benzene rings to the electronic structures of the ground states of the conjugate bases of these compounds. An explanation of this conclusion is given.

Recent studies of the effect of a group X in the 3′- or 4′-position on the reactivity of a substituent Y in the 4-position of a substituted biphenyl have raised some question as to the ability of the biphenyl system to transmit substituent effects by resonance hybridization involving the quinonoid structure I.[1] The studies thus far reported[1a,2] have been concerned with substituted biphenyls of type II, where X = Br or NO_2 and Y = COOR (R = H or alkyl). While these studies demonstrated that substituent effects are transmitted through the biphenyl system, the substituents were of such a nature that strong resonance interactions of type III would not be expected.

We have prepared 3′- and 4′-nitro-4-hydroxybiphenyl (II, X = NO_2, Y = OH) and measured their dissociation constants. These have been com-

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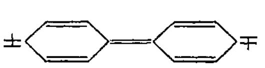
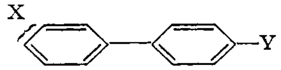
[1] For reviews see (a) E. Berliner and E. Blommers, THIS JOURNAL, **73**, 2479 (1951), and (b) G. H. Beaven, D. M. Hall, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 854 (1952).

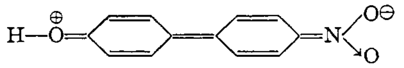
[2] N. N. Lichtin and H. P. Leftin, THIS JOURNAL, **74**, 4207 (1952).



I



II



III

pared with the dissociation constants of 3- and 4-hydroxybiphenyl in order to evaluate the contribution of structures of type III to the ground state of the corresponding systems. In addition, similarly substituted fluorene derivatives were studied in order to assess the importance of coplanarity of the benzene nuclei as required by III for the transmission of substituent effects of resonance.

Methods and Results

Available Phenols.—3-Phenylphenol, 4-phenylphenol and 3,5-dimethylphenol were Eastman Kodak Co. samples purified by recrystallization following Norit decolorization. Melting points duplicated literature values in each case.

4'-Nitro-4-hydroxybiphenyl.—This material was prepared in 31% over-all yield by the procedure of Jones and Chapman,[3] nitrating 4-phenylphenyl benzoate with fuming nitric acid and hydrolyzing the resulting nitro ester. The purified product had a m.p. 202–204° in agreement with the literature.[3]

3'-Nitro-4-hydroxybiphenyl.—*p*-Iodoanisole was prepared by reaction of diazotized *p*-anisidine with potassium iodide solution. The product, obtained in 50% yield, had m.p. 47–50° in essential agreement with the literature.[4] *m*-Iodonitrobenzene, m.p. 35–38°, was prepared by action of potassium iodide solution on diazotized[5] *m*-nitroaniline after the general method of Dennett and Turner.[6]

p-Iodoanisole (34.8 g.) and *m*-iodonitrobenzene (19 g.) were mixed and heated to 225–235°, whereupon bronze powder (25 g.) was added with stirring during a 40-minute period. After an additional 45-minute period of heating and stirring, the mixture was cooled, pulverized and extracted with ether in a Soxhlet thimble for 5 hours. The ether was evaporated from the extract and the residue was steam distilled. The non-volatile residue, recovered by ether extraction, was 12 g. of brown, low-melting solid. This was leached with four 50-ml. portions of warm hexane. Evaporation led to a gummy yellow solid. Repetition of the hexane treatment followed by crystallization from hexane produced 2.9 g. (16%) of impure 3'-nitro-4-methoxybiphenyl, m.p. 72–76°. Recrystallization from methanol (30 ml.) gave 1.8 g. of reasonably pure product, m.p. 75–77°.

Anal. Calcd. for $C_{13}H_{11}O_3N$: C, 68.11; H, 4.83. Found: C, 68.94; H, 4.94.

The above methoxy compound (1.43 g.) was dealkylated by addition of constant boiling hydrobromic acid (3.5 ml.) over ten minutes to its refluxing solution in acetic acid (12 ml.). Refluxing was continued until a test sample of the reaction mixture was completely soluble in 5% potassium hydroxide solution. The mixture was thrown into water (150 ml.) and the product was extracted into ether. Solvent evaporation gave a residue which was dissolved in boiling 5% potassium hydroxide solution (100 ml.). Cooling produced red crystals. These were treated with 4 *N* hydrochloric acid (12 ml.) during 16 hours, whereupon a green-yellow solid, 0.68 g., m.p. 102–107°, resulted. This was purified by three recrystallizations from benzene, followed by vacuum sublimation. The pure 3'-nitro-4-hydroxybiphenyl so obtained had m.p. 108–108.5°.

Anal. Calcd. for $C_{12}H_9O_3N$: C, 66.97; H, 4.21. Found: C, 66.82; H, 4.31.

2-Hydroxyfluorene.—This material was prepared in 24% yield *via* diazotized 2-aminofluorene.[7] It had m.p. 170–170.5°, in agreement with the recorded value.[8]

2-Nitro-7-hydroxyfluorene.—2,7-Dinitrofluorene, m.p. *ca.* 330°, was obtained in 42% yield by the method of Courtot.[9] This was partially reduced to 2-amino-7-nitrofluorene using ammonium sulfide after the procedure of Cislak and Hamilton.[10] The crude nitrated amine was purified first by extraction with hot, dilute hydrochloric acid, then by continuous extraction with ether for 20 hours. Solvent evaporation gave a 15% yield of material of m.p. 220°, which was employed without further purification. This product (1.33 g.) was dissolved in hot, dilute sulfuric acid (175 ml. of acid, 500 ml. of water). The solution was cooled to 10°, precipitating a fine solid. Sodium nitrite (0.45 g.) in water (10 ml.) was added, and the mixture was allowed to stand for an hour at 10°, when the fine solid had dissolved. The solution was filtered with stirring into 6 *N* sulfuric acid (2 liters) at 80°. The mixture was boiled, then cooled and the yellow product (1.06 g.) was filtered off. The crude product was purified by chromatographing on alumina from benzene solution, developing the chromatogram with a 9:1 benzene–methanol mixture. The product so purified had m.p. 253–255° dec. The literature melting point is 250°.[11] Since our investigation, a superior preparative method has been developed.[12]

Anal. Calcd. for $C_{13}H_9O_3N$: C, 68.72; H, 3.99. Found: C, 68.71; H, 4.29.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectra of the acid and conjugate base forms of the phenols under consideration were necessary for selection of the wave lengths most suitable[13] for the quantitative determination of the concentrations of these forms present together in an equilibrium mixture. The spectrum of the acid form of each phenol was determined in aqueous 0.1 *N* hydrochloric acid, while the conjugate base spectra were obtained in 0.1 *N* sodium hydroxide solution.

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(3) B. Jones and F. Chapman, *J. Chem. Soc.*, 1829 (1952).

(4) F. F. Blicke and F. D. Smith, THIS JOURNAL, **50**, 1229 (1928).

(5) R. Manske, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 404.

(6) H. G. Dennett and E. E. Turner, *J. Chem. Soc.*, 476 (1926).

(7) W. E. Kuhn, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 447.

(8) F. E. Ray, *J. Org. Chem.*, **14**, 394 (1949).

(9) C. Courtot, *Ann. chim.*, **14**, 83 (1930).

(10) F. E. Cislak and C. S. Hamilton, THIS JOURNAL, **53**, 746 (1931).

(11) F. Bielschowsky, *Biochem. J.*, **39**, 287 (1945).

(12) J. H. Weisburger and E. K. Weisburger, *J. Chem. Soc.*, 758 (1954).

(13) M. G. Mellon, "Analytical Absorption Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 369.

Solutions were made by pipetting aliquots from a carefully prepared 95% ethanol stock solution of the appropriate phenol into the standard acid or base. A model DU Beckman quartz spectrophotometer was used for the measurements, and readings were taken every 5–10 mμ in the 240–400 mμ region. The wave lengths and molar extinction coefficients at absorption maxima are given in Table I.

Table I

Wave Lengths and Molar Extinction Coefficients at Absorption Maxima for Some Phenols at 26°

		Acid form		Conjugate base form	
No.	Compound	λmax, mμ	$\epsilon \times 10^{-3}$	λmax, mμ	$\epsilon \times 10^{-3}$
1	3-Hydroxybiphenyl	250	13.7	305	4.13
2	4-Hydroxybiphenyl	260	17.8	287.5	20.1
3	4′-Nitro-4-hydroxybiphenyl	340	14.2	400	15.1
		232	12.5	265	12.2
4	3′-Nitro-4-hydroxybiphenyl	263	24.8	294	23.4
5	2-Hydroxyfluorene	268	19.9	294	20.8
		300–312	6.1–6.3		
6	2-Nitro-7-hydroxyfluorene	370	16.7	430	17.6
		250	9.12	270	12.5
7	3,5-Dimethylphenol	271	1.17	290	2.56
		278	1.17		

In most cases wave lengths corresponding closely to those of maximum absorption of the acid and conjugate base forms were selected as suitable for analytical purposes. In some cases, spectra were partially redetermined on fresh solutions of the acid and conjugate base forms to be able to locate more precisely the wave lengths of maximum absorption.

Dissociation Constants.—The apparent dissociation constant K_a for a monobasic acid is defined as

$$K_a = (C_{H^+})(C_{A^-})/C_{HA}, \text{ so that}$$
$$pK_a = -\log (C_{A^-}/C_{HA}) + pH$$

The data required for calculation of pK_a values according to the latter equation were obtained as follows. A standard Clark and Lubs borate–boric acid buffer solution containing an aliquot of stock ethanol solution of the appropriate phenol was prepared. Optical density measurements were made on each such mixture at the two wave lengths previously chosen for analytical purposes. The *p*H of the buffer solution was checked at the temperature of the optical measurement with a standardized glass electrode in a Beckman *p*H meter. Solution temperature was maintained at 26.0 ± 0.3° in most cases during optical density measurements by the use of thermostated sample cells. The blank cell used in the spectrophotometer contained identical buffer solution as that used to dilute the stock solution of the phenol being measured. The molar concentrations of the acid and conjugate base forms of the phenols were then calculated from the optical density data by solving the two simultaneous equations

$$D_1 = \epsilon_1 \times C_{HA} + \epsilon'_1 \times C_{A^-}$$
$$D_2 = \epsilon_2 \times C_{HA} + \epsilon'_2 \times C_{A^-}$$

where D_1 and D_2 are the optical densities, ϵ_1 and ϵ_2 the molar extinction coefficients of the acid form and ϵ'_1 and ϵ'_2 the molar extinction coefficients of the conjugate base form of the phenol at the two selected wave lengths. The validity of Beer's law in the present system, and hence the validity of the above equations for calculating concentrations, is indicated by the fact that the calculated sums, $C_{HA} + C_{A^-}$, of the acid and conjugate base forms agreed in general with the known analytical concentration of phenol used to within ±2%. A slight modification[14] of the above equations was used to calculate the desired concentrations in the cases of 3-hydroxybiphenyl and 3,5-dimethylphenol. The dissociation constants observed for the phenols studied are given in Table II.

Table II

Dissociation Constants in Aqueous Boric Acid–Borate Buffers of Some Phenols at Several Temperatures

		pKa^a		
No.	Compound	19°	26°	38°
1	3-Hydroxybiphenyl[b]	..	9.50	..
2	4-Hydroxybiphenyl[c]	..	9.40	9.24
3	4′-Nitro-4-hydroxybiphenyl	9.07	8.95	8.77
4	3′-Nitro-4-hydroxybiphenyl	..	9.14	..
5	2-Hydroxyfluorene	..	9.51	..
6	2-Nitro-7-hydroxyfluorene	9.08	8.94	8.77
7	3,5-Dimethylphenol[d]	..	9.98	..

[a] Values given for No. 1 and 7 are mean values for determinations at two *p*H's. The values for the remainder of the compounds are mean values for determinations at three *p*H's at 26°, the average deviations being about 0.01 pK_a unit in each case. The values at 19 and 38° are for one *p*H only. [b] pK_a values of 9.59 and 9.60 at 25° have been found spectrophotometrically and potentiometrically in buffers for this compound. See F. Kieffer and P. Rumpf, *Compt. rend.*, **238**, 360 (1954). [c] A pK_a value of 9.51 at 25° in buffers has been reported by Kieffer and Rumpf (ref. *b*). [d] This compound has been included as a control. Literature values for its pK_a at 25° are 10.09, 10.18 (by potentiometric titration; see G. W. Wheland, R. M. Brownell and E. C. Mayo, This Journal, **70**, 2492 (1948)) and 10.15 (see F. Kieffer and P. Rumpf, *Compt. rend.*, **230**, 2302 (1950)).

The pK_a values in Table II are not corrected to zero ionic strength. As a result, some variation in the dissociation constant of each compound measured at different *p*H values would be expected as a consequence of variations in ionic strength from one Clark and Lubs buffer mixture to another. That this effect is quite small, however, is shown by the facts that the average deviation in pK_a values determined at different *p*H's was only about 0.01 unit, and that the pK_a values found for previously measured phenols were in close agreement with the literature. By considering the effect of salt concentration on the pK_a value of *m*-nitrophenol,[15] it is estimated that correction to zero ionic strength of the pK_a values in Table II would not raise each pK_a value by more than perhaps 0.1 unit.

Discussion

Comparison of the pK_a value (at 26°) of 4′-nitro-4-hydroxybiphenyl (IV), 8.95, with that of 4-hydroxybiphenyl itself, 9.40, indicates that the 4′-nitro substituent increases the acidity of 4-hydroxybiphenyl less than threefold. This observation contrasts sharply to that involving phenol itself, where introduction of a 4-nitro substituent increases the dissociation constant by a factor of almost 650.[14] In addition, comparison of the pK_a values for 4′-nitro-4-hydroxybiphenyl (IV) and 3′-nitro-4-hydroxybiphenyl (V), 9.14, shows that the former, in

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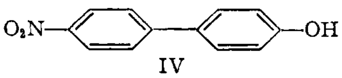
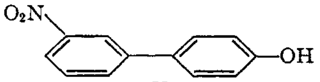
[14] C. M. Judson and M. Kilpatrick, This Journal, **71**, 3110 (1949).

[15] L. Michaelis and R. Kruger, *Biochem. Z.*, **119**, 307 (1921).

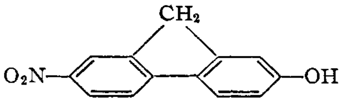
which a direct interaction III between the OH and NO_2 groups is in principle possible, is only the slightly stronger acid of the pair (K_a(IV)/K_a(V) = 1.55).



IV



V



VI

The difference (0.19 pK_a unit) is only one-sixth of that observed between *p*-nitrophenol (7.14) and *m*-nitrophenol (8.35).[14] These data force the conclusion that resonance interactions of type III are at best of only secondary importance in the ground state of the biphenyl system.

It follows that the approximate threefold enhancement of the acidity of 4-hydroxybiphenyl on introduction of a 3′- or 4′-nitro substituent must be accounted for in terms of the inductive effect. On the basis of the powerful inductive effect of the nitro group[16] and the assumption that in the nitrophenyl ring the nitrobenzene resonance is operative, it seems reasonable to regard the nitrophenyl group in the system under discussion an inductively operating, electron-attracting substituent. This view finds support in the slightly greater acidity of the 4′- over the 3′-nitro compound since in the former the nitrobenzene resonance selectively decreases the electron density at the point of attachment of the hydroxyphenyl system. The situation may be likened to that encountered in the *m*- and *p*-nitrobenzoic acids of pK_a 3.49 and 3.43, respectively,[17] and the effect is of the same order of magnitude, 0.19 *vs.* 0.06 pK unit. The slightly greater effect with change in substituent orientation in the case of the hydroxybiphenyl system is in accord with the greater susceptibility of the phenolic ionization (ρ 2.00) to substituent effects as compared to that of the benzoic acid ionization (ρ 1.00).[17]

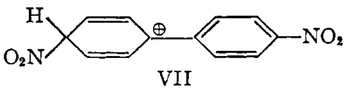
Various lines of physical evidence[1b,18] have suggested that biphenyl derivatives may not be coplanar even when lacking bulky 2,2′-substituents. We have attempted to test the hypothesis that noncoplanarity of the benzene rings in the biphenyl system is responsible for the failure of the system effectively to transmit substituent effects by resonance by a measurement of pK_a values for corresponding phenols in the essentially planar[19] fluorene system.

Table II indicates that K_a for 2-hydroxyfluorene is greater than K_a for 4-hydroxybiphenyl by a factor of only 1.29, while the acid strengths of 2-nitro-7-hydroxyfluorene (VI) and 4′-nitro-4-hydroxybiphenyl (IV) are essentially identical. These data offer no evidence for any relationship between coplanarity and acid strength in the present series, a conclusion which is at variance with that reached by Sherwood and Calvin[20] in their study of the base strengths of aminonitrobiphenyls. Conceivably the practical identity of the dissociation constants in the analogously substituted biphenyl and fluorene systems might be due to the fortuitous selection of 26° as the temperature of comparison. The data of Table II reveal, however, that this *identity* of dissociation constants in the two systems in independent of temperature, although the value of pK_a itself varies measurably with temperature in each system. Thus no differences are apparent in the enthalpies or entropies of dissociation in the two systems attributable to lack of planarity in the biphenyl system.

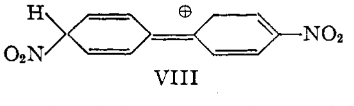
We suggest that the present failure of the biphenyl system to transmit the substituent effects anticipated is due to the high energy of the quinonoid form III occasioned by the sacrifice of the resonance energy of *two* aromatic sextets in reaching it. In *p*-nitrophenol the analogous quinonoid structure is achieved at the expense of the resonance energy of only a single benzene system.

Since the extra structures possible for the conjugate base of 4-hydroxybiphenyl, not accessible to the conjugate base of the 3-hydroxy compound, are of the quinonoid type found unimportant in the case of the above 3′- and 4′-nitro analogs, it is not surprising that there is no significant difference in the acid strengths of 3-hydroxy- and 4-hydroxybiphenyl (pK_a 9.50 and 9.40, respectively, at 26°).

The failure of the quinoid structures to contribute to the ground state of the biphenyl systems studied clearly cannot be extended to the photoexcited states, since the compounds here examined show the "resonance band" indicative of conjugation of the benzene rings in biphenyls[1b,21] (*cf.* Table I). It should be further pointed out that the absence of quinonoid contributions to the ground state and the explanation offered above in no way invalidates the attractive explanation[1a] for the formation of 2,4′- and 4,4′-dinitrobiphenyl on nitration of 4-nitrobiphenyl to the exclusion of the 3′-nitro derivative expected by analogy to the case of the dinitration of benzene. In this instance the attack of the nitronium ion *per se* raises the energy of the system in the direction of the intermediate VII. In VII one aromatic sextet has already been destroyed, so that the hybridization VII ↔ VIII ↔ etc. becomes important with consequent lowering of the barrier to substitution in the 4′-position.



VII



VIII

The data at hand do not permit a decision regarding transmission of substituent effects by resonance

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[16] G. W. Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 172.

[17] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 189.

[18] O. Bastiansen, *Acta. Chem. Scand.*, **3**, 408 (1949).

[19] G. Rieveschl and F. E. Ray, *Chem. Revs.*, **23**, 287 (1938).

[20] D. W. Sherwood and M. Calvin, This Journal, **64**, 1350 (1942).

[21] L. W. Pickett, M. Groth, S. Duckworth and J. Cunliffe, *ibid.*, **72**, 44 (1950)

across a biphenyl system in those cases where the kinetic properties of the reacting group are concerned (*e.g.*, II, X = OCH_3, Y = $COOCH_3$). It would be predicted on the basis of the results reported herein, however, that resonance transmission of substituent effects should be much less important in the biphenyl system than has been found to be the case for benzene derivatives. This view finds experimental confirmation in the study of Berliner and Liu on the comparative rates of hydrolysis of esters of benzoic and *p*-phenylbenzoic acids,[1a,22] and in the comparative reactivities found by Miller for the chlorine atoms in 4-chloro-3,5-dinitrobiphenyl and 4-chloro-3,4′,5-trinitrobiphenyl.[23] The chlorine atom in the latter compound is only 2 to 3 times as reactive as that in the former, whereas the chlorine in picryl chloride is some 6 × 10^5 times as reactive as that of 2,6-dinitrochlorobenzene.[23]

Acknowledgment.—We wish to express our appreciation to the Monsanto Chemical Company for a fellowship held by one of us (V. P. K.) which made the early completion of this work possible.

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[22] E. Berliner and L. H. Liu, This Journal, **75**, 2417 (1953).

[23] Private communication from Dr. J. Miller, University of Western Australia.

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NOTES

The Conversion of Carboxylic Acid Hydrazides to Amides with Raney Nickel

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Raney nickel has been found to cleave carboxylic acid hydrazides to form amides and ammonia. The reaction consists simply of heating a solution of the acid hydrazide in alcohol for several hours with a relatively large amount of the catalyst.

$$RCONHNH_2 \xrightarrow{\text{Raney Ni}} RCONH_2 + NH_3$$

The cleavage represented above does not take place, however, when a catalytic amount of nickel and the hydrazide are heated in an atmosphere of hydrogen. Thus, benzoic acid hydrazide with about ten parts by weight of Raney nickel was changed to benzamide. On the other hand, benzoic acid hydrazide and a trace of Raney nickel heated under an atmosphere of hydrogen in the Parr shaker did not undergo reduction. Starting material was recovered. Under similar conditions employing Adams catalyst, hydrogen was taken up and cyclohexanecarboxylic acid hydrazide[1] was obtained. That is, the benzene ring was reduced without cleavage of the N–N bond. The cyclohexanecarboxylic acid hydrazide with *excess* Raney nickel was converted to cyclohexanecarboxamide.[1]

The Raney nickel reaction was found to be general for alkyl, aryl and heterocyclic carboxylic acid hydrazides. As examples, *n*-butyric and nicotinic acid hydrazides were converted in good yield to the corresponding amides.

The reaction has been applied to *dl*-isolysergic acid hydrazide which is obtainable from the ergot alkaloids by treatment with hydrazine.[2] The configuration of the resulting amide, relative to lysergic acid or isolysergic acid, is not assigned.[3] The product, however, was identical with the amide prepared from *dl*-isolysergic acid hydrazide by the general method of Stoll[4] which employs the azide as an intermediate.[5]

Experimental[6]

General Procedure.—A mixture of 1–2 g. of the carboxylic acid hydrazide, 100 ml. of 95% ethanol and about 10 g. of moist Raney nickel was heated under reflux with stirring for approximately three hours. The nickel was removed by filtration and the filtrate was evaporated to dryness. The residue was extracted with hot water or benzene from which the amide separated on cooling. All products were compared with authentic samples and shown to be identical. In this way *n*-butyric, benzoic and nicotinic acid hydrazides were converted to the corresponding amides in 60–80% yield.

Cyclohexanecarboxylic Acid Hydrazide.—A mixture of 6.8 g. (0.05 mole) of benzoyl hydrazine, 100 ml. of 95% ethanol and 0.1 g. of Adams catalyst was shaken under an atmosphere of hydrogen for six hours. A heat lamp was employed during this time and 0.15 mole of hydrogen was taken up. The catalyst was removed by filtration and the filtrate was taken to dryness. The residue was dissolved in 100 ml. of hot benzene and, on cooling, 5 g. (70% yield) of cyclohexanecarboxylic acid hydrazide separated. A sample was recrystallized from benzene and obtained as needles, m.p. 156–157° (lit.[1] m.p. 158–159°).

Anal. Calcd. for $C_7H_{14}N_2O$: C, 59.12; H, 9.92; N, 19.70. Found: C, 59.28; H, 9.73; N, 19.87.

Cyclohexanecarboxamide.—Using the general procedure outlined above, 2 g. of cyclohexanecarboxylic acid hydrazide with about 10 g. of Raney nickel gave 1 g. of cyclohexane carboxamide, m.p. 188–189° (lit.[1] m.p. 184–185°).

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 66.34; H, 10.31; N, 11.01.

***dl*-Lysergic Acid Amide or *dl*-Isolysergic Acid Amide.**—To a solution of 1 g. of *dl*-isolysergic acid hydrazide[7] dissolved in 500 ml. of ethanol was added about 10 g. of Raney nickel. The mixture was heated under reflux for two hours with

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[1] S. Olsen and E. Enkenmeyer, *Ber.*, **81**, 359 (1948), obtained cyclohexanecarboxylic acid hydrazide from the corresponding ester and hydrazine. They reported also the conversion of this compound to cyclohexanecarboxamide by treatment with nitrous acid.

[2] A. Stoll and A. Hofmann, *Helv. Chim. Acta*, **26**, 922 (1943).

[3] The interconversion under mild conditions of lysergic and isolysergic acid derivatives is well known; see reference 4.

[4] A. Stoll and A. Hofmann, *Helv. Chim. Acta*, **26**, 944 (1943).

[5] The author is grateful to Dr. E. C. Kornfeld for a sample so prepared.

[6] Melting points were taken on a Fisher–Johns block and recorded as read. The microanalyses were performed by H. L. Hunter and Gloria Beckmann.

[7] Furnished by Dr. R. P. Pioch of this Laboratory.