STEREOSELECTIVE trans-N-CHLORINATION OF THE POTASSIUM SALT OF AZIRIDINE-2,2-DICARBOXYLIC ACID METHYL ESTER*

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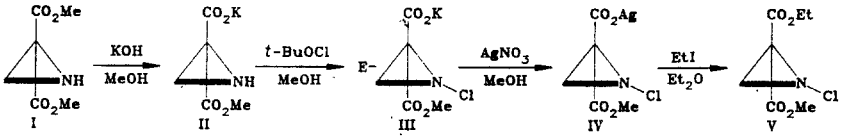
Primarily trans-1-chloroaziridine is formed in the chlorination of the potassium salt of aziridine-2,2-dicarboxylic acid methyl ester. The silver salt and then the mixed methyl ethyl ester, as well as the trimethylammonium and α-phenylethylammonium salts, were obtained from trans-1-chloroaziridine. Signals of diastereomers are observed in the PMR spectrum of the E isomer of the α-phenylethylammonium salt; this opens up the fundamental possibility of separation into antipodes.

The trans stereospecificity of nucleophilic substitution at the ester group of 1-methoxyaziridine-2,2-dicarboxylic ester [2, 3] is the basis for a scheme for complete separation into antipodes [4], as well as for the synthesis of the diastereomerically pure derivatives that are necessary for the determination of the inversion barriers with respect to the epimerization kinetics [2].

Transformations of this sort cannot be accomplished with N-chloroaziridine-2,2-dicarboxylic acid esters [5], which are dechlorinated by nucleophiles: the diethyl ester under the influence of dimethylamine in ether [5], and aziridine-2,2-dicarboxylic acid dimethyl ester [I] by the action of an equivalent amount of KOH or MeONa in absolute methanol, was demonstrated in the present research.

However, we were able to obtain N-chloroaziridine-2,2-dicarboxylic acid monomethyl ester potassium salt (III) by another method – by chlorination of monopotassium salt II, which is formed by treatment of diester I with an equivalent amount of KOH in methanol.



Salt III is formed primarily in the trans form (according to the PMR data, E/Z = 7.5), since the more solvated (in the polar solvent) carboxylate group hinders cis approach of the chlorinating reagent. The preponderance of the E isomer is retained in the subsequent transformations via the indicated scheme (see the experimental section).

It should be noted that, despite the known facile solvolytic cleavage of N-chloroaziridines by silver salts [6], N-chloroaziridine silver salt IV, which was characterized from the PMR spectrum, was obtained in quantitative yield from N-chloroaziridine potassium salt III by ion exchange. The retention of the N-chloroaziridine ring in IV was also confirmed by its conversion to mixed ester V, which, with respect to the PMR spectrum of the protons of the ring and methoxy group, is similar to dimethyl N-chloroaziridine-2,2-dicarboxylate [7]. The enrichment of ester V in the E isomer as compared with starting salt IV can be explained by steric hindrance to alkylation of the Z-IV isomer (see top of following page).

From the kinetics of E–Z isomerization of ester V we found the inversion barrier of the N atom ($\Delta G_{inv}^{\neq}$ = 24.0 ± 0.02 kcal/mole at 56°C in benzene; equilibrium ratio E/Z = 48/52),

*Communication 55 from the series "Asymmetric nitrogen." See [1] for communication 54.

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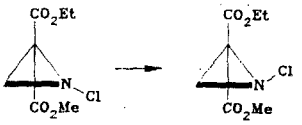
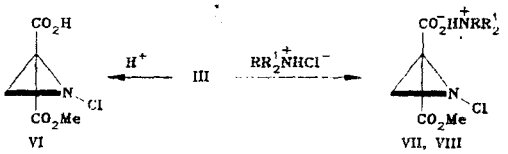


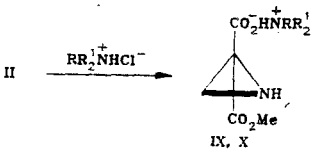
which can be regarded as an estimated value, since the rate of inversion changes significantly in the presence of uncontrollable impurities. For comparison, one can cite the known $\Delta G_{inv}^{\neq}$ values of chloroaziridines ($\Delta G_{inv}^{\neq}$ = 26.8 kcal/mole for 1-chloro-2-methylaziridine in CCl_4 at 80°C [8], and $\Delta G_{inv}^{\neq}$ = ~24 kcal/mole for 1-chloro-2,2-diphenylaziridine [9]).

From chloroaziridine potassium salt III one can obtain both free acid VI, which is stable in solution, and its trimethylammonium (VII) and α-phenylethylammonium (VIII) salts.



VII R=R¹=Me; VIII R=Ph(Me)CH, R¹=H

To confirm that dechlorination does not occur in this case we obtained genuine dechlorinated salts IX and X and demonstrated that they differ from chlorinated analogs VII and VIII (see the experimental section).



IX R=R¹=Me; X R=Ph(Me)CH, R¹=H

Thus we have demonstrated the fundamental possibility of the separation into antipodes of 1-chloroaziridine-2,2-dicarboxylic acid esters through salt III and then via the general scheme developed in [4]; there is a possibility of monitoring this separation, since the diastereomers of salt E-VIII differ with respect to the PMR spectrum of the A-H and B-H protons of the aziridine ring (see the experimental section).

EXPERIMENTAL

The PMR spectra were recorded with a Bruker WM-400 spectrometer. The IR spectra of microlayers of the compounds were recorded with a UR-20 spectrometer.

Dimethyl aziridine-2,2-dicarboxylate (I) was obtained by the method in [7] and had bp 67°C (2 mm) and n_D^{20} 1.4506.

Aziridine-2,2-dicarboxylic Acid Methyl Ester Monopotassium Salt (II). A solution of 0.56 g (10 mmole) of KOH in 10 ml of absolute methanol was added with stirring to a solution of 1.60 g (10 mmole) of diester I in 10 ml of absolute methanol, and the mixture was allowed to stand for 12 h. Absolute ether (200 ml) was then added, and precipitated salt II was separated, washed with ether, and dried in vacuo to give 1.74 g (95%) of product. PMR spectrum (CD_3OD): 2.05 (d, A-H, $^2J_{AB}$ = −1.5 Hz), 2.10 (d, B-H), and 3.74 ppm (s, CH_3O).

1-Chloroaziridine-2,2-dicarboxylic Acid Methyl Ester Potassium Salt (III). A 0.55-g (5 mmole) sample of tert-butyl hypochlorite was added in the course of 2 min to a solution of 0.92 g (5 mmole) of salt II in 30 ml of absolute methanol, and the mixture was stirred for 10 min. Salt III was characterized without isolation by means of its PMR spectrum (CD_3OD): E isomer: 2.66 (d, A-H, $^2J_{AB}$ = −2.7 Hz), 2.75 (d, B-H), 3.83 ppm (s, CH_3O); Z isomer: 2.66 (d, A-H, $^2J_{AB}$ = −2.7 Hz), 2.80 (d, B-H), 3.75 ppm (s, CH_3O); E/Z = 7.5.

1-Chloroaziridine-2,2-dicarboxylic Acid Methyl Ester Silver Salt (IV). A solution of 0.85 g (5 mmole) of $AgNO_3$ in 50 ml of absolute methanol was added to the solution of potassium salt III obtained in the preceding experiment, and the precipitated silver salt IV was removed by filtration, washed with absolute methanol (five 50-ml portions), and dried in vacuo in the dark (it darkened in light). The yield was 1.43 g (100% based on the amount of

salt II used for the chlorination). Salt IV was identified from its PMR spectrum (CD_3OD): E isomer: 2.67 (d, A-H, $^2J_{AB}$ = −2.9 Hz), 2.78 (d, B-H), 3.82 ppm (s, CH_3O); Z isomer: 2.64 (d, A-H, $^2J_{AB}$ = −2.9 Hz), 2.79 (B-H), 3.74 ppm (s, CH_3O); E/Z = 1.7. The change in the isomer ratio as compared with starting salt III was due to isomerization, since the spectrum was recorded 3 h after preparation of the solution.

Methyl Ethyl 1-Chloroaziridine-2,2-dicarboxylate (V). A 1.66-g (10 mmole) sample of ethyl iodide was added to a suspension of 1.43 g (5 mmole) of salt IV in 10 ml of absolute ether at 0°C, and the mixture was stirred at 0°C for 3 h. The precipitate was removed by filtration, and the filtrate was evaporated in vacuo to give 0.31 g (30%) of an oil with n_D^{20} 1.4648. IR spectrum: 1732, 1753 cm^{-1} (CO). PMR spectrum ($CDCl_3$): E isomer: 1.27 (t, CH_3), 2.80 (d, A-H, $^2J_{AB}$ = −2.9 Hz), 2.96 (d, B-H), 3.88 ppm (s, CH_3O); 4.24 (d, q, CH_2O), ABX_3, $\Delta\nu_{AB}$ = 1.0 Hz, $^2J_{AB}$ = $^3J_{AX}$ = $^3J_{BX}$ = 7.1 Hz); Z isomer: 1.33 (t, CH_3), 2.79 (d, A-H, $^2J_{AB}$ = −2.9 Hz), 2.96 (d, B-H), 3.78 (s, CH_3O), 4.35 ppm (m, CH_2O, ABX_3, $\Delta\nu_{AB}$ = 7.0 Hz, $^2J_{AB}$ = 6.9, $^3J_{AX}$ = $^3J_{BX}$ = 7.1 Hz); E/Z = 21. Found, %: N 6.70. $C_7H_{10}ClNO_4$. Calculated, %: N 6.74.

1-Chloroaziridine-2,2-dicarboxylic Acid Monomethyl Ester (VI). Dowex 50B × 12 200/400 ion-exchange resin was added to a solution of 0.29 g (1 mmole) of potassium salt III in 3 ml of CD_3OD, and the mixture was shaken until the solution was acidic (pH ~3). The solution was decanted, and the substance was identified from its PMR spectrum (CD_3OD): E isomer: 2.86 (d, A-H, $^2J_{AB}$ = −3.2 Hz), 2.69 (d, B-H), 3.89 ppm (s, CH_3O); Z isomer: 2.85 (d, A-H, $^2J_{AB}$ = −3.2 Hz), 2.93 (d, B-H), 3.80 ppm (s, CH_3O); E/Z = 1.6 3 h after isolation of the substance. Judging from the spectrum, monoacid VI is stable in solution at 20°C.

1-Chloroaziridine-2,2-dicarboxylic Acid Methyl Ester Trimethylammonium Salt (VII). A solution of 96 mg (1 mmole) of $Me_3N \cdot HCl$ in 1 ml of CD_3OD was added to a solution of 0.22 g (1 mmole) of salt III in 1 ml of CD_3OD, and the mixture was stirred for 30 min. The precipitated KCl was separated, and the salt was identified from its PMR spectrum (CD_3OD): E isomer: 2.62 (d, A-H, $^2J_{AB}$ = −3.0 Hz), 2.72 (d, B-H), 2.82 (s, $Me_3\overset{+}{N}$), 3.77 ppm (s, CH_3O); Z isomer: 2.62 (d, A-H, $^2J_{AB}$ = −2.6 Hz), 2.75 (d, B-H), 2.82 (s, $Me_3\overset{+}{N}$), 3.68 ppm (s, CH_3O); E/Z = 7.5.

1-Chloroaziridine-2,2-dicarboxylic Acid Methyl Ester α-Phenylethylammonium Salt (VIII). This compound was obtained as in the preceding experiment from salt III and α-phenylethylamine hydrochloride in CD_3OD and was identified from its PMR spectrum (CD_3OD): E isomer: 2.61 and 2.62 (two d, A-H, $^2J_{AB}$ = −2.7 Hz, signals of diastereomers in a ratio of 1:1 were observed), 2.75 and 2.76 (two d, B-H, signals of diastereomers in a ratio of 1:1), 3.82 ppm (s, CH_3O); Z isomer: 2.67 (d, A-H, $^2J_{AB}$ = −2.7 Hz), 2.80 (d, B-H), 3.73 ppm (s, CH_3O); for both isomers: 1.64 (d, CH_3, ^3J = 7.1), 4.46 (q, CH), 7.3-7.5 ppm (m, Ph); E/Z = 7.5.

Aziridine-2,2-dicarboxylic Acid Methyl Ester Trimethylammonium Salt (IX). This compound was obtained as in the preceding experiment from salt II and $Me_3N \cdot HCl$ in CD_3OD and was identified from its PMR spectrum (CD_3OD): 1.98 (d, A-H, $^2J_{AB}$ = 1.5 Hz), 2.04 (d, B-H), 3.68 ppm (s, CH_3O).

Aziridine-2,2-dicarboxylic Acid Methyl Ester α-Phenylethylammonium Salt (X). This compound was obtained as in the preceding experiment from II and α-phenylethylamine hydrochloride in CD_3OD and was characterized from its PMR spectrum (CD_3OD): 2.03 (broad s, A-H, $^2J_{AB}$ not observed), 2.07 (broad s, B-H), 3.73 (s, CH_3O), 1.63 (d, CH_3, J = 7.1 Hz), 4.45 (q, CH), 7.35-7.50 ppm (m, Ph).

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AZIRIDINYL KETONES AND THEIR CYCLIC ANILS.

8.* 1,2-DIARYL-1,1*a*-DIHYDROAZIRINO[1,2-*a*]QUINOXALINES FROM SUBSTITUTE o-PHENYLENEDIAMINES AND CHALCONE DIBROMIDES

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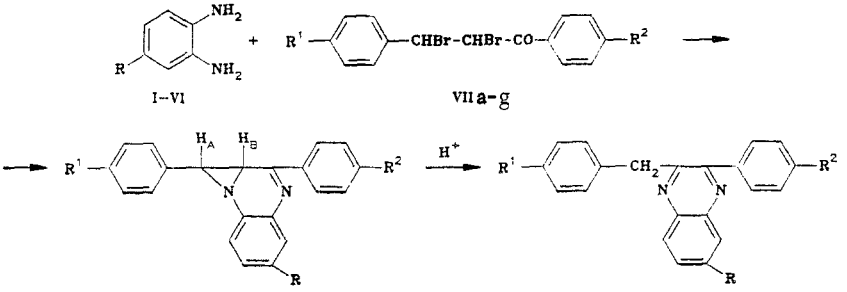
The reaction of 4-R-substituted (R = Br, Cl, OC_2H_5, C≡N, NO_2) 1,2-phenylenediamines with 1,3-diaryl-2,3-dibromo-1-propanones in the presence of triethylamine gave 1,2-diaryl-5-R-1,1*a*-dihydroazirino[1,2-*a*]quinoxalines, which undergo isomerization in an acidic medium to give 2-aryl-3-arylmethylene-7-R-quinoxalines. The dipole moments were measured, and the polarities of the synthesized compounds are discussed.

The interest in the chemistry of azirinoquinoxaline derivatives is due to the photochromism and thermochromisms that are characteristic for them and the high reactivities of the yields formed from them [1-6]. However, until now, only azirinoquinoxalines based on 1,2-phenylenediamine (I) have been described. In developing previous research [1, 5] we set out to study the products of the reaction of I and its 4-R-substituted compounds II-VI with 1,3-diaryl-2,3-dibromo-1-propanones VIIa-g; the reaction was accomplished by refluxing the starting compounds in methanol† in the presence of triethylamine:



VIIIa-g; IXa,c,g; Xa-g
XIa-g; XIIa,c,g; XIIIa,g

XIVa,c; XVa,c; XVIa

I, VIII, XIV R=H; II, IX, XV R=Br; III, X R=Cl; IV, XI R=OC_2H_5; V, XII, XVI R=CN; VI, XIII R=NO_2; VII–XVI a $R^1=R^2=H$; b $R^1=Br$, $R^2=H$; c $R^1=H$, $R^2=Br$; d $R^1=R^2=Br$; e $R^1=H$, $R^2=Cl$; f $R^1=R^2=Cl$; g $R^1=NO_2$, $R^2=H$

In all cases we obtained individual compounds, which, with respect to the results of elementary analysis and the spectral properties, correspond to the structures of 1, 1*a*-dihydroazirino[1,2-*a*]quinoxaline derivatives (Table 1).

*See [1] for communication 7.

†The use of other alcohols entails raising the boiling point of the reaction mixture and, as a consequence, accelerating secondary 1,3-dipolar-addition processes [1].

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