

TABLE I—RESULTS OF NEUTRON ACTIVATION ANALYSIS OF *l*-EPHEDRINE AND NOREPHEDRINE SILVER COMPLEX PYRIDINATES

Compound	Sample Wt., g.	Amount Ag, g.	Activity, C.p.m.	% Ag (Exptl.)	% Ag (Theor.)	% ^a Error
<i>l</i> -Ephedrine-Ag pyridinate (C ₂₀ H ₂₇ N ₃ O ₂)Ag(C ₅ H ₅ N)	0.5393	0.0541	38 ± 2	20.6	21.0	1.90
Standard AgNO ₃	0.5393	0.1665	114 ± 3	—	63.5	—
Norephedrine-Ag-pyridinate (C ₁₈ H ₂₃ N ₃ O ₂)Ag(C ₅ H ₅ N)	0.3918	0.0491	39 ± 2	22.0	22.3	1.35
Standard AgNO ₃	0.3929	0.1215	113 ± 3	—	63.5	—

^a $\frac{[\text{Percent Ag (Exptl.)} - \text{Percent Ag (Theor.)}]}{\text{Percent Ag (Theor.)}} \times 100$.

The use of this procedure in a manufacturing facility would provide a convenient analytical method for compounds of this nature.

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Keyphrases

Phenethylamine analogs—analysis
Silver complexes—phenethylamine analogs
Neutron activation—analysis

Identification of Aliphatic Amines from Rates of Cinnamoylation

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The second-order rate constants for reaction between *trans*-cinnamic anhydride and 26 aliphatic amines in acetonitrile solution are reported. The rate constant for this reaction is a discriminating criterion of identity.

EARLIER PAPERS in this series have described the identification of alcohols from rates of alkaline hydrolysis of their 3,5-dinitrobenzoate esters (1) and of sugars from their rates of oxime formation (2). Kinetic studies provide a powerful approach to the characterization of organic compounds because of the marked sensitivity of reaction rate to structure of the reactants. Because of its potential for distinguishing between closely related compounds, and its advantages of sensitivity, simplicity, and speed, rate measurement (actually rate constant measurement) should become a useful adjunct to spectroscopy and to conventional chemical methods of qualitative analysis.¹

A procedure for the determination of amines has recently been described in which the amine is

quantitatively converted to the corresponding cinnamide by acylation with *trans*-cinnamic anhydride (3). During the development of the method some cinnamoylation rates were measured, and it was noted that the acylation rate constant is dependent upon the amine structure. In the present paper this dependence is exploited to provide a new method for the characterization of primary and secondary aliphatic amines.

EXPERIMENTAL

Materials—*Trans*-cinnamic anhydride (J. T. Baker Chemical Co.) was recrystallized three times from benzene; m.p. 134–136°. Acetonitrile (Fisher Scientific Co., catalog No. A-21) was refluxed over phosphorus pentoxide and then distilled from phosphorus pentoxide through a packed column (4); b.p. 81–81.5°. Amines were purified by distillation.

Apparatus—Spectral measurements were made with a Cary model 14 recording spectrophotometer fitted with a thermostated cell compartment.

Procedure—Acetonitrile solutions of cinnamic anhydride (approximately $4 \times 10^{-6} M$) and of an amine (5.0×10^{-6} to $2.5 \times 10^{-2} M$, depending upon

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¹ An incidental benefit of this approach is the accumulation of extensive collections of rate data for related compounds under common conditions; such data may be put to valuable mechanistic use, and may also provide guidance in the development of quantitative analyses.

TABLE I—CINNAMOYLATION RATE CONSTANTS FOR ALIPHATIC AMINES

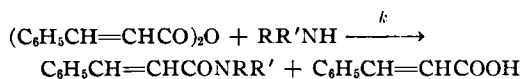
Amine	B.p., °C. ^a	k ($M^{-1} \text{ sec.}^{-1}$) ^b		pKa
		Mean ^c	Av. dev ^d	
Isopropyl-	33 (32-33)	21.42	0.09	10.63
<i>tert</i> -Butyl-	46 (44-45)	0.436	0.001	10.82
<i>n</i> -Propyl-	49 (47)	134.5	3.6	10.53
Diethyl-	55 (54)	30.3	0.6	10.98
Allyl-	56 (53)	33.8	0.5	9.69
<i>sec</i> -Butyl	63 (62)	16.95	0.07	10.56
Isobutyl-	69 (66-66.3)	115.3	0.0	10.72
<i>n</i> -Butyl-	77 (76)	158.3	0.4	10.60
Isoamyl-	95 (94-95)	156.8	5.9	10.6
<i>n</i> -Amyl-	104 (103-105)	160.8	4.5	10.64
Cyclopentyl-	105 (104-106)	46.0	0.8	9.95
Piperidine	109 (104-105)	1139	17	11.22
Di- <i>n</i> -propyl-	110 (109)	23.8	0.1	11.00
<i>n</i> -Hexyl-	128 (129-130)	168.8	5.7	10.64
Morpholine	130 (130-131)	151.6	4.1	8.70
Cyclohexyl-	134 (131-131.2)	25.9	0.3	10.64
Diisobutyl-	139 (137-139)	6.76	0.27	10.68
<i>N</i> -Methyl-cyclohexyl-	146 (146.5-147.5)	17.37	0.01	10.9
<i>N</i> -Ethyl-cyclohexyl-	164 (163-164)	0.629	0.006	11.3
<i>N</i> -Isopropyl-cyclohexyl-	174 (171-172)	0.107	0.004	11.3
<i>n</i> -Octyl-	180 (178-180)	164.4	3.7	10.65
Benzyl-	184 (181-183)	25.97	0.02	9.34
Diisoamyl-	187 (186-189)	3.69	0.05	10.94
β -Phenethyl-	198 (197-198)	58.3	0.5	9.83
Diisooctyl-	— (276)	8.34	0.03	—
Dibenzyl-	300 (285)	1.08	0.02	—

^a Values in parentheses are the author's values. ^b At 25° in acetonitrile solution. ^c Mean of 2 to 5 determinations. ^d Average deviation = $\sum |x_i - \bar{x}| / (n - 1)$.

reactivity) were equilibrated at $25.0 \pm 0.1^\circ$. Fifteen milliliters of each solution was mixed in a 50-ml. beaker and rapidly transferred to a 10-cm. cylindrical cell. The absorbance of the reaction mixture at 305 $m\mu$ was followed with time as a continuous trace on the recorder chart.

RESULTS AND DISCUSSION

The reaction studied is



For many amines this reaction is very rapid in acetonitrile solution, but the rate can be made experimentally accessible and convenient by employing low concentrations of the reactants. The amine concentration was always in excess, and first-order plots of $\log(A_t - A_\infty)$ against time were obtained.² From the slope the apparent first-order rate constant $k_{obs.}$ was calculated. This is related to the second-order rate constant k by $k_{obs.} = k$ [amine], thus permitting evaluation of k . Variation in amine concentration produced a directly proportional change in $k_{obs.}$, showing that the reaction is first order with respect to the amine.

Table I lists 26 amines, in order of increasing boiling point, with the second-order rate constants for their cinnamoylation.³ The results in Table I show that the cinnamoylation rate constant is a very discriminating criterion of identity, the maximum range

in relative rate being about 10^4 . (Aromatic amines are much less reactive than aliphatic amines.) In fact, this rate constant alone would permit one to identify most of the amines listed. By taking both boiling point and rate constant, positive identification could be made of every amine studied, except perhaps diethylamine and allylamine (and these can be distinguished by their pKa values).

A Bronsted-type plot of $\log k$ against pKa shows considerable scatter. Primary amines with no substituents on the α or β carbon atoms appear to behave well, giving a line with slope 0.78. Most of the deviations from this line can be accounted for in a qualitative way in terms of steric effects, which usually lower k , so that the reactivity (nucleophilicity) of the amine toward the anhydride is less than would be predicted from its basicity. The alicyclic secondary amines react faster than anticipated on the basis of their pKa values. Attempts to correlate the data with the use of Taft polar and steric substituent constants did not give useful results.

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² Note that for use as an identification tool, reaction kinetic studies must be designed to give first-order kinetics, because only a first-order rate constant can be evaluated without knowledge of reactant concentration. Since (presumably) the reactant identity will be unknown, its molecular weight and hence its concentration will be unknown.

³ Pyrrolidine was too reactive to be studied under first-order conditions.

Keyphrases

Amines, aliphatic—identification
Cinnamoylation rates—amine identification
UV spectrophotometry—reaction monitoring