1,1,3-Triphenyl-2-propyn-1-ol was prepared according to the procedure reported by Olah and Pittman.[21] The solid alcohol was recrystallized from petroleum ether in 66% yield: mp 80–81° (lit.[21] mp 82°); ir (CCl_4) 3599 (OH) and 2234 (C≡C) cm^{-1}; nmr (CCl_4) δ 2.70 (s, 1) and 7.40 (m, 15).

1,1-Diphenyl-3-(4-chlorophenyl)-2-propyn-1-ol was prepared in 76% yield according to the procedure described for 1,1,3-triphenyl-2-propyn-1-ol when *p*-chlorophenylacetylene was substituted for phenylacetylene: mp 74–75°; ir (CCl_4) 3600 (OH) and 2225 (C≡C) cm^{-1}.

1,1-Diphenyl-3-(4-methylphenyl)-2-propyn-1-ol was prepared as above in 75% yield: mp 64–66°; ir (CCl_4) 3600 (OH) and 2225 (C≡C) cm^{-1}.

1,1-Diphenyl-3-(4-methoxyphenyl)-2-propyn-1-ol was prepared in 70% yield as described above: mp 65–66°; ir (CCl_4) 3600 (OH) and 2225 (C≡C) cm^{-1}.

1,1-Di(4-methylphenyl)-3-phenyl-2-propyn-1-ol was prepared in 52% yield as described above: mp 82–84°; ir (CCl_4) 3600 (OH) and 2225 (C≡C) cm^{-1}.

1,3,3-Triphenyl-1-chloropropadiene (Ia) was prepared according to the procedure of Jacobs and Fenton.[2] Recrystallization from ether–ethanol afforded a 55% yield of the desired material: mp 69–70° (lit.[2] mp 70–71°); ir (CCl_4) 1964 (C=C=C) cm^{-1} (lit.[2] 1958 cm^{-1}); nmr (CCl_4) δ 7.30 (m); mol wt in benzene 926 (calcd, 302).

1-(4-Chlorophenyl)-1-chloro-3,3-diphenylpropadiene (Ib) was prepared according to the procedure described for Ia. Recrystallization from ether–ethanol gave the desired chloroallene in 80% yield: mp 84–85°; ir (CCl_4) 1926 (C=C=C) cm^{-1}.

Anal. Calcd for $C_{21}H_{14}Cl_2$: C, 74.79; H, 4.15; Cl, 21.06. Found: C, 74.69; H, 4.17; Cl, 21.10.

1-(4-Methylphenyl)-1-chloro-3,3-diphenylpropadiene (Ic) was prepared as above. Recrystallization from ether–ethanol gave the product in 70% yield: mp 127–128°; ir (CCl_4) 1926 (C=C=C) cm^{-1}.

Anal. Calcd for $C_{22}H_{17}Cl$: C, 83.42; H, 5.37. Found: C, 83.56; H, 5.53.

1-(4-Methoxyphenyl)-1-chloro-3,3-diphenylpropadiene (Id) was prepared as described above. Recrystallization from ether–ethanol gave a 67% yield of the desired product: mp 131–132°; ir (CCl_4) 1926 (C=C=C) cm^{-1}. This chloroallene exhibited marked instability. Attempts at analysis resulted in high C and H values and low Cl values. Those are consistent with rapid hydrolysis of the compound in air. Further support of this thesis comes from the observation of a C≡C bond in the ir spectrum of material allowed to stand in air for 3 days. Consequently a sample of this compound was recrystallized and dried prior to each set of kinetic runs.

1-Phenyl-1-chloro-3,3-bis(4-methylphenyl)propadiene) (Ie) was prepared as described above. Recrystallization from ligroin gave the product in 67% yield: mp 81–82°; ir (CCl_4) 1923 (C=C=C) cm^{-1}.

Anal. Calcd for $C_{23}H_{19}Cl$: C, 83.50; H, 5.79; Cl, 10.71. Found: C, 83.52; H, 5.71; Cl, 10.68.

Product Studies. A 1.01-g sample of triphenylchloroallene was transferred to a solution of 700 ml of acetone and 300 ml of distilled water at 27.8° and stirred for 6 hr (ten half-lives). At the end of this period, 500 ml of water was added and the resulting solution extracted five times with 200-ml portions of ether. The organic layer was dried over $MgSO_4$ and evaporated. The solid product (92%) showed no absorption in the 1650–1750 cm^{-1} region. Recrystallization from ligroin yielded 0.78 g (83%) of 1,1,3-triphenyl-2-propyn-1-ol, mp 80–81°. A similar experiment utilizing Id gave 0.76 g (81%) of 1,1-diphenyl-3-(4-methoxyphenyl)-2-propyn-1-ol after recrystallization. No evidence of carbonyl absorption was found in the ir spectrum of crude product.

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Intramolecular Base-Catalyzed Imidazole Catalysis

C. G. Overberger* and Chah-Moh Shen

Contribution from the Department of Chemistry and the Macromolecular Research Center, The University of Michigan, Ann Arbor, Michigan 48104.
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Abstract: A new two-step synthesis of 4(5)-(2′-hydroxyphenyl)imidazole (HPI) was utilized. Solvolysis of *p*-nitrophenyl acetate (PNPA) and *p*-nitrophenyl toluate (PNPT) catalyzed by HPI and other related imidazole or phenol model compounds, such as 1-methyl-4-(2′-hydroxyphenyl)imidazole and 4(5)-(2′-methoxyphenyl)imidazole, indicated that reaction other than simple nucleophilic catalysis by the imidazole group and phenoxide ion function of HPI must operate during the catalyzed solvolysis. The favored geometry existing between the imidazole and phenoxide groups suggests an intramolecular bifunctional catalysis involving the phenoxide and imidazole groups. The rate constant of this intramolecular base-catalyzed imidazole catalysis was estimated to be 137.4 and 6.39 l./mole min for PNPA and PNPT, respectively. The compound 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]imidazole (HPNI), which has an imidazole and phenol function joined by nine methylene units, was synthesized in seven steps from sebacic acid. The modest observed rate enhancement during the solvolysis of *p*-nitrophenyl acetate and *p*-nitrophenyl palmitate catalyzed by HPNI was attributed to a hydrophobic attraction between the substrates and the long chain model compounds.

Imidazole is known to be a nucleophilic catalyst for the solvolysis of *p*-nitrophenyl acetate (PNPA)[1] and related activated acyl compounds.[2] The simple nucleophilic catalytic process has been shown to be subject to base catalysis; the second base can be another imidazole molecule in a concentrated imidazole solution,[3] or could also be a hydroxide ion.[4] The object of this work was to introduce the second base and the imidazole group in the same molecule to test experimentally if this base-catalyzed imidazole catalysis can proceed intramolecularly in a dilute catalyst solution. Although many simple polyfunctional imidazole com-

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(2) (a) J. F. Kirsch and W. P. Jencks, *ibid.*, **86**, 837 (1964); (b) A. J. Kirby and W. P. Jencks, *ibid.*, **87**, 3209 (1965).

(3) (a) M. Caplow and W. P. Jencks, *Biochemistry*, **1**, 883 (1962); (b) T. C. Bruice and S. J. Benkovic, *J. Amer. Chem. Soc.*, **86**, 418 (1964).

(4) J. F. Kirsch and W. P. Jencks, *ibid.*, **86**, 833 (1964).

pounds, with functional groups which might be expected to have a proper geometry to interact with each other, have been synthesized,[5] no major cooperative effect between the functional groups has been noted.

4(5)-(2′-Diethylaminoethyl)imidazole and several other dialkylaminoethylimidazoles were reported to catalyze the hydrolysis of PNPA 36 times faster than imidazole at pH 7.2.[6] Many intramolecular general acid base catalysts have been observed in nonpolar solvents.[7] The effectiveness of these catalysts can be attributed to their tautomeric character, as these molecules could catalyze proton transfer without forming a high energy dipolar ion.[7c]

Experimental Section

Synthesis of Model Compounds.[8] **4(5)-(2′-Hydroxyphenyl)-imidazole (HPI).** To a stirred, refluxing ethyl acetate (250 ml) solution was added finely ground cupric bromide (112 g, 0.5 mole) followed by *o*-hydroxyacetophenone (41 g, 0.3 mole) in hot chloroform (150 ml). This mixture was refluxed on a steam bath for 3 hr with vigorous stirring. The white cuprous bromide was removed by filtration, the filtrate decolorized with Norit, and the solvent evaporated under reduced pressure. To the residue was added formamide (350 ml), and the solution was heated with stirring at 175° in an oil bath for 3 hr. The deep red mixture was then poured into hot 2 *N* hydrochloric acid (1 l.). When the solution had cooled to room temperature, its pH was adjusted to 6–7 by the addition of ammonia gas. A black polymeric material, which precipitated, was removed by filtration through Celite. The addition of further ammonia gas to the clear filtrate precipitated the crude products as a white solid, which was collected by filtration. Two recrystallizations from xylene gave pure 4(5)-(2′-hydroxyphenyl)imidazole (16.2 g, 30%) as colorless needles, mp 174.5–175.5° (lit.[9] mp 174–175°). *Anal.* Calcd for $C_9H_8N_2O$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.55; H, 5.11; N, 17.37.

4(5)-(2′-Methoxyphenyl)imidazole (MPI). *o*-Methoxyacetophenone[10] was brominated and condensed with formamide as described previously. The bromination step proceeded more readily and was completed within 30 min. The crude 4(5)-(2′-methoxyphenyl)imidazole was isolated from the aqueous formamide solution by three extractions with ether. The ether solution was evaporated under reduced pressure, after being dried over sodium sulfate, to give a brown oil which was vacuum distilled. The free base was then converted to its hydrochloride salt by reaction with hydrogen chloride gas in ether solution. One crystallization from absolute ethanol gave the salt as colorless needles, mp 237–239°; the yield was *ca.* 30%. *Anal.* Calcd for $C_{10}H_{11}ClN_2O$: C, 57.01; H, 5.26; N, 13.30. Found: C, 57.05; H, 5.14; N, 13.41.

1-Methyl-4-(2′-hydroxyphenyl)imidazole (MHPI). 4(5)-(2′-Hydroxyphenyl)imidazole (1 g, 6.2 mmoles) was methylated with excess methyl iodide (4.2 g, 30 mmoles) in refluxing acetone (20 ml) for 5 days, with the protection of a drying tube. A white solid precipitated toward the end of the reaction. The solvent was evaporated under reduced pressure, water was added to the residue, and the pH of the solution was adjusted to 8 with sodium hydroxide. The crude product, which precipitated at this pH, was recrystallized two times from aqueous ethanol (1:1) as colorless needles (0.32 g, 29%), mp 83–84°. *Anal.* Calcd for $C_{10}H_{10}N_2O$: C, 68.94; H, 5.79; N, 16.09. Found: C, 68.91; H, 5.67; N, 16.09.

Sebacic Polyanhydride (II). This compound was prepared by the procedure of Hill.[11]

ω-(*p*-Methoxyphenylcarbonyl)nonanoic Acid (III). To 184 g (1 mole) of sebacic polyanhydride in a mixture of dry nitrobenzene (250 ml) and dry tetrachloroethane (1200 ml), was added anhydrous aluminum chloride (266 g, 2 moles) with vigorous stirring at 0°. Anisole (108 g, 1 mole) was then added dropwise to the mixture. The temperature was kept below 5° during and for 3 days subsequent to the addition. The violet complex was then decomposed with 250 ml of 37% hydrochloric acid and a white solid precipitated. After a steam distillation, the oil at the bottom of the oil–water mixture solidified. The solid was purified by dissolution in 1 *N* sodium hydroxide and reprecipitated with dilute hydrochloric acid after filtration. The reprecipitated solid was further purified by extraction two times with hot water (500 ml) to remove any unreacted sebacic acid. Crystallization from 50% aqueous ethanol gave a product in 51% yield (74.3 g), mp 97–99°. Analytical sample on recrystallization from cyclohexane gave colorless needles, mp 98.0–98.5°. *Anal.* Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27; O, 21.89. Found: C, 69.83; H, 8.34; O, 22.04.

10-(*p*-Methoxyphenyl)decanoic Acid (IV). To ω-(*p*-Methoxyphenylcarbonyl)nonanoic acid (10 g, 34 mmoles) in 80 ml of diethylene glycol were added sodium hydroxide (5 g) and 85% of hydrazine hydrate (5 ml). The mixture was refluxed for 1 hr. The water formed during the reaction was distilled off slowly until the reaction temperature reached 200°. The mixture was refluxed for 3 hr at 200° and then cooled and added to 500 ml of water. The pH was adjusted to 6 with hydrochloric acid. A light yellow solid was obtained (9.75 g, 94% yield) which upon recrystallization from heptane and treatment with Norit A gave colorless products, mp 64.5–66.5°. Further recrystallization from heptane raised the melting point to 66.5–67.5°. *Anal.* Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41; O, 17.24. Found: C, 73.27; H, 9.42; O, 17.09.

10-(*p*-Methoxyphenyl)decanoyl Chloride (V). To 10-(*p*-methoxyphenyl)decanoic acid (24.5 g, 88 mmoles) was added thionyl chloride (100 ml). The mixture was refluxed for 4 hr, and the excess thionyl chloride was distilled at atmospheric pressure. The residue was then distilled to give the desired compound (14.5 g, 55% yield) as a colorless liquid, bp 160–170° (0.05 mm), $[n]^{25}D$ 1.5087. *Anal.* Calcd for $C_{17}H_{25}ClO_2$: C, 68.79; H, 8.49; Cl, 11.95. Found: C, 68.96; H, 8.53; Cl, 11.84.

α-Chloromethyl (ω-*p*-Methoxyphenyl)nonyl Ketone (VI). To 14.5 g (50 mmoles) of 10-(*p*-methoxyphenyl)decanoyl chloride was added excess diazomethane (prepared from 34.3 g of *N*-nitroso-*N*-methylurea) at 0° under a nitrogen atmosphere and anhydrous conditions. After being stirred for a further 45 min, dry hydrogen chloride gas was passed into the solution until the yellow color disappeared. After stirring for an additional 45 min at 0°, the ether solution was washed with three 100-ml portions of ice water and once with 100 ml of 0.1 *N* sodium bicarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the ether gave 13.2 g (87% yield) of colorless crystals, mp 59–61°. An analytical sample was recrystallized from heptane, mp 60.5–61°. *Anal.* Calcd for $C_{18}H_{27}ClO_2$: C, 69.55; H, 8.76; Cl, 11.41. Found: C, 69.39; H, 8.64; Cl, 11.46.

4(5)-[ω-(*p*-Methoxyphenyl)nonyl]imidazole (VII). To anhydrous diethylene glycol (250 ml) were added α-chloromethyl (ω-*p*-methoxyphenyl)nonyl ketone (14 g, 45 mmoles) and dry formamidine acetate (18.3 g, 175 mmoles). The mixture was heated for 50 hr at 135° under a nitrogen atmosphere, during which time the solution became brown. The diethylene glycol was removed *in vacuo* and the residual oil, dissolved in a small amount of 90% ethanol–water, was added to a Dowex 50w × 8 ion-exchange resin (NH_4^+ form). After washing with 1 l. of 90% ethanol–water, the desired compound was released by treatment with 0.1 *N* ammonium hydroxide in 90% ethanol–water. Removal of the solvent yielded a brown oil, which upon distillation at 180° (0.025 mm) gave the product as a light yellow, waxy solid (5 g, 37% yield), mp 58–73°. The analytical sample was recrystallized from ethyl malonate, mp 74–76°. *Anal.* Calcd for $C_{19}H_{28}N_2O$: C, 75.95; H, 9.39; N, 9.33. Found: C, 75.86; H, 9.24; N, 9.31.

4(5)-[ω-(*p*-Hydroxyphenyl)nonyl]imidazole (VIII). A solution of crude 4(5)-[ω-(*p*-methoxyphenyl)nonyl]imidazole (1.56 g, 5.2 mmoles) in glacial acetic acid (12 ml) was saturated with dry hydrogen bromide gas (6 g). The reaction mixture was maintained at room temperature for 24 hr, at 50° for 2.5 hr, and finally at 70° for 1 hr. The acetic acid was distilled off and the residue was suspended in anhydrous ether. After a filtration, the ether was then evaporated under reduced pressure yielding the product as a light yellow solid, which was crystallized from 50% ethanol–water, mp 104–106.5° (0.77 g, 25% yield). Further recrystallization from 60% ethanol–water gave colorless needles, mp 106.0–108.5°. *Anal.*

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(8) Melting points are uncorrected. Analyses were performed by Spang Laboratory, Ann Arbor, Mich.

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(10) K. V. Auwers, *Justus Liebigs Ann. Chem.*, **408**, 212 (1915).

(11) J. W. Hill, *J. Amer. Chem. Soc.*, **54**, 4105 (1932).

Calcd for $C_{18}H_{26}N_2O$: C, 75.48; H, 9.15; N, 9.78. Found: C, 75.34; H, 9.03; N, 9.80.

Substrates. *p*-Nitrophenyl Acetate. This compound is a product of Pierce Chemical Co. and was sublimed *in vacuo* before being used, mp 77.5–78.0° (lit.[12] mp 79.5–80.0°, lit.[1b] 77.5–78.0°).

***p*-Nitrophenyl Toluate.** Equivalent amounts of *p*-nitrophenol, *p*-toluly chloride, and triethylamine were refluxed in benzene for 30 min. After removal of the solvent under reduced pressure, the solid residue was washed with water, recrystallized from 50% acetone–water, and then sublimed under vacuum to yield *p*-nitrophenyl toluate, mp 117.5–118.5°; the yield was *ca.* 80%. *Anal.* Calcd for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31; N, 5.45. Found: C, 65.28; H, 4.41; N, 5.50.

***p*-Nitrophenyl Palmitate.** This compound is a product of K and K Laboratories, Inc., mp 60.5–63.0° (lit.[13] 62–64°).

Potentiometric Titration. The model compounds containing imidazole and/or phenolic functions (6–30 mg, 10^{-2} mole) were dissolved in 10 ml of 30% (v/v) 1-propanol–water in a constant temperature cell at 26°. After the addition of 2 *N* HCl (100 μl), the titration was carried out with 1.0 *N* NaOH solution added from a micropipet. The response of the glass electrode of the Radiometer (Type TT T1c) used to follow the titrations was checked repeatedly against two Beckmann buffer solutions. A blank titration curve was obtained by substituting 30% (v/v) 1-propanol–water for the model compound solution in the cell. Differential titration curves were derived graphically by the method of Park and Davis.[14]

Kinetic Measurements. Stock solutions, *ca.* 5×10^{-3} *M*, were prepared by dissolving the model compound in 30% (v/v) 1-propanol–water. To produce the standard catalyst solutions, 5 ml of these stock solutions was diluted to 50 ml with 30% (v/v) 1-propanol–water buffers [with tris(hydroxymethyl)aminomethane (Tris) (0.02 *M*)·HCl at pH 7–9; with 3-(*N*,*N*′-dimethylamino)propanol (0.02 *M*)·HCl or triethylamine (0.02 *M*)·HCl at pH above 9]. The ionic strengths of these catalyst solutions were also adjusted to 0.02 by the addition of potassium chloride. For each kinetic measurement, 3 ml of standard catalyst solution (*ca.* 5×10^{-4} *M*) was treated with a suitable amount of substrate solution (for *p*-nitrophenyl acetate (PNPA), 200 μl of 30% (v/v) 1-propanol–water solution; for *p*-nitrophenyl toluate (PNPT), 50 μl of pure 1-propanol solution; for *p*-nitrophenyl palmitate (PNPP), 200 μl of pure 1-propanol solution), the final substrate concentration in the reaction mixture being *ca.* 5×10^{-5} *M*. The solvolysis reaction was followed by monitoring the appearance of the *p*-nitrophenoxide ion at 400 mμ in a spectrophotometer. All the observed data followed first-order kinetics. The pseudo-first-order rate constant k_{measd} (with catalyst) and k_{blank} (without catalyst) were treated by the expression, $k_{obsd} = k_{measd} - k_{blank}$ and $k_{cat} = k_{obsd}/[catalyst]$, where [catalyst] is the molar concentration of imidazole and/or phenol model compound. Blank rates were obtained at different pH values for all esters employed.

Results and Discussion

The compound 4(5)-(2′-hydroxyphenyl)imidazole (HPI) was synthesized by reacting formamide with 2-bromo-2′-hydroxyacetophenone, which was obtained from 2′-hydroacetophenone by reaction with cupric bromide as described by King and Ostrum.[15] This revised two-step synthesis, which gives an overall yield of 30%, is considerably simpler than previously described methods.[9]

The model compound, 4(5)-(2′-methoxyphenyl)imidazole (MPI), was also synthesized and characterized. Methylation of HPI with methyl iodide in refluxing acetone gave only one product as indicated by tlc and a sharp melting point; the nmr spectrum of this compound also showed only one sharp singlet at τ 6.39 ($CDCl_3$), corresponding to three protons ($CH_3N{=}$). Methylation on the oxygen of the starting material was excluded since 4(5)-(2′-methoxyphenyl)imidazole was obtained by an unambiguous route and it exhibited a singlet at τ 6.17 in the same solvent which was assigned to CH_3O protons. Methylation of a 4(5)-substituted imidazole usually gave a mixture of 1,4 and 1,5 isomers. The fact that the methylation of HPI gave only the 1,4 isomer can be justified by two factors. (1) Steric considerations: the methylation of 4(5)-phenylimidazole gave predominately 1,4 isomer,[16] alkylation taking place selectively on the less hindered site. (2) Basicity constant: the 1,5-monomethylated product of 4(5)-substituted imidazole, substituted by an electron-withdrawing group, would be more basic than the parent compound. Protonation of the methylated product would involve the more basic nitrogen atom, which is located away from the electron-withdrawing substituent.[16b] The titration results (Table I) indicated

Table I. Dissociation Constants of Substituted Imidazolium Ions.

Compound	pK_a	*N*-Methyl derivatives pK_a (4 isomer)	pK_a (5 isomer)
4(5)-Nitroimidazole[a]	−0.05	−0.53	2.13
4(5)-Phenylimidazole[a]	6.00	5.78	
4(5)-(2′-Hydroxyphenyl)-imidazole[b]	6.00	5.65	

[a] J. H. Ridd and B. V. Smith, *J. Chem. Soc.*, 1364 (1960). [b] Measured in 30% (v/v) 1-propanol–water at 26°, μ = 0.02.

the methylation product of HPI would be the 1,4 isomer. Methylation of 4(5)-phenylimidazole also gave the 1,4 isomer, which is less basic than its parent compound. The phenyl group was regarded as the electron-withdrawing group.[17]

The compound 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]-imidazole (HPNI) (VIII) was synthesized in seven steps from sebacic acid (I) (Scheme I). A Friedel–Crafts reaction between the polydibasic anhydride (II) and anisole according to the method of Hill[11] gave ω-(*p*-methoxyphenylcarbonyl)nonanoic acid (III). The keto acid (III) was reduced and treated with thionyl chloride to give V, which was treated with diazomethane and hydrogen chloride to give the α-chloromethyl ketone (VI). A condensation reaction between VI and amidine acetate gave VII. Treatment of VII with hydrogen bromide in glacial acetic acid gave 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]imidazole (HPNI) (VIII). The overall yield was 4.4%. The compounds II–VIII were characterized by elemental analysis and infrared and nuclear magnetic resonance spectra. In addition, a potentiometric titration curve for compounds VII and VIII was obtained. Titrations were carried out at 26°. The dissociation constants obtained were listed in Table II.

The dissociation constants of the various imidazolium cations indicate that a 4(5)-(2′-hydroxyphenyl) group has the same effect as a 4(5)-phenyl group in reducing the basicity of the imidazole function.[17]

Effects of 4(5)-(2′-Hydroxyphenyl)imidazole (HPI) on the Solvolyses of Esters. Studies on the solvolytic reactions of *p*-nitrophenyl acetate (PNPA) and *p*-nitrophenyl toluate (PNPT) catalyzed by 4(5)-(2′-hydroxyphenyl)imidazole (HPI) were undertaken in 30% (v/v) 1-propanol–water buffered solutions at 26°. The catalyst (HPI) was found to be much more

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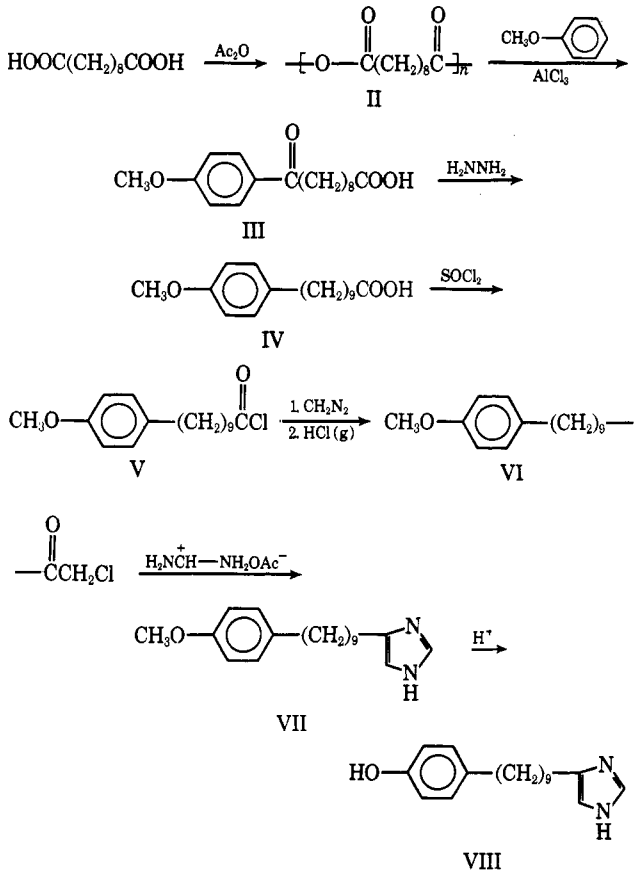
Scheme I



effective in solutions of high pH values, which indicated that the high efficiency of HPI is associated with the phenoxide ion in the structure.

Table II. Results of Potentiometric Titrations of Imidazole- and/or Phenol-Containing Model Compounds Measured in 30% (v/v) 1-Propanol–Water at 26°, Ionic Strength 0.02

Compound	pK^{IMH^+}	pK^{PhOH^+}
Imidazole	7.00	
4(5)-(2′-Hydroxyphenyl)imidazole	6.00	10.75
1-Methyl-4-(2′-hydroxyphenyl)imidazole	5.65	11.03
4(5)-(2′-Methoxyphenyl)imidazole	6.15	
4(5)-[ω-(*p*-Hydroxyphenyl)nonyl]imidazole	6.77	11.18
4(5)-[ω-(*p*-Methoxyphenyl)nonyl]-imidazole	6.75	
p-Cresol		11.30
Imidazole	7.00	

A study of the dependence of the solvolytic rates on the HPI concentration at pH 10.02 (where the phenol functions of HPI are 15.7% dissociated) revealed that the catalytic rates for the solvolysis of PNPA and PNPT were directly proportional to the concentration of HPI (Figure 1). These results indicated that the solvolysis is first order with respect to the catalysts for both PNPA and PNPT.

Both meta- and para-substituted phenols have been reported to act as nucleophiles during the transesterification of *p*-nitrophenyl acetate (PNPA). The second-order rate constant for the reaction was found to be dependent upon the pK_a of the phenols *via* the Brønsted relationship.[18] In the case of the reaction between the

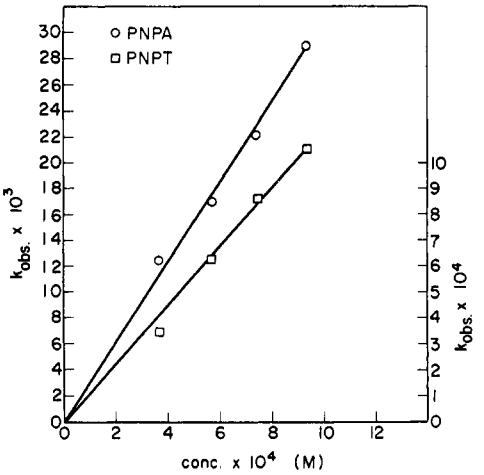
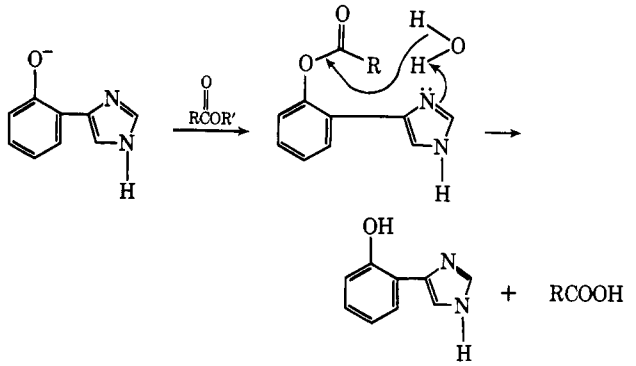


Figure 1. First-order observed rate constants for the solvolysis of PNPA (○, left scale) and PNPT (□, right scale) as a function of the concentration of HPI in 30% *n*-PrOH–H_2O, pH 10.02, ionic strength 0.02, 26°.

phenolic function of HPI and PNPA or PNPT, we assume that transesterification was followed by an intramolecular imidazole-catalyzed solvolysis as indicated in Scheme II.[19]

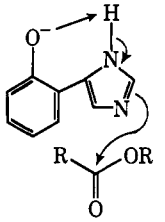
Scheme II



As an alternative procedure, the transesterification reaction could have been followed by solvolysis using water and hydroxide ion.[19b]

The favored geometry between the phenoxide ion and imidazole in 4(5)-(2′-hydroxyphenyl)imidazole (HPI) suggests an intramolecular phenoxide ion catalyzed imidazole catalysis

Scheme III



The total rate equation for the solvolytic reaction of PNPA and PNPT catalyzed by 4(5)-(2′-hydroxyphenyl)-imidazole (HPI) can be written in the following form

$$\text{rate} = [\text{ester}](k_n[\text{Im}] + k_n'[\text{PhO}^-] + k_{gb}[\text{Im}][\text{OH}^-] + k_n''[\text{PhO}^-] + k_{intra}[\text{PhO}^-]) \quad (1)$$

(18) T. C. Bruice and R. Lapinski, *J. Amer. Chem. Soc.*, **80**, 2265 (1958).

(19) (a) G. L. Schmir and T. C. Bruice, *ibid.*, **80**, 1173 (1958); (b) S. M. Felton and T. C. Bruice, *ibid.*, **91**, 6721 (1969).

In basic solution, the phenolic group of the HPI molecule is either free or dissociated, whereas the imidazole function remains predominately in its neutral form. The first two terms of eq 1 described the catalyses by the imidazole functions of the free HPI and the dissociated HPI, respectively. The third term is associated with a hydroxide ion catalyzed imidazole catalysis. The k_n'' term is associated with the previously mentioned nucleophilic catalysis catalyzed by the phenoxide portion of the catalyst molecule; the rate measured (the generation of phenoxide ion) should correspond to the formation of transesterification product, 4(5)-(2′-acetoxyphenyl)imidazole, which in turn depends upon the concentration of the substrate and the phenoxide ion of HPI. The last term of eq 1, k_{intra}, is associated with the proposed intramolecular phenoxide ion catalyzed imidazole catalysis. At pH above 8, the imidazole group of the HPI is present predominately in the neutral form while the phenolic functions are partially dissociated to phenoxide ion. This intramolecular process, therefore, will only depend on the phenoxide ion concentration in the catalyst molecule. The other modes of catalysis, such as general base catalysis by imidazole,[20] and imidazole-catalyzed imidazole catalysis were not considered. These modes of catalysis would not be expected for the conditions employed, *i.e.*, a dilute catalyst solution and substrates containing good leaving groups.

Equation 1 could also be written

$$k_{obsd} = [HPI][k_n(1 - \alpha) + k_n'\alpha + k_{gb}(OH^-) + k_n''\alpha + k_{intra}\alpha] \quad (2)$$

where k_{obsd} is the pseudo-first-order rate constant, α is the fraction of HPI existing as the phenoxide ion, and [HPI] is the molar concentration of 4(5)-(2′-hydroxyphenyl)imidazole.

Solvolytic reactions of the neutral substrates, *p*-nitrophenyl acetate (PNPA) and *p*-nitrophenyl toluate (PNPT), catalyzed by model compounds, such as 4(5)-(2′-methoxyphenyl)imidazole (MPI) and 1-methyl-4-(2′-hydroxyphenyl)imidazole (MHPI), were studied in 38% 1-propanol–water solutions at 26° at various pH levels with a constant ionic strength of 0.02. The results are listed in Tables III and IV.

Since there is no appreciable increase in the rate of solvolysis for both PNPA and PNPT in the presence of 4(5)-(2′-methoxyphenyl)imidazole at pH *ca.* 10 over that observed at pH *ca.* 7 (Table III), we can conclude that the hydroxide ion catalyzed imidazole catalysis (k_{gb}) must be very small in 4(5)-(2′-methoxyphenyl)-imidazole catalysis at pH values up to *ca.* 10. These results agree with previous studies[4] that the hydroxide ion catalyzed reaction of imidazole with *p*-nitrophenyl acetate could not be detected; at pH 11, the rate of hydrolysis of PNPA in the presence of 0.2 mole of imidazole was completely accounted for by the rate of the uncatalyzed reaction of imidazole and the rate of alkaline hydrolysis. The compounds 4(5)-(2′-hydroxyphenyl)imidazole (HPI) and 4(5)-(2′-methoxyphenyl)-imidazole (MPI) have a similar pK^{IMH^+} (Table II); thus the k_{gb} term in eq 2 can, therefore, also be neglected.

(20) B. M. Anderson, E. H. Cordes, and W. P. Jencks, *J. Biol. Chem.*, **236**, 455 (1961).

Table III. Solvolysis of Esters Catalyzed by 4(5)-(2′-Methoxyphenyl)imidazole in 30% (v/v) 1-Propanol–Water at 26°, μ = 0.02

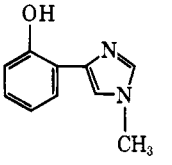
Ester	pH	k_{cat}, l./mol-min
PNPA	7.00	2.35
PNPA	9.97	Small[a]
PNPT	7.88	1.51×10^{-2}
PNPT	9.97	Small[a]

[a] k_{cat} value is small. Since k_{blank} is approximately equal to k_{measd}, an accurate determination of k_{cat} was not possible.

Table IV. Solvolysis of Esters Catalyzed by 1-Methyl-4-(2′-hydroxyphenyl)imidazole in 30% (v/v) 1-Propanol–Water Solution at 26°, μ = 0.02

Ester	pH	k_{cat}, l./mol min
PNPA	7.08	0.15
PNPA	9.72	2.02
PNPA	10.68	19.23
PNPT	7.88	0.58×10^{-2}
PNPT	9.72	3.08×10^{-2}
PNPT	10.68	15.89×10^{-2}

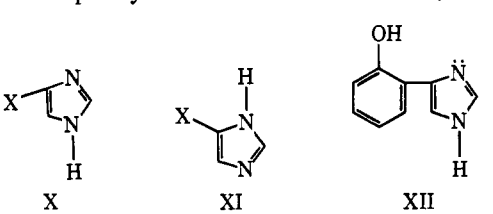
The literature indicates that free rotation around the internuclear bond in 4(5)-phenylimidazole is inhibited by conjugation between the two aromatic nuclei and that the rings are coplanar.[21] Since 1-methyl-4-(2′-hydroxyphenyl)imidazole (MHPI) (IX) has a similar structure, it should have the following conformation where the *N*-methyl group of the ortho substituent is directed away from the phenoxide group.



IX

Because the *N*-methyl group of 1-methyl-4-(2′-hydroxyphenyl)imidazole (MHPI) (IX) is removed from the phenoxide ion in the same molecule, the steric environment of the phenoxide ion in both MHPI and 4(5)-(2′-hydroxyphenyl)imidazole (HPI) are essentially identical. Also, the possibility of an intramolecular imidazole-catalyzed decomposition of a neighboring acetate group, such as shown in Scheme II, exists for both MPHI and HPI. Therefore, the use of 1-methyl-4-(2′-hydroxyphenyl)imidazole (IX) as a model compound to study the solvolysis of PNPA and PNPT, catalyzed by the phenoxide ion of 4(5)-(2′-hydroxyphenyl)imidazole (HPI), seems justified.

The tautomeric ratio (X:XI) of the imidazole group could be modified by the substituent at the 4(5) position.[16b] A phenyl substituent favors the 1,4 tautomer



(X) as indicated by the basicity constant of its *N*-methyl

(21) T. Hayashi and H. Midorikawa, *Sci. Pap. Inst. Phys. Chem. Res., Tokyo*, **58**, 139 (1964); *Chem. Abstr.*, **62**, 10317*f* (1965).

derivative.[16b] Results of potentiometric titrations (Table II) indicate that 4(5)-(2′-hydroxyphenyl)imidazole also exists predominately as its 1,4 tautomer (XII).

The facts that 4(5)-(2′-hydroxyphenyl)imidazole (HPI) (XII) and 1-methyl-4-(2′-hydroxyphenyl)imidazole (MHPI) (IX) utilized the same imidazole nitrogen (3 position) to catalyze ester solvolysis and that methyl substitution on the 1 position of imidazole has only a slight effect on its catalytic activity[1] further justify the choice of 1-methyl-4-(2′-hydroxyphenyl)imidazole (MHPI) as a good model compound to study the solvolysis of PNPA and PNPT, catalyzed by the imidazole group of 4(5)-(2′-hydroxyphenyl)imidazole (HPI).

The absence of an N–H group in the model compound MHPI precluded interference from an intramolecular phenoxide ion catalyzed imidazole catalysis reaction.

On these grounds we can use the solvolytic data on PNPA and PNPT in the presence of 1-methyl-4-(2′-hydroxyphenyl)imidazole (MHPI) (IX) and its dissociation constants (Table II) to estimate the catalytic effects by the phenoxide and imidazole functions of 4(5)-(2′-hydroxyphenyl)imidazole (HPI).[22] The combined values for the first, second, and the fourth terms of eq 2 at pH 10.02 are of the order of 9.78 l./mole min for PNPA and 0.08 l./mole min for PNPT. From these values, the slope of Figure 1, and the α value (α = 0.157 at pH 10.02) (eq 2), the k_{intra} for 4(5)-(2′-hydroxyphenyl)-imidazole could be estimated at 137.4 l./mole min and 6.39 l./mole min for PNPA and PNPT, respectively.

The simple nucleophilic imidazole catalysis factor (k_n of eq 2) can be obtained from the rate constant of 4(5)-(2′-hydroxyphenyl)imidazole at pH *ca.* 8 (Table V)

Table V. Solvolysis of Esters Catalyzed by 4(5)-(2′-Hydroxyphenyl)imidazole in 30% (v/v) 1-Propanol–Water Solution at 26°, μ = 0.02

Ester	pH	k_{cat} l./mol min	k_{intra}, l./mol min
PNPA	7.90	5.24	137.4
PNPT	8.82	0.11	6.39

where essentially no phenoxide ion is present and most of the imidazole groups exist in the neutral, active form.

By comparing the values of k_{intra} and k_n (Table V), it is clear that an intramolecular phenoxide ion does catalyze the imidazole catalysis quite efficiently, especially for esters such as *p*-nitrophenyl toluate (PNPT). Previous studies[4] have indicated that the solvolysis of this ester with imidazole is catalyzed by a hydroxide ion.

Intramolecular base-catalyzed imidazole catalysis also appears to operate during the hydrolysis of *p*-nitrophenyl acetate in the presence of 4(5)-(2′-dialkylaminoethyl)imidazole[6] where the base is an amine instead of a phenoxide ion.

Effects of 4(5)-[ω-(*p*-Hydroxyphenyl)nonyl]imidazole on the Solvolyses of Esters. Solvolytic reactions of *p*-nitrophenyl acetate (PNPA), catalyzed by 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]imidazole (HPNI), 4(5)-[ω-(*p*-methoxyphenyl)nonyl]imidazole (MPNI), *p*-cresol, and imidazole have been studied in 30% (v/v) 1-propanol–water at several different pH values. The results are listed in Table VI.

Table VI. Solvolysis of *p*-Nitrophenyl Acetate Catalyzed by Imidazole and or Phenol-Containing Compounds in 30% (v/v) 1-Propanol–Water at 26°, Ionic Strength 0.02

Catalyst	k_{cat}, l./mol min, at pH 7.08	7.90	8.98	9.97
HPNI	12.12	18.30	21.20	22.31
MPNI	14.01	19.25	23.60	24.24
Imidazole	8.42	11.52	11.80	9.91
p-Cresol	0.21	0.96	2.80	6.14

When comparing the catalytic rate constant of 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]imidazole (HPNI) at pH 9.97, where the hydroxyl and imidazolium groups are 5.81 and *ca.* 100% dissociated, respectively, with the catalytic rate constants of imidazole and *p*-cresol at the same degree of dissociation, there is very little, if any, cooperative effect operating between the phenoxide and imidazole function of HPNI during the solvolysis of *p*-nitrophenyl acetate (PNPA). Under conditions where there would be no participation of phenoxide ion during the solvolysis of PNPA, such as the reaction catalyzed by 4(5)-[ω-(*p*-methoxyphenyl)nonyl]imidazole (MPNI) and 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]imidazole (HPNI) at a pH less than 8, the catalytic rate constants of these long-chain compounds (MPNI and HPNI) are too large to be attributed to the imidazole function alone.

Polyvinylpyrrolidone in aqueous solution displays a strong binding affinity toward dissolved aromatic compounds, such as nitrobenzene, accompanied by an entropy gain. These binding forces have been attributed to both the hydrophobic attraction and the interaction of the π electrons of the aromatic compounds with the water-soluble polymer.[23] An increase in the dimerization constants of alkylcarboxylic acids[24] and the linear increase in the effectiveness of the enzyme inhibitors, 1-alkyl-3-aminocarbonylpyridinium chloride,[25] as the chain length increases from C_1 to C_{17} and C_3 to C_{11}, respectively, has also been explained in terms of increased hydrophobic interaction.

The small acceleration of the reaction catalyzed by the long-chain compounds (HPNI and MPNI) must be due to the presence of the long methylene chain, which increases the hydrophobic interaction between the substrate *p*-nitrophenyl acetate (PNPA) and the long-chain compounds. If this is the case, a long-chain substrate such as *p*-nitrophenyl palmitate would be solvolyzed more efficiently by a long-chain compound (HPNI or MPNI) than imidazole and *p*-cresol. Solvolytic studies of *p*-nitrophenyl palmitate (PNPP) catalyzed by 4(5)-[ω-(*p*-hydroxyphenyl)nonyl]imidazole (HPNI) and imidazole- or phenol-containing model compounds have been studied in 34% (v/v) 1-propanol–water at 26°. The results are listed in Table VII.

(22) In order to make this estimation, it was assumed that both HPI and MHPI have the similar catalytic rate constants (k_n, k_n', and k_n'' of eq 2). In reality, MHPI should be a better catalyst overall than HPI to catalyze the solvolysis of PNPA and PNPT. The pK values (Table II) indicated that MHPI should have a larger k_n'' and a smaller k_n' than HPI. The larger magnitude of k_n'' should outweigh its k_n' value and still make MHPI a better catalyst than HPI. Subsequently, the k_{intra} obtained should then be a little smaller than its real value.

(23) P. Molyneux and H. P. Frank, *J. Amer. Chem. Soc.*, **83**, 3169, 3175 (1961).

(24) (a) E. E. Schrier, M. Pottle, and H. A. Scherager, *J. Amer. Chem. Soc.*, **86**, 3444 (1964); (b) P. Mukerjee, *J. Phys. Chem.*, **69**, 2821 (1965).

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Table VII. Solvolysis of *p*-Nitrophenyl Palmitate Catalyzed by Imidazole and/or Phenol-Containing Compounds in 30% (v/v) 1-Propanol–Water at 26°, Ionic Strength 0.02

Catalyst	k_{cat}, l./mol min, at pH 7.08	7.90	8.98	9.97
HPNI	7.20	9.61	10.86	12.56
MPNI				14.58
p-Cresol				1.10
Imidazole	2.15	2.74	2.08	2.43

The results in Table VII indicate that imidazole and *p*-cresol are less efficient in catalyzing the solvolysis of a long-chain substrate than a short-chain substrate (Table VI). The decrease in catalyst efficiency can be attributed to steric hindrance caused by the long aliphatic chain located at the acyl portion of the substrate. The imidazole-catalyzed hydrolysis of esters of *p*-nitrophenol have been reported to be subject to steric hindrance.[26] The steric hindrance should be even larger if the long-chain compounds HPNI and MPNI are used as the catalyst.

In spite of more severe steric crowding, the MPNI- or HPNI-catalyzed solvolysis of *p*-nitrophenyl palmitate (PNPP) was more efficient (relative to imidazole) than the solvolysis of *p*-nitrophenyl acetate (PNPA) as previously expected. Polyoxyethylene (23) lauryl alcohol was reported[27] not to form micelles in aqueous solutions which contain 25% (by volume) or more of an additive, such as ethanol or 1,4-dioxane. The small observed rate enhancement during the solvolysis of PNPP catalyzed by long-chain compounds can, therefore, be attributed to a hydrophobic attraction between the substrate and the catalyst.

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Electron Transfer in the Type II Photoelimination of α-Aminoacetophenones

Albert Padwa,*[1] William Eisenhardt, Robert Gruber, and Deran Pashayan

Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214.
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Abstract: The type II photoelimination reaction of a series of α-aminoacetophenones has been studied. Quantum yields and rate constants for product formation were determined in several solvents. These ketones were found to undergo photoelimination with extraordinarily high rates but with modest quantum efficiency. Photoelimination of α-amino ketones with low-lying π–π^* triplet states also occurs with enhanced reaction rates. Attachment of an electron-withdrawing benzoyl group to the nitrogen atom decreases the rate of photoelimination. The results can best be rationalized by an electron-transfer route for which the rate constant may exceed diffusion control.

Studies of the photochemistry of ketones that possess a hydrogen-bearing γ carbon have shown that two major reaction pathways are available.[2-21] The first involves a photoelimination reaction, commonly called the Norrish type II cleavage,[22] to yield olefins and smaller carbonyl compounds, and the second involves the formation of cyclobutanols.[23] Both reactions appear to be intramolecular with little or no detectable side reactions and have been visualized as arising from a common biradical intermediate. In the case of aryl alkyl ketones, both reactions proceed by way of a triplet which leads to a 1,4-biradical intermediate which may either cyclize, undergo cleavage, or revert to starting ketone by reabstraction of hydrogen. The lines of evidence implicating the reversibility of the hydrogen transfer step are based on kinetic data[4,24] and are reinforced by stereochemical[25,26] and deuterium isotope effects.[21,27,28]

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