TABLE I

N-Cyclohexenimine derivative	M.p., °C.	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
p-Chlorobenzoyl	100–101	66.2	6.0	5.9	66.4	6.1	5.9
p-Iodobenzoyl	127–128	47.7	4.3	4.3	47.7	4.3	4.5
p-Nitrobenzoyl	128–129	63.4	5.7	11.4	63.1	5.7	11.0
p-Bromobenzenesulfonyl	110–112	45.6	4.5	4.4	45.3	4.5	4.5
p-Iodobenzenesulfonyl	104	39.7	3.9	3.9	39.7	3.9	3.8

Experimental Section

Pyrolysis of N-Benzoylcyclohexenimine (Ia).—Compound Ia, prepared as described,[12] had a melting point of 78–80° (lit. m.p. 77–78°,[12] 70–72°[2]). A 3.0-g. sample was heated at 125–135° for 25 min., then distilled, b.p. 172° (11 mm.). Four equal fractions were collected without residue or forerun. Each fraction had a melting point of 78° and was shown to be unchanged starting material. The same result was obtained when a solution of Ia in benzene was heated in a metal bomb at 150° for 10 hr.

A solution of 1.0 g. of compound Ia in 8 ml. of benzene was heated in metal bomb at 200–210° for 9 hr. Evaporation of the benzene gave a solid residue, which was recrystallized from hexane, giving N-(2-cyclohexenyl)benzamide (III), m.p. 101–103°, undepressed on admixture with an authentic sample of III, m.p. 101–103° (lit.[13] m.p. 101.8–102.8°).

The previously unreported **N-phenylcarbamyl derivative of cyclohexenimine** was prepared by reaction of the imine with phenyl isocyanate in heptane solution, m.p. 159–160° after recrystallization from ethanol.

Anal. Calcd. for $C_{13}H_{16}N_2O$: C, 59.76; H, 5.78; N, 61.08. Found: C, 59.92; H, 5.80; N, 15.90.

Reaction of Cyclohexenimine with Methyl Iodide.—Treatment of cyclohexenimine with methyl iodide in benzene or ether at room temperature gave as the only isolable product up to 67% yield of *dl-trans*-N,N-dimethyl-2-iodocyclohexylammonium iodide, colorless needles, m.p. 159–160° after recrystallization from ethanol (lit.[9] m.p. 153–154°). A band due to the NH bond was observed in the infrared absorption spectrum at 3.35 μ.

Anal. Calcd. for $C_8H_{17}I_2N$: C, 25.21; H, 4.50; N, 3.67. Found: C, 25.28; H, 4.54; N, 3.38.

Reaction of N-Methylcyclohexenimine with Methyl Iodide.—A mixture of the imine and excess methyl iodide in ethanol was allowed to stand for several weeks at room temperature, during which time colorless crystals of *dl-trans*-N,N,N-trimethyl-2-iodocyclohexylammonium iodide separated, m.p. 110–111.5° (lit.[9] m.p. 107 dec.).

N-(*trans*-2-Iodocyclohexyl)benzamide (IVa).—A solution of 412 mg. of N-benzoylcyclohexenimine (Ia) and 2.2 g. of sodium iodide in 100 ml. of acetonitrile was stirred for 24 hr. The solvent was evaporated and the solid residue was washed with water to remove inorganic salts. By titration of the aqueous solution with hydrochloric acid to the methyl orange end point it was found to contain the equivalent of 0.5 mmole (25% yield) of sodium hydroxide. The water-insoluble material was dried and extracted with hexane. The hexane-soluble fraction contained 132 mg. (32%) of unreacted Ia. Recrystallization of the hexane-insoluble fraction from alcohol gave 99 mg. (15%) of the iodo amide IVa, m.p. 163–165°.

Anal. Calcd. for $C_{13}H_{16}INO$: C, 47.43; H, 4.90; N, 4.25. Found: C, 47.18; H, 5.01; N, 4.14.

Similar results were obtained when the reaction was run in acetone at room temperature or under reflux. Compound IVa was also prepared by the addition of concentrated aqueous hydroiodic acid to an acetone solution of Ia.

Reaction of N-(4-Nitrobenzoyl)cyclohexenimine (Ib) with Sodium Iodide.—A solution of 500 mg. of Ib and 1.0 g. of sodium iodide in 100 ml. of acetonitrile was refluxed for 24 hr. The solvent was evaporated and the residue was washed with water, giving a 95% yield of crude oxazoline Vb, m.p. 118–119° (lit. m.p. 120–121°,[14] 116.5–118.5°[15]).

When a similar reaction in acetone was interrupted after 2 hr. and the crude product was extracted with hexane, the hexane-insoluble material after recrystallization from benzene consisted of a 6% yield of N-(*trans*-2-iodocyclohexyl)-4-nitrobenzamide (IVb), m.p. 167–168°.

Anal. Calcd. for $C_{13}H_{15}IN_2O_3$: C, 41.73; H, 4.04; N, 7.49. Found: C, 42.36; H, 4.33; N, 7.29.

Oxazoline Vb was found in the hexane-soluble fraction.

Treatment of Iodo Amide IVa with Sodium Ethoxide.—To a solution of sodium ethoxide made from 1.0 g. of sodium and 100 ml. of ethanol was added 75 mg. of iodo amide IVa. After 1 day at 25° and 30 min. at 50°, an attempt was made to isolate oxazoline Va by way of the known picrate,[11] without success.

Three benzoyl and two benzenesulfonyl derivatives of cyclohexenimine were prepared in the usual way. Their melting points and analyses are shown in Table I.

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Synthesis of Benzyl Esters of α-Amino Acids

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With the increasing use of benzyl esters in peptide synthesis, new methods for their preparations have been developed from time to time. α-Amino acids on treatment with benzyl alcohol in the presence of acid catalysts such as polyphosphoric acid,[1] benzenesulfonic acid,[2] *p*-toluenesulfonic acid,[3] or sulfuryl chloride,[4] in such solvents as carbon tetrachloride are converted into benzyl esters.

The important advantage offered by benzyl esters over alkyl esters is that benzyl groups can be removed reductively by either catalytic hydrogenolysis[5] or sodium in liquid ammonia.[6] Looking to the usefulness of the benzyl ester group as a carbon-protecting group in peptide chemistry, we report a simple method for the synthesis of the benzyl esters of glycine, L-phenylalanine, L-glutamic acid, and S-benzyl-L-cysteine using thionyl chloride as a catalyst and a dehydrating agent. This catalyst has been used earlier in the synthesis of alkyl esters of amino acids.[7]

Experimental Section

The amino acid to be esterified was suspended in benzyl alcohol, and cooled to 5°. Thionyl chloride was added slowly, over a period of 20 min., and the reaction mixture was then heated on a steam bath for 5 hr. Dry ether was added to the

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TABLE I

EXPERIMENTAL DETAILS FOR PREPARATION OF BENZYL ESTER HYDROCHLORIDES FROM α-AMINO ACIDS

Product	Amount of starting material, g. (mmoles)	Benzyl alcohol, ml.	Thionyl chloride, ml.	M.p., °C. Obsd.	M.p., °C. Lit.	Yield, g. (%)
L-Phenylalanine benzyl ester (HCl)	3.3 (20)	125	20	202	203[a]	5.2 (90)
Glycine benzyl ester (HCl)	1.5 (20)	140	15	130	131–132[b]	3.0 (76)
S-Benzyl-L-cysteine benzyl ester (HCl)	2.11 (10)	125	20	92–93	91–97[a]	3.33 (100)
L-Glutamic dibenzyl ester (HCl)	2.94 (20)	105	20	93–95	94–95[c]	5.0 (69)

[a] Ref. 1. [b] Ref. 2. [c] B. Hargitay, A. J. Hubert, and R. Buyle, *Makromol. Chem.*, 56, 104 (1962).

solution until turbidity appeared. The mixture was then refrigerated for a few hours, during which time the benzyl ester hydrochloride crystallized. The product was collected by filtration and recrystallized from an absolute ethanol–ether mixture. Details for individual preparations are shown in Table I; the melting points obtained are in agreement with values reported in the literature. Important bands in the infrared spectra of all compounds included 2941 ($^+NH_3$ stretching), 1754 (ester carbonyl), 1205–1250 (C–O– stretching vibration), 738–727 cm.$^{-1}$ (monosubstituted benzene). The infrared data indicate the benzylation to have occurred at the carboxyl groups and not at the amino groups.

The Polonovski Rearrangement of Benzylideneaminoacetic Acid N-Oxides with Acid Anhydrides

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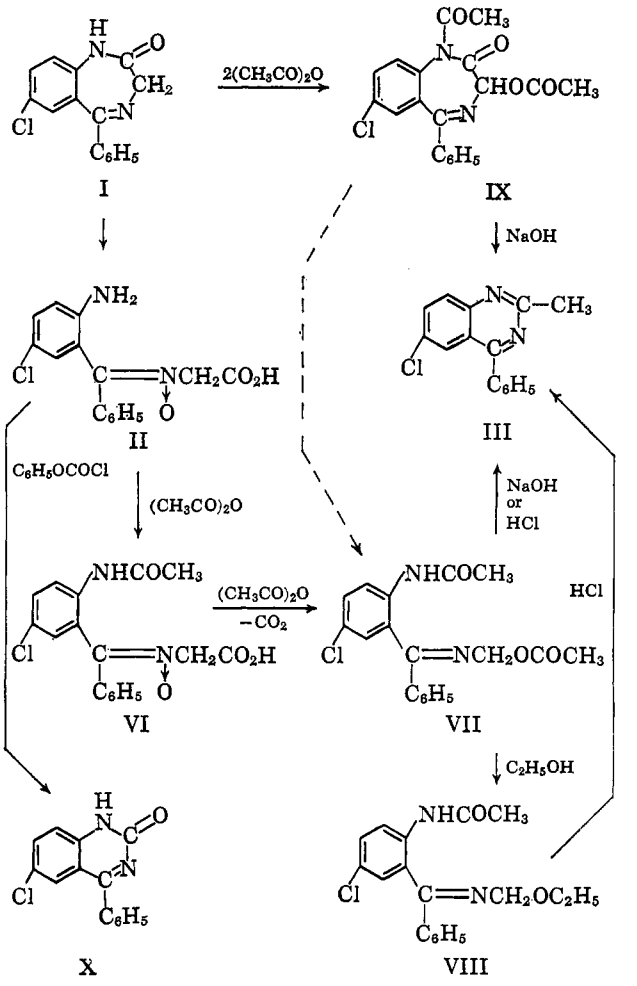
The formation of stable acetoxy compounds from a Polonovski-like rearrangement of N-oxides of cyclic compounds such as 7-chloro-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one 4-oxide (I)[1,2] has recently been reported.[3–7] Hence it was of interest to examine the reaction of acetic anhydride with a similar noncyclic N-oxide, 2-amino-5-chloro-α-phenylbenzylideneaminoacetic acid N-oxide (II),[1,2] prepared by hydrolysis of I (see Scheme I).

Vigorous treatment of II with acetic anhydride and isolation of the product by basification with sodium hydroxide unexpectedly gave 6-chloro-2-methyl-4-phenylquinazoline (III).[8] Compound II underwent analogous rearrangements with formic acetic anhydride and with chloroacetic anhydride, giving 6-chloro-4-phenylquinazoline (IV) and 6-chloro-2-chloromethyl-4-phenylquinazoline (V),[8] respectively.

In order to determine the course of the production of III, the isolation of the intermediates was attempted.

SCHEME I



Mild treatment of II with acetic anhydride gave the acetanilide (VI). More strenuous treatment of II (or similar treatment of VI) with acetic anhydride yielded 2′-(α-acetoxymethyliminobenzyl)-4′-chloroacetanilide (VII). Compound VII would result from the expected introduction of an acetoxy group onto the adjacent saturated methylene group of VI, accompanied by a facile decarboxylation of the intermediate. The infrared absorption spectrum of VII confirmed the presence of ester (5.73 μ) and amide (5.92 μ) functions and the absence of a carboxylic acid group. The n.m.r. spectrum ($CDCl_3$) of VII showed two methyl singlets (δ 2.00, 2.15) and one methylene singlet (δ 5.20). Treatment of VII with alkali or acid afforded III. Apparently the initial step with either acid or base is

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