of color. Both methyl vinyl sulfoxide and β-chloroethyl methyl sulfoxide showed one strong band in this region; the former a sharp band at 7.19 μ, the latter a broad band at 7.17–7.20 μ.

## Discussion

Analysis of the copolymerization data for the pair styrene ($M_1$)–methyl vinyl sulfoxide ($M_2$) according to the equation[7]

$$r_2 = \frac{M_1}{M_2}\left[\frac{dM_2}{dM_1}\left(1 + \frac{M_1}{M_2} - r_1\right) - 1\right]$$

gave values of $r_1 = 4.2 \pm 0.2$ and $r_2 = 0.01 \pm 0.01$. From these values of the copolymerization ratios for this system, the values of the resonance stabilization factor, $Q_2$, and the electrical factor, $e_2$, were calculated from the equations of Alfrey and Price.[8]

$$r_1 = Q_1/Q_2\, e^{-e_1(e_1-e_2)}$$
$$r_2 = Q_2/Q_1\, e^{-e_2(e_2-e_1)}$$

Using the values of $Q_1 = 1.0$ and $e_1 = -0.8$ for styrene[9] we obtain the values of $Q_2 = 0.10$ and $e_2 = 0.9$.

The value of 0.9 for $e$ for methyl vinyl sulfoxide, somewhat smaller in magnitude than $e = 1.2$ for methyl vinyl sulfone,[3] is reasonable in view of the smaller $\sigma$ constant for the methyl sulfoxide group (0.5) compared to the methyl sulfonyl group (0.7).[10]

The $Q$-value for methyl vinyl sulfoxide (0.10) is low, like methyl vinyl sulfone ($Q = 0.07 - 0.15$) as compared to methyl vinyl sulfide ($Q = 0.33 - 0.34$), indicating little resonance interaction between the sulfoxide group and the carbon free radical intermediate in polymerization.

$$R\cdot + CH_2{=}CH \longrightarrow RCH_2CH\cdot$$
$$\qquad\quad |\qquad\qquad\quad |$$
$$\qquad SOCH_3 \qquad\quad SOCH_3$$

Since the sulfoxide group retains an unshared pair of electrons on the sulfur and in this way resembles the sulfide more than the sulfone, it was surprising to find such a low $Q$ factor. However, the data on the ultraviolet spectra are in agreement since they too indicate little conjugation between the sulfoxide group and the carbon–carbon double bond for methyl vinyl sulfoxide; $\lambda_{max}$ 229 mμ, log ε 3.32. Mohler[11] reports that β-chloroethyl sulfoxide shows $\lambda_{max}$ 220 mμ, log ε 3.1.

This is a relatively small change in spectra when compared with the shift occurring for the sulfide: β-chloroethyl sulfide,[11] $\lambda_{max}$ 205 mμ, log ε 3.5; methyl vinyl sulfide,[3] $\lambda_{max}$ 240 mμ, log ε 4.0.

The ineffective resonance interaction between the sulfur–oxygen bond and the carbon–carbon bond is further indicated by the identity of the 7.19 μ bands for the saturated and unsaturated sulfoxides.[12] This contrasts with the shift of the carbonyl frequency from 5.81 μ in methyl ethyl ketone[13] to 5.95 μ in methyl vinyl ketone.[14]

(7) F. M. Lewis, C. Walling, W. Cummings, E. R. Briggs and F. R. Mayo, THIS JOURNAL, **70**, 1519 (1948).
(8) T. Alfrey and C. C. Price, *J. Polymer Sci.*, **2**, 101 (1947).
(9) C. C. Price, *ibid.*, **3**, 772 (1948).
(10) C. C. Price and J. J. Hydock, THIS JOURNAL, **74**, 1943 (1952).
(11) H. Mohler, *Helv. chim. acta*, **20**, 1188 (1937).
(12) It is not certain whether this 7.19 μ band is that of the sulfur–oxygen or the sulfur–carbon bond. If the former, resonance interaction should shift it to longer wave length, if the latter, to shorter wave length.
(13) H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 166.
(14) C. Cherrier, *Compt. rend.*, **225**, 997 (1947).

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

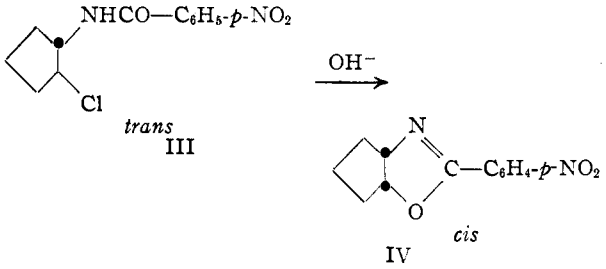
# A New Reaction: The Rearrangement of the Hydrochloride of *cis*-2-Aminocyclopentyl *p*-Nitrobenzoate

BY EUGENE E. VAN TAMELEN

The hydrochloride of *cis*-2-aminocyclopentyl *p*-nitrobenzoate rearranges when heated to *trans*-N-*p*-nitrobenzoyl-2-chlorocyclopentylamine. Experimental evidence is presented which points to an oxazoline intermediate. The scope of this reaction is reported and discussed.

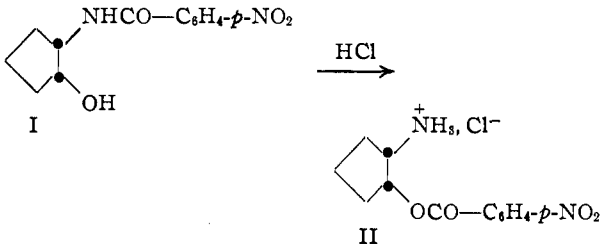
During an investigation concerned with the mechanism of acyl migrations, the author had occasion to attempt a N ⟶ O acyl transfer with *cis*-2-*p*-nitrobenzamidocyclopentanol (I). After the latter substance was refluxed for three hours in dry dioxane which had been previously saturated with dry hydrogen chloride, a 19% yield of the expected hydrochloride of *cis*-2-aminocyclopentyl *p*-nitrobenzoate (II) crystallized on cooling. In an attempt to account for the remainder of the material, the solvent was evaporated from the filtrate and a solid isolated. The product was found, however, to be neither II nor starting material, but a new substance (III), whose melting point (125–126°) was raised to 127.0–127.5° by crystallization from benzene. Compound III (i) was insoluble in water, (ii) gave a positive Beilstein halogen test but no precipitate with alcoholic silver nitrate, and (iii) exhibited strong absorption in the infrared at 6.04 microns, characteristic of the amide function. The analysis corresponded to the empirical formula $C_{12}H_{13}O_3N_2Cl$. These data are consistent with the formulation of III as N-*p*-nitrobenzoyl-2-chlorocyclopentylamine. The ready conversion of III to the known[1] (*cis*) oxazoline (IV) through the agency of alcoholic sodium hydroxide confirms this assignment; the type of ring closure exemplified here characterizes N-acyl-2-haloalkylamines. In addition, the transformation provides evidence for the stereochemistry of III. Winstein[2] and Carter[3] have amply demonstrated the generality of ring closure of N-acyl-2-amino-

(1) G. E. McCasland and D. A. Smith, THIS JOURNAL, **72**, 2190 (1950).
(2) S. Winstein and R. Boschan, *ibid.*, **72**, 4669 (1950).
(3) G. E. McCasland, R. K. Clark and H. E. Carter, *ibid.*, **71**, 637 (1949).




alkyl tosylates to oxazolines *via* internal displacement of the tosyloxy anion with inversion. Applying this finding to the case at hand, one can readily deduce that only a *trans*-N-acyl-2-chloroalkylamine III should easily afford the *cis*-oxazoline represented as IV. Actually, the formation of IV from III, as described above, is practically instantaneous.[4] The structure and stereochemistry are further confirmed by the formation of IV through dehydrohalogenation with silver acetate in wet acetic acid.[5]

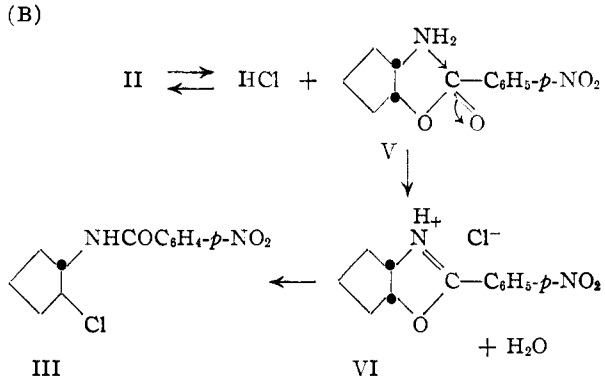
After the structure of the rearrangement product had been demonstrated, attention was turned to a consideration of the mechanistic route by which the product might have arisen. One possibility involved a *direct* replacement of hydroxyl by halogen with hydrogen chloride—a simple SN1 displacement which would result in the more stable configuration, probably *trans*. The step finds analogy in the conversion of *cis*-2-benzamidocyclohexanol to *trans*(?)-N-benzoyl-2-chlorocyclohexylamine by means of thionyl chloride.[5] It could be demonstrated, however, that the formation of the migration product II must precede—at least preponderantly—the formation of III, in that a 61% yield of II could be obtained by reducing the reaction time from three hours to several minutes.[6] Under these conditions the yield of III was negligible. The



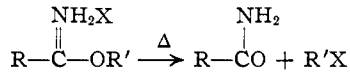

evidence for the presence of II in the reaction sequence was strengthened by the observation that II itself could be transformed into III by refluxing a dioxane suspension—with or without hydrogen chloride added—for three hours. The somewhat poorer yield by this route may be ascribed to side reactions favored by the inhomogeneity of the reaction medium.

Two possible schemes can be envisioned which account for the transformation of the ester hydrochloride II to the rearranged III. In (A), a thermally-induced equilibration between (i) the hydrochloride II, (ii) hydrogen chloride and free base (V), and, incidentally, (iii) dioxane hydrochloride, must be assumed to be an initial step. The acylate ion of V is subsequently displaced by chloride ion to *trans*-2-chlorocyclopentylamine and *p*-nitrobenzoic acid,[7] followed by amide formation from the two latter components. Perhaps more satisfactory is scheme (B). Here, thermal equilibration

(B)




of II is again an initial step, but is followed by ring closure to the oxazoline (IV) hydrochloride (VI).[1] At this point, one is on firm ground, since the thermal rearrangement of oxazoline hydrochlorides to 2-chloroalkyl amides is a known reaction.[8] It should be pointed out that this last-named reaction is simply a cyclic modification of the well-known pyrolytic rearrangement of iminoester hydrohalides to alkyl halides and amides, a reaction reported by Pinner,[9] discussed by Winstein,[2] and studied recently in detail by McElvain.[10]




In any event, the possibility of VI intermediating the reaction under consideration was confirmed by the finding that IV was converted to III in 77% yield by refluxing in dioxane–hydrogen chloride; presumably the hydrochloride VI is formed initially and is then converted to III. Final confirmation of scheme (B) was obtained by running both the I → III and the II → III conversions in the presence of added, equimolar amounts of carboxylic acids. Acid exchange experiments should lead to the chloroamide of the added acid if the intermolecular (A) is correct; on the other hand, (B) proceeds by an intramolecular mechanism, and added acids should have no effect on its course. Actually, in the presence of either benzoic or *o*-nitrobenzoic acid, III was apparently the only chloroamide formed; it was freed from the added acid by the addition of strong base, which simultaneously converted III to oxazoline IV, the identified end-product.

In an effort to investigate the scope of the reaction, *cis*-2-*p*-nitrobenzamidocyclohexanol (VII) and 2-*p*-nitrobenzamidoethanol (IX) were refluxed separately in dioxane–hydrogen chloride for several

(4) The proof of the configuration of III cannot be considered to be conclusive without a comparison of reactivity with its stereoisomer. Investigations in this direction are underway in this Laboratory.

(5) W. S. Johnson and E. N. Schubert, THIS JOURNAL, **72**, 2187 (1950).

(6) E. E. van Tamelen, *ibid.*, **73**, 5773 (1951).

(7) Such a step finds precedent in the work of Tronov and Ssibgatullin, *Ber.*, **62B**, 2850 (1929), who have shown the kinetics of the following reaction type to be consistent with an SN1 mechanism.

$$R—CO—OR' + HBr \longrightarrow R—CO—OH + R'Br$$

(8) E. M. Fry, *J. Org. Chem.*, **14**, 887 (1949).

(9) A. Pinner and F. Klein, *Ber.*, **10**, 1892 (1877).

(10) S. M. McElvain and B. E. Tate, THIS JOURNAL, **73**, 2233 (1951).

hours. In neither case could the chloroamide, corresponding to III, be isolated; only the amino ester hydrochlorides (VIII and X, respectively) resulting from acyl migration were identified. These failures may be interpreted to indicate that the ester and aminohydro halide functions must be most favorably oriented in space (as in II), in order that a reasonably rapid reaction rate may be expected. It should be emphasized as well, that rigorously and freshly purified reagents are required for a clean I → III or II → III conversion; otherwise the reaction product is low-melting and difficult to purify. In view of these several rigid requirements, it is perhaps not surprising that no reaction of the type described herein has been heretofore reported.

## Experimental[11]

*d,l-trans*-N-*p*-Nitrobenzoyl-2-chlorocyclopentylamine (III). A. From *d,l-cis*-2-*p*-Nitrobenzamidocyclopentanol (I).—A solution of 500 mg. (2 mmoles) of *cis*-2-*p*-nitrobenzamidocyclopentanol[1] in 50 ml. of freshly dried dioxane[12] was saturated with anhydrous hydrogen chloride gas (with careful exclusion of atmospheric moisture). A reflux condenser equipped with a calcium chloride drying tube was attached to the reaction flask and the solution gently refluxed for three hours. In order to induce crystallization of the *cis*-2-aminocyclopentyl *p*-nitrobenzoate hydrochloride, the solution was frozen and then allowed to warm to room temperature. The hydrochloride was filtered off and the filtrate evaporated to dryness *in vacuo*. The solid remaining was triturated thoroughly with hot water and filtered off with suction. The yield of nearly pure (m.p. 125–126°) chloroamide was 330 mg. (62%). Two recrystallizations from benzene afforded material of constant melting point (127–127.5°).

*Anal.* Calcd. for $C_{12}H_{13}O_3N_2Cl$: C, 53.63; H, 4.89; Cl, 13.29. Found: C, 53.83; H, 4.79; Cl, 13.14.

B. From *d,l-cis*-2-Aminocyclopentyl *p*-Nitrobenzoate Hydrochloride (II).—Two hundred and fifty mg. of *cis*-2-aminocyclopentyl *p*-nitrobenzoate hydrochloride[1] was suspended in 25 ml. of dry dioxane. Refluxing for three hours was accompanied by gradual solution of the solid. The isolation was carried out as described in (A) above. The crude chloroamide (m.p. 115–118°) weighed 160 mg.; recrystallization from benzene gave 100 mg. (50%) of material which melted at 125–126°. A mixed melting point determination showed this product to be identical with that described in (A). A comparable yield was obtained when the hydrogen chloride saturation was omitted from the above procedure.

C. From *d,l-cis*-2-*p*-Nitrophenyl-4,5-trimethyleneoxazoline (IV).—Three hundred mg. (1.30 mmoles) of oxazoline IV[1] was dissolved in 30 ml. of dioxane; the procedure described under (A) was followed, except that refluxing was continued for only 1.5 hours. The chloroamide obtained weighed 270 mg. (77%) and melted at 123–124°; it was identical with the material previously obtained.

Conversion of III to *d,l-cis*-2-*p*-Nitrophenyl-4,5-trimethyleneoxazoline (IV). D.—The chloroamide III (134 mg., 0.5 mmole) was dissolved in 1 ml. of hot 95% ethanol. An aliquot, consisting of 40 mg. (1 mmole) of sodium hydroxide dissolved in 0.8 ml. of 75% ethanol, was added in one portion and the resulting solution heated on the steam-bath for about one minute. The resulting mixture was poured into 4 ml. of water. The yield was 100 mg. (86%). The melting point (137–139°) of the oxazoline was undepressed upon admixture with an authentic sample,[1] m.p. 137.5–139.5°.

E.—One-half mmole of III was refluxed in 10 ml. of wet (two drops of water in 50 ml.) acetic acid solution along with 125 mg. of silver acetate for three hours. The reaction mixture was cooled and the silver chloride removed by filtration. The filtrate was evaporated *in vacuo* to a volume of 3–4 ml. After dilution with an equal volume of water, a slight excess of concentrated aqueous ammonia was added. The mixture was finally diluted with water to a volume of 20 ml. The precipitated oxazoline weighed 65 mg. (56%); crystallization from absolute ethanol afforded 30 mg. of pure material (m.p. 137–138°). The mixed melting point was undepressed.

Attempted Exchange Reactions with Benzoic and *o*-Nitrobenzoic Acids in the I → III and II → III Conversions.—The procedure followed was that described under (A) or (B), with the exception that an amount of benzoic acid equivalent to one mmole of I or II was dissolved in the reaction medium. The solid mixture obtained by evaporation of the dioxane solvent was dissolved in 1 ml. of hot ethanol. After the addition of 60 mg. of sodium hydroxide, dissolved in 1 ml. of 80% ethanol, the oxazoline was isolated as described under (D). A third attempt at exchange was made using *o*-nitrobenzoic acid in the I → III transformation. In each case, the previously obtained *p*-nitrophenyl oxazoline (IV) was the only product isolated, always directly in a high state of purity. Yields, based on I or II as starting materials, ranged from 45–50%. The identity was checked by a mixed melting point determination in each case.

Acyl Migration of *d,l-cis*-2-*p*-Nitrobenzamidocyclohexanol (VII).—One millimole (265 mg.) of the amide[1] was subjected to the reaction conditions outlined in (A). After being refluxed, the solution was allowed to cool. The crystalline material which precipitated melted at 235° (dec.) and thus appeared to be the hydrochloride of *cis*-2-aminocyclohexyl *p*-nitrobenzoate (VIII), reported m.p. 235–236°.[1] This was confirmed by converting the salt with strong, aqueous base to starting material *via* a reverse acyl migration. The expected rearrangement product, N-*p*-nitrobenzoyl-2-chlorocyclohexylamine, is known and has the melting point 181°.[1] The yield of the N → O migration product was 120 mg. (40%). From the mother liquors which resulted from the above work there could be isolated only starting amide.

Acyl Migration of 2-*p*-Nitrobenzamidoethanol (IX).—Four hundred and twenty milligrams of IX[13] was added to 25 ml. of dioxane–hydrogen chloride and the resulting solution refluxed for four hours. After cooling, the crystalline 2-aminoethyl *p*-nitrobenzoate hydrochloride (X) which had previously separated was removed by filtration and dried. Recrystallization from ethanol failed to raise the melting point (199–201°). The yield was 61%. The mother liquors yielded an amount of impure, water-insoluble material insufficient for purification.

*Anal.* Calcd. for $C_9H_{11}O_4N_2Cl$: C, 43.83; H, 4.49. Found: C, 43.80; H, 4.83.

The structure of the hydrochloride was confirmed by its reconversion to starting amide by means of aqueous alkali.

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(11) All melting points are corrected.

(12) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Company, Boston, Mass., 1941, p. 369.

(13) S. Frankel and M. Cornelius, *Ber.*, **51** 1654 (1918).