ester in the hydrolyzing solution and was found not to effect the kinetics of the reaction.) The alcoholic mixture was placed in a dry 25-ml volumetric flask immersed in a constant-temperature bath. A hydrolyzing solution of the desired pH (borate, phosphate, or acetate buffers when necessary), concentration of nucleophile, and ionic strength (adjusted with sodium nitrate) was also immersed in the bath. After reaching bath temperature, a measured quantity of hydrolyzing solution (to give a solution 2.5×10^{-3} M in MOFB) was injected vigorously into the sample flask. The time of injection was taken as the initial reaction time. At intervals over three half-lives, samples were taken from the reaction mixture and quenched in a hydrochloric acid solution at a pH ~2. (Investigation had shown that the hydrolysis essentially is stopped at this pH.)[11] The absorbances of the quenched solutions were read on a Beckman DU spectrophotometer using a blank of hydrolyzing solution at pH 2. The very rapid runs were sampled using a Cornwall continuous pipettor immersed in the bath.

The large difference in the ultraviolet absorption at 260 mμ between methyl *o*-formylbenzoate and its hydrolysis product, *o*-formylbenzoic acid, in acid media was used in determining the concentrations of the reactants as a function of time. Using standard equations,[12] excellent pseudo-first-order plots were obtained. In a study of the reproducibility of duplicate runs, a variation of less than 2% in the rate constants was observed for a test group of runs. All pH measurements were made using a Beckman Model 76 expanded-scale pH meter. The error in pH, including buffer standardizations, was assumed to be no greater than ±0.07 pH units.

Registry No.—Piperazine, 110-85-0.

(11) Reference 2b gives a difference of 10^7 in the rate constants for hydroxide ion and hydronium ion catalyzed reactions.

(12) A. Frost and R. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1961, p 28.

On the Structure of N-Acyl-α-amino Ketones Obtained from 2-Alkylidenepseudoxazolones

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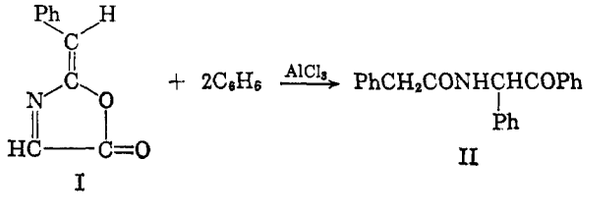
Received March 29, 1967

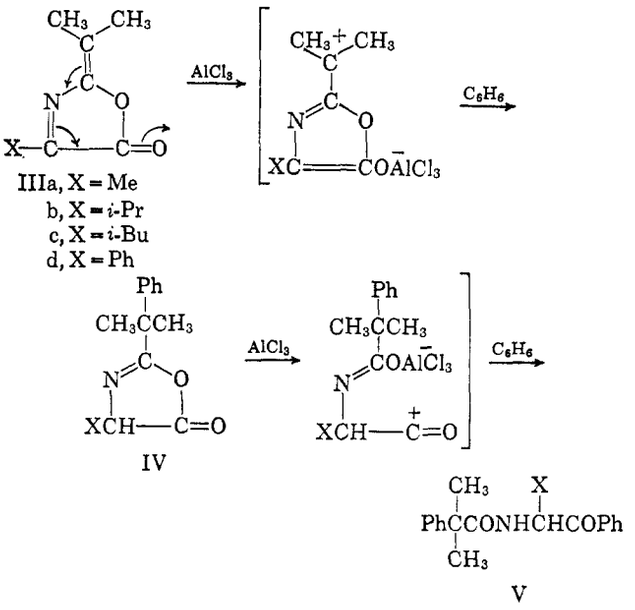
Filler[1] reported that 2-benzylidene-3-oxazolin-5-one (I) reacts with 2 equiv of benzene to give N-phenylacetyl-α-amino ketone II under Friedel–Crafts reaction conditions by the addition to C-4 and then ring opening at C-5 position. However, we have found that



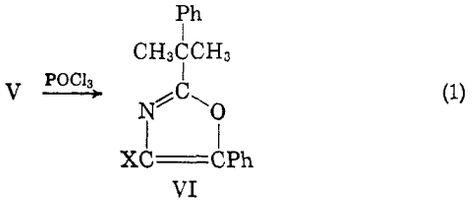
I II

2-isopropylidene-4-substituted 3-oxazolin-5-ones[2] (III) also reacted with benzene to give 1:2 adducts, N-(α-phenylisobutyryl)-α-amino ketones (V), by a reverse mode of 1,4-addition reaction at both C-5 and the isopropylidene *exo* double bond in the presence of anhydrous aluminum chloride. In III, the replacement of the hydrogen at C-4 could be the reason for lack of reaction at C-4. A suggested mechanism for the formation of V is *via* the formation of 1:1 adduct intermediate IV by increased electrophilic character of the isopropylidene substituent caused by the coordination of aluminum chloride to the carbonyl group, followed by its subsequent ring opening with benzene[3,4] (Scheme I).

SCHEME I



Elemental analyses and yields are summarized in Table I. The structure of V was confirmed by the infrared and the nmr spectral data as shown in Table II. The fact that V was readily cyclized to oxazole VI[5] (eq 1) by the treatment of dehydrating agent such as phosphorus oxychloride and to thiazole by phosphorus pentasulfide[6] is more convincing evidence of the structure V. The elemental analyse sand yields are shown in Table III.



Experimental Section

Reaction of 3-Oxazolin-5-ones with Benzene.—A sample of IIIb[2] (6.7 g, 0.04 mole) in 200 ml of dry benzene was added dropwise to a stirred slurry of 23.2 g (0.175 mole) of anhydrous aluminum chloride in 50 ml of dry benzene.[1] After the solution had been stirred for 2 hr, 120 ml of 18% HCl was added. The benzene layer was separated and washed twice with 100-ml portions of water and dried over anhydrous sodium sulfate. After removal of benzene, the resulting solid was recrystallized from ethanolic water to give N-(α-phenylisobutyryl)-α-aminoisobutyrophenone (Vb, 8 g), mp 78–81°, mol wt 290 (calcd 323.4) measured by vapor pressure osmometer in benzene. 2,4-Dinitrophenylhydrazone was obtained by refluxing with 1 equiv of 2,4-dinitrophenylhydrazine in ethanol: mp 125–127°.

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(2) Y. Iwakura, F. Toda, and Y. Torii, *Tetrahedron Letters*, 4427 (1966).

(3) R. Filler, *Advan. Heterocyclic Chem.*, **4**, 82 (1965).

(4) R. Filler and Y. S. Rao, *J. Org. Chem.*, **27**, 2403 (1962); A. Mustafa, A. E. Sammour, M. M. N. Eldeen, T. Salama, and M. K. Hilmy, *Ann.*, **689**, 189 (1965); A. Mustafa, A. E. Sammour, M. M. M. Eldeen, T. Salama, and H. K. Hilmy, *ibid.*, **689**, 189 (1965).

(5) P. T. Frangopol, A. T. Balaban, L. Birladeanu, and E. Cioranescu, *Tetrahedron*, **16**, 59 (1961).

(6) R. P. Kurkjy and E. V. Brown, *J. Am. Chem. Soc.*, **74**, 5778 (1952).

TABLE I

N-ACYL-α-AMINO KETONES (V)

X	Mp, °C	Yield, %	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
Me[a]	86–88.5	59	77.26	7.17	4.74	77.24	7.12	4.81
i-Pr[a]	79–81	62	77.98	7.79	4.33	77.94	7.63	4.64
i-Bu[a]	90–92	67	78.30	8.07	4.15	78.70	8.15	4.09
Ph[b]	109–112	73	80.64	6.49	3.92	80.24	6.69	3.91

[a] Solvent for crystallization, water–ethanol. [b] Solvent for crystallization, benzene–cyclohexane.

TABLE II

INFRARED AND NMR SPECTRAL DATA OF N-ACYL-α-AMINO KETONES (V)

	ν_{NH}^{Nujol}, cm^{-1}	$\nu_{C=O}^{Nujol}$,[a] cm^{-1}	$\nu_{C=O}^{Nujol}$,[b] cm^{-1}	τ (in 10% CCl_4); *J* values; area ratio
Me	3380	1670	1645	8.54 (s);[c] 3.86 (q);[d] 8.80 (d); J = 7.2 cps; 6:1:3
i-Pr	3420	1680	1660	8.48, 8.50 (s); 4.49 (d); 9.13, 9.54 (d); J = 7.2 cps; 3:3:1:3:3
i-Bu	3280	1685	1640	8.54 (s); 4.25 (t); 9.05, 9.26 (d); J = 5.4 cps; 6:1:3:3
Ph	3380	1675	1655	8.50, 8.59 (s); 3.46 (s); 3:3:1

[a] Ketone–carbonyl absorption. [b] Amide-I absorption. [c] Two methyl groups of α-phenylisobutyryl substituent. [d] α-Methynyl hydrogen.

TABLE III

OXAZOLES (VI)

X	Bp (mm) or mp, °C	Yield, %	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
Me	140–160 (0.5)	79	82.28	6.91	5.05	80.86[c]	6.99	5.13
Picrate[a]	130–131	..	59.28	4.38	11.06	59.46	4.37	10.86
i-Pr[b]	64.5–66	83	82.58	7.59	4.59	82.60	7.82	4.73
i-Bu[b]	47–49	83	82.72	7.89	4.38	82.79	7.95	4.29

[a] Solvent for crystallization, ethanol. [b] Solvent for crystallization, water–ethanol. [c] A satisfactory analysis was presumably not obtained by vaporization.

Anal. Calcd for $C_{27}H_{29}N_5O_5$: C, 64.40; H, 5.81; N, 13.91. Found: C, 64.36; H, 5.54; N, 13.88.

Ring Closure of Vb to 2-(α-Phenylisopropyl)-4-isopropyloxazole (VIb).—A solution of Vb (1.044 g) and phosphorus oxychloride (3 g) in toluene (10 ml) was refluxed for 4 hr and then water (10 ml) was added carefully to the solution. The reaction mixture was neutralized by 10% NaOH solution. The resulting mixture was extracted twice with each 100 ml of ether and the combined ether extract was washed with water and dried over anhydrous sodium sulfate. The oil that remained after the solvent was removed crystallized when cooled to room temperature. The product (VIb) was recrystallized from 20 ml of ethanol–water mixture to yield 0.82 g (83%): $\nu_{C=N}^{Nujol}$ 1550 cm^{-1};[7,8] nmr, τ 8.23 (s), 8.67 (d), 6.79 (septuplet); 6:6:1 in 10% CCl_4.[9] VIc showed $\nu_{C=N}^{Nujol}$ 1555 cm^{-1}; nmr, τ 8.25 (s), 9.03 (d); 6:6 in 10% CCl_4; λ_{max} 210 and 270 mμ in cyclohexane. VIa showed $\nu_{C=N}^{liq\ film}$ 1550 cm^{-1}; nmr, τ 8.28 (s), 7.69; 6:6 in 10% CCl_4. The picrate of VIa was obtained by heating with picric acid in ethanol.

Cyclization of Vb to 2-(α-Phenylisopropyl)-4-isopropylthiazole.—A mixture of Vb (927 mg) and phosphorus pentasulfide (291 mg) in dioxane (10 ml) was refluxed for 2 hr. Then 10 ml of water and 2 ml of concentrated HCl were added and the mixture was refluxed for 1 hr. The mixture was distilled under reduced pressure to remove distillable materials. Then residue was neutralized with 10% NaOH and the solution was extracted twice with 50-ml portions of ether. The combined ether extract was dried over anhydrous sodium sulfate. After removal of the ether by distillation, the resulting crystals were recrystallized from ethanol: mp 90–92°; yield, 65%; $\nu_{C=N}^{Nujol}$ 1530 and 1600 cm^{-1};[7,10] nmr, τ 8.20 (s), 8.74 (d), 6.93 (septuplet); 6:6:1 in 10% CCl_4.[9]

Anal. Calcd for $C_{21}H_{23}NS$: C, 78.46; H, 7.21; N, 4.36; S, 9.97. Found: C, 78.23; H, 7.07; N, 4.34; S, 9.82.,

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(9) P. Haake and W. B. Miller, *J. Am. Chem. Soc.*, **85**, 4044 (1963).
(10) J. Chouteau, G. Davidovics, J. Metzger, M. Azzaro, and M. Poite, *Bull. Soc. Chim. France*, 1794 (1962).

Registry No.—Va, 13318-37-1; Vb, 13341-90-7; Vb 2,4-dinitrophenylhydrazone, 13341-91-8; Vc, 13342-75-1; Vd, 13342-76-2; VIa, 13342-77-3; VIa picrate, 13342-78-4; VIb, 13342-79-5; VIc, 13342-80-8; 2-(α-phenylisopropyl)-4-isopropylthiazole, 13342-81-9.

Rearrangement of 2,6-Dibromocyclohexanone Ketals

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Received February 28, 1967

Recently it was reported that cyclopentadienone ketals can be prepared and used for synthetic purposes in place of the extremely reactive parent compound.[1] Since we were interested in preparing Michael adducts of cyclohexadienone, it appeared that cyclohexadienone ketals might be stable enough to isolate as starting materials for this purpose. They could then hopefully be hydrolyzed *in situ* in the presence of acidic addends to form the desired 3,5-disubstituted cyclohexanones.

Our approach was to brominate the appropriate ketal of cyclohexanone by the method of Garbisch[2] to give the 2,6-dibromocyclohexanone ketals. However, we were not able to isolate any cyclohexadienone ketal

(1) P. E. Eaton and R. A. Hudson, *J. Am. Chem. Soc.*, **87**, 2769 (1965).
(2) E. W. Garbisch, Jr., *J. Org. Chem.*, **30**, 2109 (1965).