

lized from benzene, yielded pure, optically inactive¹² pinocembrin, m.p. 201–203°.

Anal. Calcd. for C₁₅H₁₂O₄: C, 70.30; H, 4.72. Found: C, 70.17; H, 4.80; OCH₃, 0.00.

Identity was confirmed by mixture melting point and infrared spectral comparison with an authentic specimen of pinocembrin.¹³ The ultraviolet spectrum was in agreement with that published by Erdtman.¹⁴

Attempted molecular weight determination by Rast's method: A portion of a mixture of 13.7 mg. of pinocembrin and 163.5 mg. of camphor melted in a capillary at 120°.

(12) Pinocembrin from pine wood is optically active, $[\alpha]_D -56^\circ$, but racemizes on sublimation [G. Linstedt, *Acta Chem. Scand.*, **3**, 755 (1949)].

(13) The literature records variable melting points for pinocembrin. Racemization does not result in depression¹⁴; rather, the synthetic specimens (inactive) are recorded with the highest melting points.¹⁵ We are indebted to Dr. Holger Erdtman, Royal Institute of Technology, Stockholm, for a specimen of levorotatory pinocembrin. Its infrared spectrum and that of our inactive preparation were superimposable.

(14) H. Erdtman, *Svensk Kem. Tid.*, **56**, 26 (1944).

(15) J. Shinoda and S. Sato, *J. Pharm. Soc. (Japan)*, **48**, 109 (1928).

On further heating the melt turned solid, melting again at 164°.

Acetylation of a sample with acetic anhydride–sodium acetate under reflux for 1 hr. followed by recrystallization from boiling ethanol led to pinocembrin diacetate, m.p. 142–143°. The same treatment, prolonged for 5 hr., yielded the 2',4',6'-triacetoxychalcone, m.p. 117–119°. These constants are in agreement with those reported in the literature.^{14,15}

Saponification of the pinocembrin acetate with ethanolic potassium hydroxide revealed two acetyl groups per molecule of 257 (molecular weight of pinocembrin, 256.25).

Oxidation of pinocembrin with aqueous alkaline potassium permanganate at room temperature yielded benzoic acid, purified by sublimation *in vacuo*, m.p. 122°, identified by mixture melting point (no depression) and infrared spectral comparison with an authentic sample.

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Imidazole Catalysis. IV.¹ The Reaction of General Bases with *p*-Nitrophenyl Acetate in Aqueous Solution

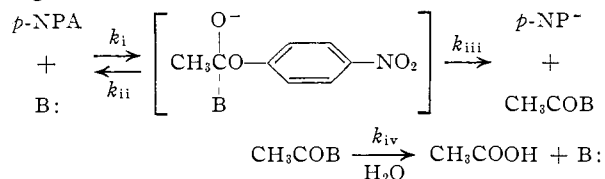
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The second-order rate constant for the reaction of OH⁻, CN⁻, HPO₄²⁻, CH₃COO⁻, H₂O, C₆H₅O⁻, *p*-ClC₆H₄O⁻, *p*-CH₃OC₆H₄O⁻, C₆H₅NH₂, *p*-CH₃C₆H₄NH₂ and *p*-CH₃CONHC₆H₄NH₂ with *p*-nitrophenyl acetate have been determined. When the log *k*₂ values for the reaction of the bases studied herein as well as those for the imidazoles and pyridines of a previous study are plotted *vs.* *pK*'_a, in the conventional Brönsted manner, it is found that the nitrogen bases are more efficient nucleophiles toward *p*-nitrophenyl acetate than are the negatively charged oxygen (or CN⁻) bases.

As part of a program to study the base catalytic properties of imidazoles, the catalysis of the hydrolysis of *p*-nitrophenyl acetate (*p*-NPA) by imidazole and substituted imidazoles was investigated.^{1a,1b} Certain observations made during these earlier studies indicated that the imidazoles were, as compared to other general bases, particularly reactive toward *p*-NPA. It has been the purpose of this study to compare the nucleophilicity of imidazoles and other general bases toward *p*-NPA.

In accord with present concepts of the mechanisms of B_{AC}²² displacement reactions at the ester carbonyl group the over-all reaction of *p*-NPA with a general base (B:) would be



In the instance where B: is OH⁻, the ratio $[(k_i + k_{iii})/(k_i + k_{ii})]$ is probably quite large since, in the closely allied reaction of OH⁻ with phenyl benzoate in H₂O¹⁸ solvent, there is no back incorporation of O¹⁸ into ester.³ For other bases it is possible that

(1) For previous papers in this series see: (a) T. C. Bruce and G. L. Schmir, *THIS JOURNAL*, **79**, 1663 (1957); (b) **80**, 148 (1958); (c) G. L. Schmir and T. C. Bruce, *ibid.*, **80**, 1173 (1958).

(2) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 754.

(3) C. A. Bunton and D. N. Spatcher, *J. Chem. Soc.*, 1079 (1956).

the ratio of forward to reverse rate constants are smaller as was shown by Bender for the alkaline hydrolysis of alkyl benzoates.⁴

In the reaction of *p*-NPA with imidazoles and pyridines the hydrolysis of the CH₃COB intermediates (acetylimidazole⁵ and/or acetylimidazolium salt^{1a} and acetylpyridinium salt⁶) is very rapid. Thus the catalytic constant for the reaction of imidazole with *p*-NPA is sufficiently large to give pseudo first-order kinetics even when the concentration of base was equal to or smaller than that of the substrate.^{1a} In comparison, for bases such as phenolate and aniline the decomposition of CH₃COB would be rate limiting since the solvolyses of phenyl acetate and acetanilide proceed at much lower rates than for *p*-NPA. When a large excess of base is employed the accumulation of CH₃COB does not effectively lower the concentration of B:. Under these conditions the reaction of all bases with *p*-NPA may be treated by first-order kinetic expressions thus obviating the necessity of solving expressions for parallel first- and second-order reactions. The value of the second-order rate constant (*k*₂) for the displacement reaction (*i.e.*, B: + *p*-NPA → CH₃COB + *p*-NP⁻) may then be obtained at any fixed *pH* and concentration of B: from the expression $(k_{\text{obs}} - k_w)/(\text{B:}) = k_2$, where *k*_{obs} is the observed *pseudo* first-order rate constant, *k*_w is the solvolysis constant in the absence of B:

(4) M. L. Bender, *THIS JOURNAL*, **73**, 1626 (1951).

(5) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1652 (1957).

(6) V. Gold, *et al.*, *J. Chem. Soc.*, 1406 (1953).

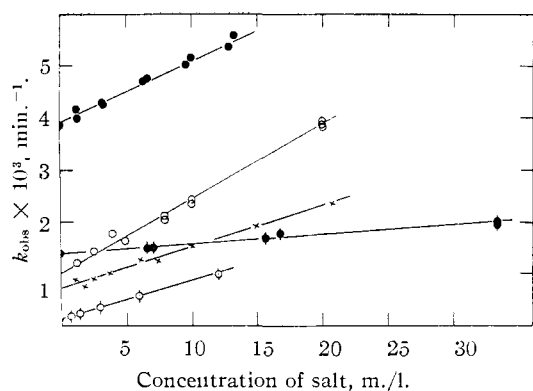


Fig. 1.—Plots of total concentration of salts vs. log of k_{obs} : KCN $\times 10^{-4}$ at pH 8.0, ●; KCN $\times 10^{-3}$ at pH 7.0, ●; $[KH_2PO_4 + K_2HPO_4] \times 10^{-2}$ at pH 8.0, ○; $[KH_2PO_4 + K_2HPO_4] \times 10^{-2}$ at pH 7.0, ○; $CH_3COONa \times 10^{-2}$ at pH 6.0, x.

and (B:) is the concentration of the catalytically active species of the base [the apparent second-order rate constant (k_2') is obtained if (B:) is replaced by (B: + BH)]. Alternatively a plot of k_{obs} vs. (B:) gives as its slope k_2 and as its intercept k_w . The values of k_2 are then an index of the efficiency of various bases to participate in the displacement of p -NP⁻ from p -NPA.

Experimental

Materials.—All inorganic salts employed were of reagent grade. The organic compounds were Eastman Kodak Co. White Label and were recrystallized or redistilled prior to use.

Apparatus.—The constant temperature bath is described in a previous paper.^{1a} Spectrophotometric readings were made with a model DU Beckman spectrophotometer and pH determinations were made with a model G Beckman pH meter.

pK_a' determinations were made by the method of half-neutralization and serial dilution.^{1b} The second ionization constant for phosphoric acid was determined in a previous study.^{1c}

Kinetics.—All reactions were run at 0.55 M ionic strength provided by buffer and KCl. The solvent was 28.5% ethanol-water (v./v.) and the temperature $30 \pm 0.1^\circ$. The mechanical procedures employed in performing the rate determinations are described in earlier papers.¹

Results

In a previous study it was noted that the rate of solvolysis of p -NPA was markedly dependent on the nature and concentration of buffer.^{1b} In Table I are recorded the values of k_2' , k_2 and k_w obtained from plots of k_{obs} vs. total phosphate and acetate concentration (Fig. 1).

TABLE I

Base	pK _a '	pH	k_2' l. mole ⁻¹ min. ⁻¹ $\times 10^2$	k_2 l. mole ⁻¹ min. ⁻¹ $\times 10^2$	k_w $\times 10^4$ min. ⁻¹
CH ₃ COO ⁻	4.7	6.0	0.090	0.095	0.72
HPO ₄ ²⁻	7.0	7.0	0.736	1.47	1.4
HPO ₄ ²⁻	7.0	7.5	1.17	1.54	} 1.51 \pm 0.02 4.0
HPO ₄ ²⁻	7.0	8.0	1.38	1.52	

The value of k_w for the phosphate and acetate experiments of Table I are given by the expression

$$k_w = k_{H^+}(H_3O^+) + k_{H_2O}(H_2O) + k_{OH^-}(OH^-)$$

For the hydrolysis of p -NPA the value of k_{H^+} has

been shown previously to be quite small⁷ and at the pH values employed the quantity $k_{H^+}(H_3O^+)$ may be ignored. A plot (Fig. 2) of k_w vs. OH⁻ concentration then gives as its slope k_2 for OH⁻ (990 l. mole⁻¹ min.⁻¹) and the intercept divided by the concentration of water affords k_2 for H₂O (1.54×10^{-6} l. mole⁻¹ min.⁻¹). The value of k_2 for OH⁻, as determined, is in essential agreement to that of 485 l. mole⁻¹ min.⁻¹ reported by Tommila and Hinshelwood⁷ for experiments carried out in 60% acetone-water, but differs markedly from the value of 30,600 l. mole⁻¹ min.⁻¹ reported by Bender and Turnquest when 5% aqueous dioxane was employed as solvent.⁵ Also, our value of k_2 for H₂O is much smaller than that of 5.9×10^{-5} l. mole⁻¹ min.⁻¹ reported by these workers.

With phosphate as buffer, plots of k_{obs} vs. total cyanide concentration afford k_2' values of 0.177 l. mole⁻¹ min.⁻¹ and 1.18 l. mole⁻¹ min.⁻¹ at pH 7.0 and 8.0, respectively (Fig. 1). Employing a pK_a' of 9.1 for HCN the calculated values of k_2 for CN⁻ become 17.9 and 16.1 l. mole⁻¹ min.⁻¹, respectively.

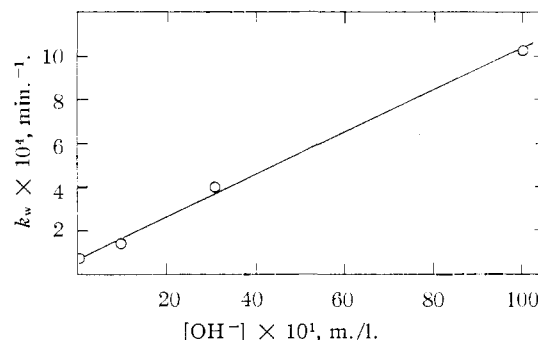


Fig. 2.—The relation of k_w to hydroxide ion concentration.

The second-order rate constants for the phenols and anilines were determined from the values of k_{obs} obtained at two different concentrations of the nucleophile at pH 8.0 (Table II).

TABLE II

Base	pK _a '	k_2 , l. mole ⁻¹ min. ⁻¹
C ₆ H ₅ O ⁻	9.9 ⁸	19.0 \pm 3.0
p -ClC ₆ H ₄ O ⁻	9.3 ⁸	9.6 \pm 1.8
p -CHOC ₆ H ₄ O ⁻	7.6 ⁸	0.5 \pm 0.1
C ₆ H ₅ NH ₂	4.5	.023 \pm .001
p -CH ₃ C ₆ H ₄ NH ₂	5.0	.052 \pm .005
p -CH ₃ CONHC ₆ H ₄ NH ₂	4.4	.020 \pm .000

Discussion

In Fig. 3 the log k_2 values for the reaction of the bases studied herein as well as those for the imidazoles and pyridines of a previous study^{1b} are plotted vs. pK_a' in the conventional Brønsted manner. Inspection of Fig. 3 reveals that a single linear-free energy diagram does not suffice to correlate all the data. Thus, HPO₄²⁻ and imidazole are both characterized by pK_a' values of 7.0, but their second-order rate constants differ by 10³ and hydroxide ion (pK_a' 15.7) is not as good a nucleophile as the anion of 6-nitrobenzimidazole (pK_a' 10.6).

(7) E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938).

(8) O. Gawron, M. Duggen and C. J. Grelecki, *Anal. Chem.*, **24**, 969 (1952).

The plots of Fig. 3 are not unusual in that reactions known to proceed by general base catalysis yield separate Brönsted equations for radically different types of bases.⁹ It is generally found that all bases characterized by O^- as the attacking nucleophile fall into a single line and this may be noted to be so for the phenols and CH_3COO^- . The divergence of HPO_4^{--} from this line is due to the fact that the pK_a' is not truly a measure of its proton affinity. A suitable statistical correction places this point much closer to the plot for other O^- bases. It may also be noted that the value of $\log k_2$ for H_2O falls above that which would be predicted from plots for O^- and $\geq\text{N}$: species, but the value of $\log k_2$ for OH^- is considerably lower than expected. It is usual to have the value of k_0 for H_2O near to that expected from the Brönsted plot, but k_0 for OH^- is generally lower. Probably of greatest interest is the magnitude of the essentially parallel displacement of the lines connecting the points for bases of similar type from the Brönsted plot ($\log k_2 = 0.8pK_a' - 4.3$) for the imidazoles and the decidedly greater nucleophilicity of the nitrogen as compared to the negative oxygen (and CN^-) bases when the affinity for the proton is used as standard.

The inability to correlate displacement reactions on carbon to pK_a' has been treated by Swain and Scott¹⁰ who suggest the equation $\log k/k_0 = sn$ for non-solvolytic nucleophilic displacement reactions on carbon. According to Swain, plots of the $\log k_2$ relative to water (*i.e.*, $\log k/k_0$) *vs.* derived nucleophilic constants (n) afford linear plots with slope s . When the equation of Swain is applied to the bases studied herein for which values of n are available (CH_3COO^- , pyridine, HPO_4^{--} , OH^- , aniline and CN^-) a value of $s = 1.16$ is obtained and the median deviation is $0.6 n$ unit. The major deviant is OH^- ($3.4 n$ units). Swain noted a large deviation for OH^- ($3.74 n$ units) in its reaction with β -propiolactone and suggested this to be due to the particularly relative effectiveness of OH^- as a nu-

(9) R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941, Chapt. V.

(10) C. G. Swain and C. B. Scott, *THIS JOURNAL*, **75**, 141 (1953).

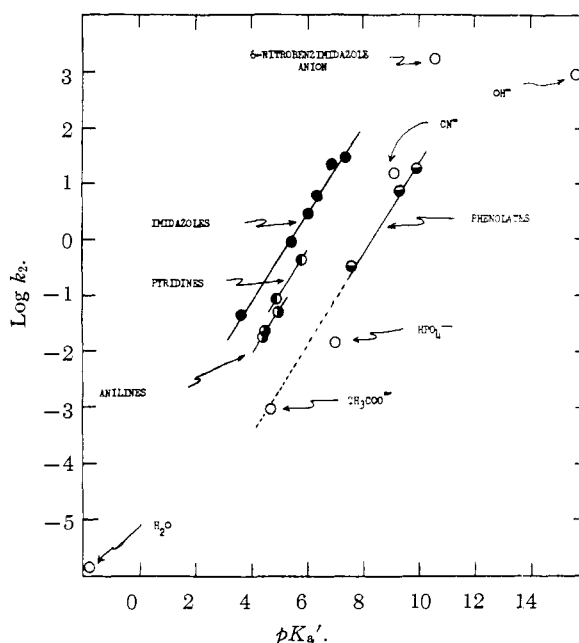


Fig. 3.—A Brönsted type plot of $\log k_2$ *vs.* pK_a' for the reaction of general bases with *p*-nitrophenyl acetate.

cleophile in displacement reactions on the ester carbonyl group. A derived value of $n = 8.0$ for OH^- from the β -propiolactone rate data brings the point for the reaction of OH^- with *p*-NPA into line with the other nucleophiles studied. The application of the more recent dual basicity equation of Edwards¹¹ corrects for the large deviation of OH^- by allowing suitable weighting of pK_a' values in comparison with the nucleophilic constant, but the plot then acquires the same characteristics as the Brönsted plot (Fig. 3).

Acknowledgment.—This work was supported by a grant from the Institute of Arthritis and Metabolic Diseases, National Institutes of Health.

(11) J. O. Edwards, *ibid.*, **76**, 1540 (1954); **78**, 1819 (1956).

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Electronic Structure and Auxin Activity of Benzoic Acid Derivatives

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The π -electron distribution of various benzoic acid derivatives has been calculated by a molecular orbital method. A distinct parallelism is found between the electronic structure and the auxin activity of these compounds. A discussion of the mechanism of plant growth action is given. A strong resemblance is pointed out between the plant growth action of these compounds and the carcinogenic action of aromatic compounds.

Since the discovery of the natural plant growth substance, indole-3-acetic acid, numerous active substances have been synthesized, and in order to elucidate the mechanism of hormonal action of these compounds, many studies¹⁻⁹ have been made.

(1) R. M. Muir, C. Hansch and A. H. Gallup, *Plant Physiol.*, **24**, 359 (1949); C. H. Hansch and R. M. Muir, *ibid.*, **25**, 389 (1950); R. M. Muir and C. Hansch, *ibid.*, **28**, 218 (1953).

(2) R. L. Wain, *J. Sci. Food Agr.*, 101 (1951).

The mechanism of the action of these plant growth hormones nevertheless has remained elusive.

(3) R. M. Muir and C. Hansch, *Plant Physiol.*, **26**, 309 (1951).

(4) C. Hansch, R. M. Muir and R. L. Metzner, *ibid.*, **26**, 812 (1951).

(5) J. M. F. Leaper and J. R. Bishop, *Bot. Gaz.*, **112**, 250 (1951).

(6) J. Bonner and R. S. Bandurski, *Ann. Rev. Plant Physiol.*, **3**, 59 (1952).

(7) A. Rhodes and R. de B. Ashworth, *Nature*, **169**, 76 (1952).

(8) H. Veldstra, *Ann. Rev. Plant Physiol.*, **4**, 151 (1953).

(9) C. J. Schoot and K. H. Klassens, *Rec. trav. chim.*, **75**, 271 (1956).