[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY, LEWISBURG, PENNA.]

The Isomerization of Aziridine Derivatives. V. The Formation of 1-Aryl-Δ^2-1,2,3-triazolines from 1-Arylazoaziridines[1]

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A new method for the preparation of 1-aryl-Δ^2-1,2,3-triazolines by the isomerization of 1-arylazoaziridines is reported.

Introduction

Syntheses of Δ^2-1,2,3-triazolines have heretofore involved either the addition of an aryl azide to an olefinic linkage such as occurs in N-arylmaleimides,[2] benzoquinones,[3,4] styrenes,[5,6] α-dicyclopentadienes,[6] α,β-unsaturated ketones,[6] cyclopentene,[6] acrylonitriles,[7] N,N-diethylethylene sulfonamide[8] and unsaturated esters[9] or the addition of diazomethane to anils.[5,10–12] A new method of synthesizing 1-aryl-Δ^2-1,2,3-triazolines by the isomerization of 1-arylazoaziridines is described in this paper. No general method for the synthesis of monosubstituted Δ^2-1,2,3-triazolines has been reported previously.

Results

The 1-arylazoaziridines (I) were prepared according to a published procedure[13] with slight but important modifications and subsequently isomerized in acetone solutions containing iodide ion or in one instance thiocyanate ion into the corresponding 1-aryl-Δ^2-1,2,3-triazolines (III). Table I summarizes the triazolines prepared by this method.

Most of the 1-arylazoaziridines prepared were oils that decomposed upon attempted distillation. In these cases the crude oils were immediately dissolved in acetone and isomerized. 1-Arylazoaziridines containing an *o*-substituent on the aryl moiety, such as 1-(2-methyl-4-bromophenylazo)-aziridine and 1-(2-methyl-5-nitrophenylazo)-aziridine, were very unstable. Both compounds exploded violently after standing at room temperature for 20–30 minutes. Other 1-arylazoaziridines, 1-(*p*-bromophenylazo)-aziridine and 1-(3-nitro-4-methylphenylazo)-aziridine, for example, decomposed vigorously with a shower of sparks when exposed to fumes of hydrogen bromide or hydrogen chloride.

Evidence supporting the triazoline structure was obtained by converting 1-phenyl-Δ^2-1,2,3-triazoline (III, Ar = C_6H_5) into N-2-chloroethylaniline hydrochloride(IV) by reaction with hydrochloric acid. The N-2-chloroethylaniline hydrochloride was identified by comparison of infrared spectrum and mixed melting point with an authentic sample.[14] The conversion of Δ^2-1,2,3-triazolines into N-2-chloroethylamino derivatives by treatment with hydrochloric acid is a known reaction.[6]

Thermal decomposition of 1-(*m*-chlorophenyl)-Δ^2-1,2,3-triazoline (III, Ar = *m*-ClC_6H_4) in refluxing heptane into 1-*m*-chlorophenylaziridine (V) constituted additional proof for the triazoline structure. Identification of V was made by comparison of infrared spectrum with a sample prepared by the alkaline solvolysis of N-2-chloroethyl-*m*-chloroaniline.[15] The thermal degradation of Δ^2-1,2,3-triazolines into aziridines has been reported several times[2,3,4,6] (see, however, ref. 12).

Other evidence supporting the triazoline structure was garnered by n.m.r. spectroscopy. The n.m.r. spectrum of 1-*p*-nitrophenyl-Δ^2-1,2,3-triazoline showed the two methylene functions as distinct, as would be expected, while the starting material, 1-(*p*-nitrophenylazo)-aziridine, does not show this difference.[16]

TABLE I

1-ARYL-Δ^2-1,2,3-TRIAZOLINES BY ISOMERIZATION OF 1-ARYLAZOAZIRIDINES

ArNN=NCH$_2$CH$_2$ Ar =	Yield, %	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
p-BrC_6H_4–[a]	84	121–122	18.58	18.65
m-$O_2NC_6H_4$–[a]	64	128–129	29.14	29.14
p-$O_2NC_6H_4$–[a]	98	145–146	29.14	28.85
3,4-$Cl_2C_6H_3$–[b]	83	94–96	19.44	19.44
p-ClC_6H_4–[c]	68	99–100.5	23.13	22.85
m-ClC_6H_4–[c]	60	54–55	23.13	22.81
p-$CH_3C_6H_4$–[c]	76	79–80.5	26.06	25.64
3-NO_2–4-$CH_3C_6H_3$–[d]	90	99–100.5	27.17	26.92
C_6H_5–[d]	80	90–91.5	28.54	28.32
p-IC_6H_4–[e]	85	146–147	15.38	15.31

[a] Recrystallized by adding petr. ether (b.p. 30–60°) to a warm solution of benzene until the solution became cloudy, followed by cooling in a Dry Ice–acetone-bath and filtering. [b] Recrystallized by adding petr. ether (b.p. 30–60°) to a solution of ether until solution became cloudy, followed by cooling in a Dry Ice–acetone-bath and filtering. [c] Recrystallized from petr. ether (b.p. 30–60°). [d] Recrystallized from cyclohexane. [e] Recrystallized by adding cyclohexane to a warm solution of benzene until the solution became cloudy, followed by cooling in a Dry Ice–acetone-bath and filtering. Yields are based on the weight of crude 1-aroylazoaziridine.

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(1) Aided by Grant No. T-143 A from the American Cancer Society.

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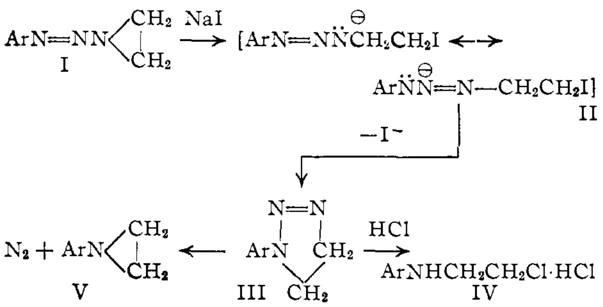
The rearrangement of 1-(*p*-nitrophenylazo)-2-methylaziridine was also studied. A compound having the same nitrogen content as the starting reagent and melting with decomposition at 121° was obtained. It is presumed (see Discussion) that 1-(*p*-nitrophenyl)-4-methyl-Δ^2-1,2,3-triazoline is the product of isomerization.

Many of the triazolines darken and decompose after a week or two standing at room temperature.

Discussion

The isomerizations probably occur by a nucleophilic attack of iodide ion on the aziridinyl carbon to yield the ion II which subsequently displaces an iodide ion by the negatively charged nitrogen



The mechanism is analogous to that proposed for the isomerizations of 1-aroylaziridines,[17] 1-N-arylbenzimidoylaziridines,[18] 1-aziridinecarboxanilides,[19] 1-aziridinethiocarboxanilide[19] and 2-(1-aziridinyl)-quinoxalines[20] by nucleophiles. Electron-withdrawing groups attached to the aryl group facilitated the isomerization. For example, 1-(*p*-nitrophenylazo)- and 1-(3,4-dichlorophenylazo)-aziridines rearranged at room temperature in 15–20 minutes with the evolution of heat. This would seem to indicate that the first step in the mechanism depicted above is rate determining.

It is conjectured that in the case of 1-(*p*-nitrophenylazo)-2-methylaziridine the iodide ion reacted at the less hindered methylene carbon of the aziridine ring. Expulsion of the iodide ion by the negatively charged nitrogen would give 1-*p*-nitrophenyl-4-methyl-Δ^2-1,2,3-triazoline. This would be analogous to the isomerization of 1-*p*-nitrobenzoyl-2-methylaziridine by sodium iodide into 2-*p*-nitrophenyl-4-methyl-2-oxazoline.[19]

The triazolines show medium infrared absorption at 10.1–10.3 μ and strong infrared absorption at 10.90–10.99 μ. Medium intensity bands at 10.1–10.2 μ have also been observed for the triazolo ring.[21]

Experimental

1-Arylazoaziridines.—A mixture of 0.05 mole of an aromatic amine, 19 ml. of 12 *N* hydrochloric acid and 17 ml. of water were heated until a clear solution was obtained. The mixture was poured with stirring onto 70 g. of ice in a beaker that was cooled externally. When the temperature reached 0–5° a cold solution (8°) of 3.6 g. of sodium nitrite dissolved in 30 ml. of water was added with vigorous stirring over a period of 2 minutes. Stirring was continued for an additional 15 minutes with ice (51–187 g.) being supplied to maintain a temperature of 0–5°. The solution was filtered by suction into a flask containing 100 g. of ice to which was added 100 ml. of a cold (10°) saturated solution of sodium acetate. Solid sodium acetate trihydrate (100–150 g.) was then introduced portionwise until the *p*H of the solution was 5.6–5.9. The temperature was held at 0–5° by ice (57–140 g.) during the buffering period. Aziridine was added dropwise and in great excess (9 g.) over a period of 5–10 minutes. At this point 50 g. of sodium chloride was added and stirring continued 5 minutes. The temperature during these two operations was held at 0–5° by addition of ice. The 1-arylazoaziridine separated either as an oil or a solid. The solid 1-arylazoaziridine was filtered immediately and washed several times with 10-ml. portions of ice-water. The material was promptly pressed between sheets of filter paper, placed in a desiccator containing anhydrous calcium chloride, and in this manner stored overnight in a refrigerator. The crude 1-arylazoaziridines were usually isomerized into the corresponding Δ^2-1,2,3-triazolines the following day. 1-(*p*-Bromophenylazo)-aziridine was prepared in 74% yield based on *p*-bromoaniline and melted at 56–57°. The compound had been prepared previously[13] in 33% yield, m.p. 56–56.5°. 1-(*p*-Nitrophenylazo)-aziridine was synthesized in 95% yield and melted after several recrystallizations from benzene–petroleum ether (b.p. 30–60°) at 92–93°. The recorded value[13] for the melting point of this compound was 70–70.5°.

Anal. Calcd. for $C_8H_8N_4O_2$: N, 29.14. Found: N, 28.85.

1-(3-Nitro-4-methylphenylazo)-aziridine was isolated in 89% yield and after recrystallization from petroleum ether (b.p. 30–60°) melted at 44.5–45.5°.

Anal. Calcd. for $C_9H_{10}N_4O_2$: N, 27.17. Found: N, 26.63.

1-(*p*-Nitrophenylazo)-2-methylaziridine was prepared in 54% yield and melted at 47–49° after recrystallization from petroleum ether (b.p. 30–60°).

Anal. Calcd. for $C_9H_{10}N_4O_2$: N, 27.17. Found: N, 26.69.

The 1-arylazoaziridines which were oils were separated from the reaction mixture by extracting repeatedly with chloroform (500 ml.). Each extract was poured into a flask immersed in an ice-bath until the extraction process was complete. The pooled extracts were divided into two portions and the chloroform quickly evaporated by means of compressed air. Dark red oils remained as well as a small quantity of water. The organic layer was separated by means of a separatory funnel and dried for 1 hour over anhydrous sodium carbonate. The oils were kept in a refrigerator during this period of drying. Transformation of these oils into tars will result if the drying operation is continued much beyond an hour. Suction filtration into a tared flask gave the crude yield of 1-arylazoaziridine. These oils were then isomerized immediately to the triazolines. Deletion of the drying procedure gave almost the same quality of crude product in the isomerization step.

Isomerization of 1-Arylazoaziridines.—Usually 0.0185 mole of 1-arylazoaziridine was dissolved in 35 ml. of anhydrous acetone containing 0.5 g. of sodium iodide. The reaction mixtures were kept at room temperature for 30 minutes when the aryl moiety was *p*-$O_2NC_6H_4$–, *m*-$O_2NC_6H_4$–, 3,4-$Cl_2C_6H_3$–, 3-O_2N–4-$H_3CC_6N_3$–; otherwise the reaction mixture was refluxed for 1 hour. The solvent was evaporated and 5 ml. of cold water was added to the solid residue. The crude 1-aryl-Δ^2-1,2,3-triazoline was filtered, washed with two 5-ml. portions of cold water and recrystallized from an appropriate solvent (see Table I). On occasion a crude triazoline separated as an oil upon evaporation of the acetone. In such cases the oily triazoline was taken up in 10 ml. of ether. A little petroleum ether was added and the mixture cooled in a Dry Ice–acetone-bath whereupon the triazoline precipitates.

The presumed 1-*p*-nitrophenyl-4-methyl-Δ^2-1,2,3-triazoline was recrystallized from benzene. It decomposed at 121°.

Anal. Calcd. for $C_9H_{10}N_4O_2$: N, 27.17. Found: N, 26.90.

N-(2-Chloroethyl)-aniline Hydrochloride from 1-Phenyl-Δ^2-1,2,3-triazoline.—Two milliliters of 12 *N* HCl was added to 300 mg. of the triazoline. A vigorous evolution of gas

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occurred and the solution turned a deep red in color; after standing for 10 minutes the solution was evaporated by means of compressed air. A dark-colored oil was obtained which changed into a solid, m.p. 145–150°, and weighed 382 mg. (87%). Four recrystallizations from anhydrous acetone gave a light gray material, m.p. 155–157°. A mixed melting point with an authentic sample[14] melted at 157–158° and infrared spectra of the two samples were identical.

1-(*m*-Chlorophenyl)-aziridine.—A mixture of 352 mg. of 1-(*m*-chlorophenyl)-Δ^2-1,2,3-triazoline and 75 ml. of heptane was refluxed 20 hours. The mixture was cooled and several pellets of sodium hydroxide added to prevent polymerization of the formed aziridine.[15] The heptane was evaporated until a volume of 9.5 ml. remained. An infrared spectrum of an authentic sample[15] of 1-(*m*-chlorophenyl)-aziridine dissolved in heptane was identical with a spectrum of the reaction mixture. All the heptane was then evaporated and the residual oil was removed from the pellets of sodium hydroxide. The crude 1-(*m*-chlorophenyl)-aziridine (210 mg.) had an infrared spectrum that identically corresponded in every respect to the spectrum of the true sample.

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[CONTRIBUTION FROM THE EVANS CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY, COLUMBUS 10, O.]

Synthesis and Reactions of 4-Trichloromethyl-2,4,5-trimethyl-2,5-cyclohexadienone[1]

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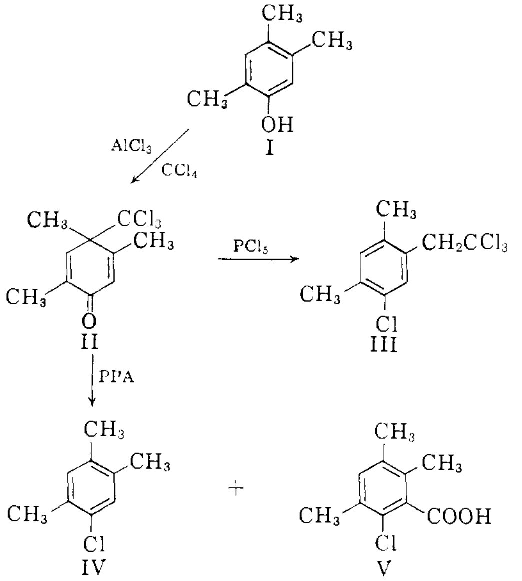
2,4,5-Trimethylphenol (I), aluminum chloride and carbon tetrachloride react to give 4-trichloromethyl-2,4,5-trimethyl-2,5-cyclohexadienone (II) in 70% yield; II reacts with phosphorus pentachloride to yield 2,4-dimethyl-5-(β,β,β-trichloroethyl)-chlorobenzene (III) in 91% yield, and with polyphosphoric acid to yield 2,4,5-trimethylchlorobenzene (IV) (*ca.* 20%) and 2-chloro-3,5,6-trimethylbenzoic acid (V) (*ca.* 40%).

The reactions of *p*-cresol[3a,4] and 3,4-dimethylphenol[5] with carbon tetrachloride and aluminum chloride to form 4-methyl-4-trichloromethyl-2,5-cyclohexadienone and 3,4-dimethyl-4-trichloromethyl-2,5-cyclohexadienone, respectively, have been described. In view of the interesting reactions of these dienones with phosphorus pentachloride[5,6] and polyphosphoric acid[6] (PPA), we have extended our studies to 2,4,5-trimethylphenol (I).

On reaction in carbon tetrachloride solution with aluminum chloride, Compound I was converted smoothly into 4-trichloromethyl-2,4,5-trimethyl-2,5-cyclohexadienone (II). The latter was converted into 2,4-dimethyl-5-(β,β,β-trichloroethyl)-chlorobenzene (III) by treatment with phosphorus pentachloride and into a mixture of 2,4,5-trimethylchlorobenzene (IV) and 2-chloro-3,5,6-trimethylbenzoic acid (V) by treatment with polyphosphoric acid. Thus, the chemistry of I and II is similar to that of their analogs.[5,6] The formation of products is satisfactorily explained by the mechanisms previously postulated.[5,6] Of interest is the relatively large yield of the acid V which results from the 1,3-migration of the trichloromethyl group to a position on the nucleus which has two *ortho* groups, methyl and chloro. In the case of the analogous rearrangement of 3,4-dimethyl-4-trichloromethyl-2,5-cyclohexadienone with PPA, two acids were formed[6]; namely, 2-chloro-4,5-dimethylbenzoic acid (in the 50–60% yield range) and 2-chloro-5,6-dimethylbenzoic acid (in 3% yield). Since the formation of the latter acid involves migration to a position having two *ortho* substituents, it was of interest to see what would happen if there were only such a position open in the starting dienone. The results herein reported show that rearrangement of a trichloromethyl group to a hindered position on the ring occurs readily.



The structure of III was established as follows. Dehydrochlorination yielded 5-(β,β-dichlorovinyl)-2,4-dimethylchlorobenzene (VI) which was oxidized to 5-chloro-2,4-dimethylbenzoic acid (VIIa). As the latter was unknown, its structure was established by conversion into dimethyl 2,4-dimethyl-1,3-benzenedicarboxylate[7] (VIIIb).

The structure of IV was proved by oxidation of durene[8] by nitric acid[9] to an acid which must be

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[3] Postdoctoral fellow, 1960–1961.

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[8] We acknowledge with thanks the gift of a sample of durene from the Humble Oil and Refining Co., Baytown, Tex.

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