for 3 hr., then diluted with ether, and extracted with 10% acetic acid. The aqueous phase, which was deep red, was further acidified with dilute hydrochloric acid, whereupon the color changed to yellow. The acidified aqueous mixture was extracted with ether–ethyl acetate. The organic extract was washed with water until neutral and dried over sodium sulfate. On partial evaporation of the solvent, there crystallized 165 mg. of V (28.3%) as fine orange needles: m.p. 208–212° dec., lit.[5] m.p. 211° dec.; $\lambda_{max}^{dioxane}$ 6.05, 6.14 μ; $\lambda_{max}^{ethanol}$ 285 mμ (ϵ 18,350), lit.[5] log ϵ 4.27.

Aziridines. XIII. Reactions of Cyclohexenimine Derivatives[1]

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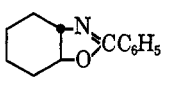
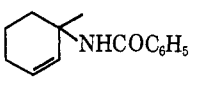
In 1956, it was reported[2] that pyrolysis of a sample of N-benzoylcyclohexenimine (Ia), m.p. 70–72°, at 120° followed by distillation at 180° (20 mm.) and chromatography on alumina gave a 20% yield of a product to which was ascribed the isomeric *trans*-oxazoline structure II. The assignment of structure was based only on the observation of a melting point of 66–67° (lit. m.p. 66.2–67.6°[3] and 68.5–69.0°[4] for authentic II) and an elemental analysis for nitrogen. In view of the similarity of melting points of Ia and II, this conclusion seems open to question. Furthermore, by analogy with a number of reported pyrolytic isomerizations of acyl aziridines, the anticipated product is the unsaturated amide III.[5,6]

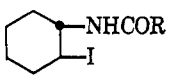
Ia, R = C_6H_5
b, R = $C_6H_4NO_2$-*p*



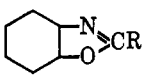
II



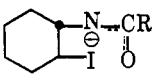
III



IVa, = R C_6H_5
b, = $C_6H_4NO_2$-*p*



Va, R = C_6H_5
b, R = $C_6H_4NO_2$-*p*



VIa, R = C_6H_5
b, R = $C_6H_4NO_2$-*p*

Therefore a reinvestigation of the pyrolysis was undertaken. It was found that heating compound Ia either alone as described,[2] or in a benzene solution at 150° for 10 hr., gave only unreacted starting material. In benzene solution at 200–210°, compound Ia was isomerized to the unsaturated amide III, which was conclusively identified by comparison with an authentic sample. The pyrolysis of Ia is therefore not anomalous, but follows the previously observed pattern.

In previous papers in this series we described the preparation of the quaternary methiodides of cycloheptenimine, cyclooctenimine, and *trans*-cyclododecenimine.[6,7] These are all stable, crystalline compounds which were found to be particularly suitable for structure determination by the three-dimensional single-crystal X-ray diffraction technique.[8] In contrast, it was reported that attempted quaternization of cyclohexenimine gave only ring-opened products.[9] These observations were confirmed in our laboratory. In view of these results, we prepared a number of N-aroyl and N-arenesulfonyl derivatives of cyclohexenimine containing a heavy element. Of these, the N-*p*-iodobenzenesulfonyl derivative was found suitable for X-ray study, and its structure was determined in the laboratory of L. M. Trefonas.[8]

A comparison of the structures reported by Trefonas for cyclohexenimine and cycloheptenimine provides an excellent rationalization for the difference in stability of the quaternary iodides. The six-membered ring of cyclohexenimine is very nearly planar and presumably there are no axial hydrogens to obstruct the nucleophilic back-side attack by iodide ion. In contrast, the seven-membered ring in cycloheptenimine is considerably puckered and appears to have four hydrogens in approximately axial positions which can block back-side approach of the iodide ion.

Examples of the isomerization of N-acyl aziridines by treatment with sodium iodide in acetone or acetonitrile have been reported,[5] and an iodo amide was suggested as a possible intermediate in this reaction. We have now found that treatment of N-benzoylcyclohexenimine Ia with sodium iodide in acetonitrile or acetone indeed gives an iodo amide, N-(*trans*-2-iodocyclohexyl)benzamide (IVa). On the other hand, the analogous *p*-nitrobenzoyl derivative Ib on treatment with sodium iodide in acetone gave primarily the oxazoline Vb, and only a small amount of the iodo amide IVb. In acetonitrile, Vb was formed exclusively, in 95% yield.

A possible explanation of this difference in reactivity is that the more strongly basic intermediate ion VIa preferentially abstracts a proton from the solvent (which may possibly contain some water) to form the amide IVa, whereas the more stable and less basic ion VIb undergoes cyclization.[10]

The iodo amide IVa was not cyclized to the oxazoline Va even on treatment with sodium ethoxide in ethanol, a result which was unexpected in view of the ready cyclization of the corresponding tosylate.[11]

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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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