$NaHCO_3$, 5 mL of H_2O, and 5 mL of saturated NaCl, dried (Na_2SO_4), and evaporated to yield 820 mg of nearly colorless oil. TLC (C_6H_6) and NMR analyses indicated a complex mixture of compounds. IR (neat) spectroscopy revealed a weak but significant SH band at 2560 cm^{-1}. The oil was chromatographed over 15 g of silica gel with benzene as eluant to give (a) 300 mg (36%) of 1,6-diphenyl-1,6-hexanedithiol (**21**) as an oil [ca. 70% pure by TLC and NMR; NMR (CCl_4) δ 7.2 (s), 3.8 (m, CHSH), 3.3–2.9 (m, impurity), 2.0–0.9 (m), with 1.7 (d, J = 5 Hz, SH)] and (b) fractions containing mixtures of **21** and 1,6-diphenyl-6-ethoxy-1-hexanethiol (TLC and NMR as above). The impure dithiol (fraction a) could not be crystallized, and it decomposed in the gas chromatograph.

Attempted Synthesis of 4,9-Diphenyl-1,2,3-trithionane (18). To 146 mg (0.55 mmol) of reagent **7** stirred at room temperature in 100 mL of CCl_4 was added dropwise over a 5-h period a solution of 151 mg (0.50 mmol) of the impure dithiol **21** (obtained above) in 100 mL of CCl_4. TLC (C_6H_6, hexanes) 2.5 h after complete addition indicated the absence of elemental sulfur and dithiol **21**. The reaction mixture, after being allowed to stand overnight, was concentrated under reduced pressure to a 5-mL volume, filtered, and evaporated to give a viscous oil. IR and NMR spectroscopy indicated no significant amount of thiol: NMR (CCl_4) δ 7.1 (br s, 6.3 H), 4.2–3.6 (br t?, 1 H), 3.4–3.0 (br, 0.4 H), 2.3–1.5, 1.5–0.9 (br, 5.5 H); IR (neat) 3010, 2900, 2840, 1600, 1585, 1490, 1450, 1070, 1030, 790, 760, 700 cm^{-1}. Crystallization attempts failed. TLC (8:2 hexanes–$CHCl_3$) indicated several components, possibly a mixture of oligomers. Column chromatography over 20 g of silica gel (8:2 hexanes–$CHCl_3$ eluant) yielded only a few milligrams of each of the first 4 or 5 components, which were not characterized.

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Registry No. 6 (n = 5), 928-98-3; **6** (n = 6), 1191-43-1; **6** (n = 8), 1191-62-4; **7**, 65952-73-0; **8** (n = 5), 76583-30-7; **8** (n = 6), 76583-31-8; **8** (n = 8), 76583-32-9; **9**, 3354-86-7; **10**, 76583-65-8; **11**, 17749-54-1; **13**, 76583-66-9; **14**, 76599-27-4; **15**, 76583-67-0; **16** (meso), 53585-65-2; **16** (*dl*), 53585-66-3; **17a**, 2506-33-4; **17b**, 57819-14-4; **19** (meso), 39997-18-7; **19** (*dl*), 39997-17-6; **20**, 76583-68-1; **21**, 76583-69-2; thiourea, 62-56-6; α,α'-dibromo-*o*-xylene, 91-13-4; α,α'-dimercapto-*o*-xylene, 41383-84-0; 2,2′-bis(bromomethyl)biphenyl, 38274-14-5; 2,2′-bis(hydroxymethyl)biphenyl, 3594-90-9; *meso*-α,α'-dibromoadipic acid, 3425-65-8; *meso*-α,α'-dimercaptoadipic acid, 35605-89-1; *meso*-2,5-dibromohexane, 54462-67-8; 5,8-dimethyl-1,2,3,4-tetrathiocane, 76583-70-5; 1,4-dibenzoylbutane, 3375-38-0; 1,6-dichloro-1,6-diphenylhexane, 58819-38-8; 1,6-diphenyl-6-ethoxy-1-hexanethiol, 76583-71-6; hexanedioic acid, 124-04-9.

Synthesis of 2,2-Dichloro-1,3-diarylaziridines by Reduction of Trichloroacetophenone Imines

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2,2-Dichloro-1,3-diarylaziridines, usually obtained by addition of dichlorocarbene to benzylideneanilines, were synthesized by reaction of *N*-aryl-α,α,α-trichloroacetophenone imines with lithium aluminium hydride in ether.

Introduction

Since the first preparation of a 2,2-dichloroaziridine by Fields and Sandri in 1959,[2] several methods have been developed for the synthesis of the title compounds. The most stable members of this series are 2,2-dichloro-1,3-diarylaziridines and are generally accessible by reaction of substituted benzylideneanilines with dichlorocarbene, the latter being generated by a variety of methods.[2-7] Another method involves the base-induced ring closure of α-aryl-β,β,β-trichloroalkylanilines[8,9] and *N*-(trichloroethyl)benzamides.[10] The latter methods are the only two examples hitherto of a dichloroaziridine synthesis in which the final carbon skeleton is already present in the starting materials. We would like to report another example of the synthesis of 2,2-dichloro-1,3-diarylaziridines in which the products result from an intramolecular displacement reaction.

Table I. Synthesis of 1-Aryl-2,2-dichloro-3-phenylaziridines 5[a]

compd	R	% yield[b]	mp, °C	lit. mp, °C	reacn conditions[c]
5a	H	66	99	99–100[d] 98–99[e]	Δ, 1 h
5b	*p*-Me	81	70	70–71[d]	Δ, 15 min
5c	*m*-Me	64	59		Δ, 20 min
5d	*p*-OMe	71	93	92–93[d]	30 min at room temp, Δ, 2 min

[a] Compounds 5 gave satisfactory N analyses. [b] Isolated yield, starting from ketimines 2 (two steps). [c] Reflux period for the reaction of α,α,α-trichloro ketimines 3 with 8 equiv of lithium aluminium hydride in ether. [d] Reference 20. [e] Reference 2.

Results

Recently, the reaction of mixed metal hydrides with α-halogenated imino compounds was developed as a method for the synthesis of aziridines.[11-14] When the reaction

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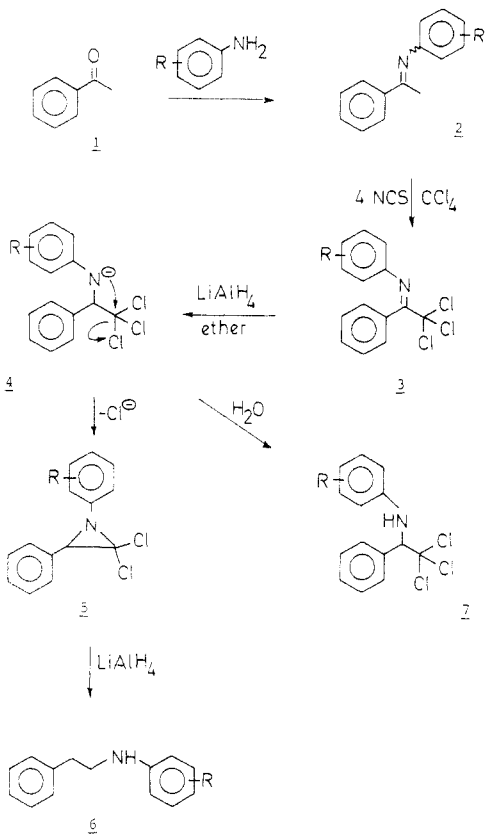
Scheme I



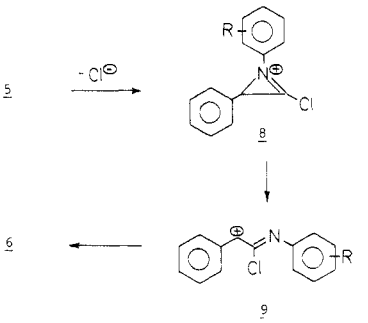
was carried out on an α,α,α-trichloromethylketimine, fitted in a steroidal frame, the resulting bicyclic 1,3-dialkyl-2,2-dichloroaziridine suffered further ring opening to give a ring-expanded product.[15]

We have found now that *N*-(2,2,2-trichloro-1-phenylethylidene)anilines (**3**), easily obtained by chlorination of *N*-arylacetophenone imines (**2**) with *N*-chlorosuccinimide in carbon tetrachloride, when reacted with excess lithium aluminium hydride in diethyl ether under reflux, furnished 1-aryl-2,2-dichloro-3-phenylaziridines (**5**) in 64–81% yield (yield calculated from **2**; see Table I and Scheme I).

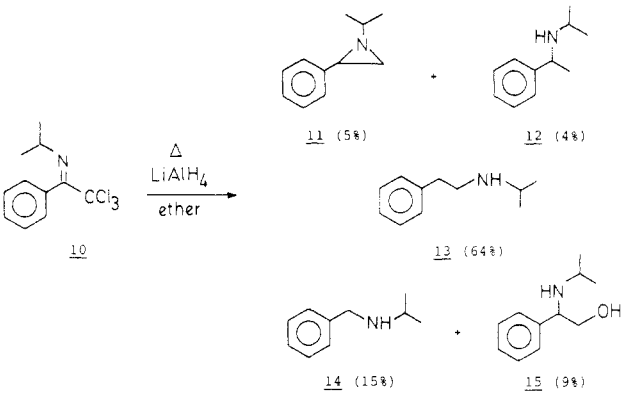
These products were identical in all aspects with the 2,2-dichloroaziridines prepared according to the phase-transfer-catalyzed reaction of benzylideneanilines with chloroform and aqueous 50% sodium hydroxide.[6] In our experiments, catalytic Triton B solution was used instead of TEBA.[6]

The mechanism of formation of 2,2-dichloroaziridines **5** involves addition of hydride at the carbon–nitrogen double bond, followed by intramolecular nucleophilic substitution. Regular sampling indicated the presence of *N*-(1-phenyl-2,2,2-trichloroethyl)anilines (**7**) as evidenced by NMR analysis. It is possible to isolate compounds **7** by carrying out the reaction with 1 or 2 equiv of lithium aluminium hydride in ether or tetrahydrofuran at −30 °C. Purification was performed by using column chromatography (Florisil; CCl_4 as eluent); 2,2-dichloroaziridines **5** were detected in the reaction mixture (NMR) prior to column chromatography but they did not emerge from the column (decomposition, hydrolysis). The reaction of **3** with $LiAlH_4$ in ether under reflux was in fact a useful route to *N*-phenethylanilines **6**. As an example, *N*-(2,2,2-trichloro-1-phenylethylidene)-*m*-toluidine (**3c**) was converted

Scheme II



Scheme III



with $LiAlH_4$ (8 equiv, Δ, 24 h) into *N*-phenethyl-*m*-toluidine (**6c**) in 66% isolated yield.

The dichloroaziridines **5** suffered ring opening at such a rate that it can interfere with the dichloroaziridine formation. Opening of dichloroaziridines **5** with hydride to phenethylanilines **6** is a known reaction[16,17] and is found in those cases where the reaction times are too long. It is therefore highly advisable to perform a regular sampling of the reaction mixture. The samples are conveniently analyzed (after aqueous workup; see Experimental Section) by NMR spectrometry, which clearly shows the characteristic spin systems of the three compounds involved, i.e., the AB system of the CHNH moiety of trichloroamine **7**, the CHN singlet of dichloroaziridine **5** and the A_2B_2 system of phenethylanilines **6**.

The conversion of 2,2-dichloroaziridines **5** into phenethylanilines **6** by lithium aluminium hydride involves initial loss of a chloride anion to generate an azirinium chloride **8**, isomerization into an α-imino carbenium ion **9** and further transformation into ring-opened products **6** (Scheme II). This reaction pattern parallels the general solvolytic[2,18–21] and thermal[22,23] behavior of dichloroaziridines.

Our efforts toward the extension of the dichloroaziridine synthesis, presented in this paper, to the *N*-alkyl analogues failed because more drastic reaction conditions were required, i.e., larger excess of $LiAlH_4$ and longer reflux period (8 equiv of $LiAlH_4$, ether, Δ, 4 h and subsequently plus 8

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equiv of $LiAlH_4$, ether, Δ, 3 h). In the *N*-isopropyl case, the initially formed 2,2-dichloroaziridine did not survive these conditions and a variety of reaction products were noticed. Preparative gas chromatographic analysis indicated the presence of (in consecutive order as eluted from the gas chromatograph, SE-30 column) 4% *N*-(1-phenylethyl)-*N*-isopropylamine (**12**), 15% *N*-benzyl-*N*-isopropylamine (**14**), 5% 1-isopropyl-2-phenylaziridine (**11**), 64% *N*-phenethyl-*N*-isopropylamine (**13**), and 9% *N*-(2-hydroxy-1-phenylethyl)-*N*-isopropylamine (**15**) (Scheme III). When the reaction was carried out with $LiAlH_4$ (12 equiv) in tetrahydrofuran under reflux (16 h) the reaction mixture consisted of 27% **12**, 6% **14**, and 64% **13**.

Aziridine formation[11-14] is apparently also the process of choice as evidenced by the isolation of aziridine **11** and ring-opened product **13** and by the presence of β-hydroxyamine **15**, resulting from hydroxide-induced opening of aziridine **11** during aqueous workup. The small amount of nonrearranged amine **12** points to the competitive nucleophilic substitution of the halides in the starting material as compared to nucleophilic addition at the imino bond. Finally, *N*-benzyl-*N*-isopropylamine (**14**) originates from a haloform-type reaction.

Experimental Section

IR spectra were measured with a Perkin-Elmer Model 257 spectrophotometer. NMR spectra were recorded with a Varian T-60 NMR spectrometer and mass spectra were obtained from a AEI MS 20 mass spectrometer coupled with a Pye Unicam gas chromatograph (Model 104, 1.5% SE-30, 1.5 m, He carrier gas). GLC analyses were performed with a Varian Model 920 gas chromatograph (5% SE-30, 3 m, H_2 carrier gas). *N*-Aryl ketimines **2** were obtained by condensation of acetophenone (**1**) with anilines in ether in the presence of titanium tetrachloride.[24]

Preparation of *N*-(2,2,2-Trichloro-1-phenylethylidene)-anilines 3. A solution of 0.05 mol of *N*-aryl ketimine **2** in 120 mL of dry carbon tetrachloride was treated with 0.2 mol of *N*-chlorosuccinimide (the apparatus was fitted with an air condenser and a calcium chloride tube). Under vigorous swirling, the mixture was heated by a Bunsen flame until a vigorous reaction started (this requires usually 1–2 min and the flask was immediately put into a cold-water bath (~10 °C) after which the mixture was further magnetically stirred for 1 h. Succinimide was filtered and washed twice with dry carbon tetrachloride and the filtrate was evaporated in vacuo (12 mmHg). The last traces of carbon tetrachloride were removed by using a high-vacuum pump (0.01–0.001 mmHg). The remaining clear oil consisted of essentially pure α,α,α-trichloro ketimine **3** and was used as such in further experiments. Yields were almost quantitative in all cases. The spectrometric data of compounds **3** are presented in a table as supplementary material.

Synthesis of 1-Aryl-2,2-dichloro-3-phenylaziridines 5 (General Procedure). A cooled (10 °C) and stirred suspension of 0.06 mol of lithium aluminium hydride in 40 mL of freshly distilled dry ether was treated dropwise with a solution of 0.03 mol of α,α,α-trichloro ketimine **3** in 30 mL of dry ether. After complete addition, the reaction mixture was refluxed for a time indicated in Table I. Workup involved pouring the reaction mixture into a mixture of ice and water covered by ether. The organic layer was separated and the aqueous layer twice extracted with ether. The combined ethereal extracts were dried ($MgSO_4$) and evaporated to leave an oil, which crystallized on standing. Recrystallization was performed with hexane/carbon tetrachloride (freezer).

It is absolutely necessary to take regular samples of the reaction mixture, starting after the complete addition of the substrate to the hydride suspension, because the substitution pattern in the starting material and the reactivity and quality of the lithium aluminium hydride used play a predominant role. When no such precautions are taken the presence of anilines **6** and **7** may inhibit crystallization of dichloroaziridines **5**. The sampling is executed by mixing 0.5 mL of the reaction mixture with a mixture of 10 mL of water and 2 mL of ether. After this mixture (test tube) is shaken, the ethereal layer is syringed into a conical flask and evaporated to leave a colorless oil, which is analyzed by NMR.

Isolation of *N*-[2,2,2-Trichloro-1-(4-chlorophenyl)ethyl]-aniline. *N*-[2,2,2-Trichloro-1-(4-chlorophenyl)ethylidene]aniline (0.02 mol scale) was treated with lithium aluminium hydride (0.01 mol) in tetrahydrofuran at −30 °C (30 min) as described in the general procedure for the synthesis of 2,2-dichloroaziridines **5**. The residual oil, obtained after aqueous workup, was eluted with carbon tetrachloride over a 30-cm Florisil column. The β,β,β-trichloro amine was obtained as the sole product in the first fractions (yield 32%), despite the presence of about 40% of the corresponding dichloroaziridine, as evidenced by NMR analysis of the reaction mixture. *N*-[2,2,2-Trichloro-1-(4-chlorophenyl)-ethyl]aniline: NMR (CCl_4) δ 5.06 (1 H, d, AB, J = 7.4 Hz, CHN), 4.59 (1 H, br d, AB, J = 7.4 Hz, NH, signal disappears on shaking with D_2O), 6.4–7.4 (5 H, m, C_6H_5N), 7.49 and 7.26 (2 × 2 H, 2 d, J = 8.5 Hz, p-ClC_6H_4); IR (NaCl) 3400 (ν_{NH}), 1602 and 1504 cm^{-1} ($\nu_{aromatic}$).

Synthesis of *N*-Phenethyl-*m*-toluidine (6c). *N*-(1-Phenyl-1-ethylidene)-*m*-toluidine (**2c**, 0.03 mol) was chlorinated with NCS as described above and the crude α,α,α-trichloro ketimine **3c** thus obtained was treated with 0.06 mol of lithium aluminium hydride in ether under reflux during a period of 24 h as given in the general procedure. Usual workup afforded an oil which was distilled in vacuo to give 4.2 g (66%; two-step synthesis) of *N*-phenethyl-*m*-toluidine (**6c**): bp 114–125 °C (0.01 mmHg); NMR (CCl_4) δ 2.23 (3 H, br s, CH_3), 2.85 (2 H, m, AA'BB', CH_2Ph), 3.32 (2 H, m, AA'BB', CH_2N), 4.63 (1 H, br s, NH), 7.19 (5 H, s, C_6H_5), 6.2–7.2 (4 H, m, *m*-tolyl); IR (NaCl) 3390 cm^{-1} (ν_{NH}); mass spectrum, m/e (relative abundance) 211 (M^+, 3), 120 (100), 91 (21), 77 (6), 65 (9), 51 (3).

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Registry No. 2a, 1749-19-5; **2b**, 4209-15-8; **2c**, 26625-24-1; **2d**, 2743-00-2; **3a**, 76772-99-1; **3b**, 76757-56-7; **3c**, 76757-57-8; **3d**, 76757-58-9; **5a**, 3543-98-4; **5b**, 10295-36-0; **5c**, 76773-00-7; **5d**, 10295-35-9; **6c**, 1958-56-1; **10**, 76757-59-0; **11**, 4164-23-2; **12**, 65757-60-0; **13**, 52007-97-3; **14**, 102-97-6; **15**, 68058-02-6; *N*-[2,2,2-trichloro-1-(4-chlorophenyl)ethylidene]aniline, 76757-60-3; *N*-[2,2,2-trichloro-1-(4-chlorophenyl)ethyl]aniline, 76757-61-4.

Supplementary Material Available: Table containing spectrometric properties of *N*-(2,2,2-trichloro-1-phenylethylidene)amines **3** and **10** (1 page). Ordering information is given on any current masthead page.

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