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Synthesis of 2-Chloro-2-imidoylaziridines via Aza-Darzens-type Reaction of 3,3-Dichloro-1-azaallylic Anions and *N*-(Arylsulfonyl)imines

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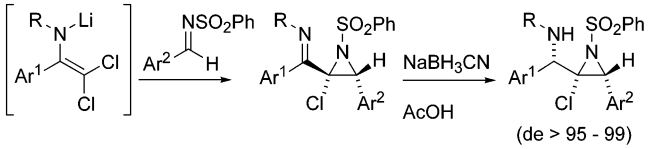
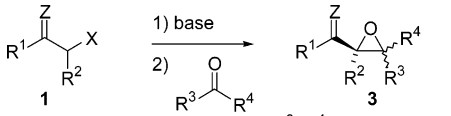


3,3-Dichloro-1-azaallylic anions, generated by deprotonation of α,α-dichloroketimines **10** with lithium diisopropylamide, reacted with *N*-sulfonylaldimines **7** to produce the Mannich-type products *N*-[2,2-dichloro-3-(*N*-alkylimino)-1,3-diarylpropyl]benzenesulfonamides **11**. The latter stable compounds were hydrolyzed at the imino functionality to afford *N*-[2,2-dichloro-3-oxo-1,3-diarylpropyl]benzenesulfonamides **12** in excellent yields. *N*-[2,2-Dichloro-3-(*N*-alkylimino)-1,3-diarylpropyl]benzenesulfonamides **11** were cyclized to *cis*-3-aryl-2-chloro-2-imidoylaziridines **19** in 81−99% yield with high diastereoselectivity, representing a novel and readily available class of stable 2-chloroaziridines. Finally, a highly stereoselective entry to 2-(aminomethyl)-2-chloroaziridines **27** (70−98% yield; de > 95−99) was worked out from the reaction of *cis*-3-aryl-2-chloro-2-imidoylaziridines **19** and sodium cyanoborohydride in the presence of acetic acid. The latter 2-(aminomethyl)aziridines **27** represent stereochemically defined small azaheterocyclic rings which were scarcely reported in the literature.

Introduction

The Darzens reaction[1] is arguably one of the most powerful methods of epoxide formation, explaining that it has been widely explored. α-Halogenated esters, amides, and ketones **1** have been condensed with ketones (or aldehydes) in a basic medium to give access to various functionalized oxiranes **3** (Scheme 1). To a much more minor extent, the Darzens reaction has been worked out with α-haloimines **1** (Z = NR; R^1 = alkyl)[2] and cyclic imidates **1** (R^1−Z = O−C−C−N)[3−6] to afford the corresponding epoxides **3**.

SCHEME 1



On the other hand, since Deyrup[7] described the analogous aza-Darzens reaction, where the electrophilic ketone **2** was replaced by an imine (**4**) resulting in the synthesis of functionalized aziridines **5** (Scheme 2), few reports on this item have been reported in the literature.[7−15] α-Halogenated esters, amides, and ketones **1** have been condensed with imines **4** in a basic medium in the synthesis of various functionalized aziridines **5** (Scheme 2).

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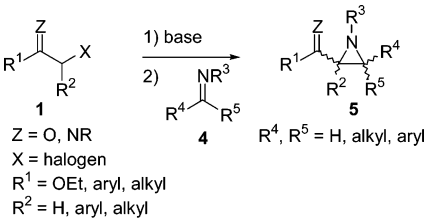
SCHEME 2



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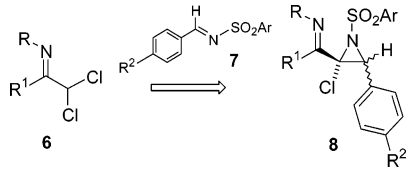

Therefore, the aza-Darzens reaction can still be considered a useful and not fully investigated tool for the construction of three-membered azaheterocycles, i.e., functionalized aziridines. Although some acid-catalyzed methods for the aza-Darzens-type reaction are known,[9] the most common route involves the use of a base.

In the present paper, the reactivity of α,α-dichloroketimines **6** and *N*-sulfonylaldimines **7** leading to the synthesis of 2-chloro-2-imidoylaziridines **8** was investigated in a novel type of the aza-Darzens-type reaction (Scheme 3).

These reactions should provide the corresponding 2-chloro-2-imidoylaziridines **8** which represent a relevant example of fairly stable 2-haloaziridines. The synthesis of 2-haloaziridines has attracted the interest of organic chemists since the early 60s because these 2-heteroatom-substituted strained rings are effective building blocks. Approaches to 2-chloroaziridines included the reaction of 2*H*-azirines with hydrogen chloride or acid chlorides (benzoyl chloride, acetyl chloride, ...), resulting in the formation of mixtures of *cis*- and *trans*-aziridines.[16] The latter aziridines were used as starting products in the synthesis of functionalized oxazoles[17,18] and oxazolines.[16,19] Reactions of 2-methyl-3-phenyl-2*H*-azirine and 2-chloromethylenemalononitrile derivatives gave rise to mixtures of chlorinated *cis*- and *trans*-aziridines.[20] Finally, 2,2-dimethyl-3-phenyl-2*H*-azirines reacted with phthalimidoacetyl chloride in benzene to give 2-chloroaziridines in 62% yield.[21] 2-Haloaziridines were also generated in poor yield by dichlorocarbene addition to benzylideneamines, followed by chlorine extrusion induced by methyllithium[22] or lithium aluminum hydride (28% yield).[23] Dehalogenation of 2,2-dihalo-1-phenylaziridines was also performed with tri-*n*-butyltin hydride to give monohalogenated aziridines.[24] Nitrene chemistry was applied to the synthesis of 2-chloroaziridines, as exemplified for 1-ethoxycarbonyl-2-chloroaziridines which were generated from the addition of ethoxycarbonylnitrene, produced by thermolysis of the corresponding azide, to vinyl chlorides.[25] The reaction of (*Z*)-*N*-trifluoromethylacetimidoyl fluoride with diazomethane afforded *N*-trifluoromethyl-2-fluoroaziridines.[26] 1-Alkyl-2-sulfonylaziridines incorporated a halogen at the 2-position when treated with carbon tetrahalides (CCl_4 or CBr_4) in *tert*-butyl alcohol in the presence of potassium hydroxide.[27] In a similar way, aziridinylphosphonates reacted with BuLi leading to 2-lithiated species which were trapped with carbon tetrachloride to give 2-chloroaziridinylphosphonates in good yields.[28] A mixture of *cis*- and *trans*-2-bromoaziridines was synthesized in poor yield (25%) when thiohydroxamic acid anhydride was photolyzed in neat $CBrCl_3$.[29] This protocol was applied to the synthesis of 2-bromoaziridine derivatives, which were used in the key step of the synthesis of (+)-9*a*-desmethoxymitomycin A and mitomycin K.[30]

Results and Discussion

A preceding Darzens-type reaction of α-chloroimines with ketones and aldehydes enabled the synthesis of 2-imidoylepoxide derivatives.[2] Remarkable to note is the lack of self-condensation and side-reaction products during the deprotonation of α-chlorinated and α,α-dichlorinated imines, a clear advantage in contrast to, for instance, α-chlorinated oximes.[31]

Knowing that the condensation reaction of α-chlorinated imine anions with an activated imine (e.g., *N*-sulfonylimine)

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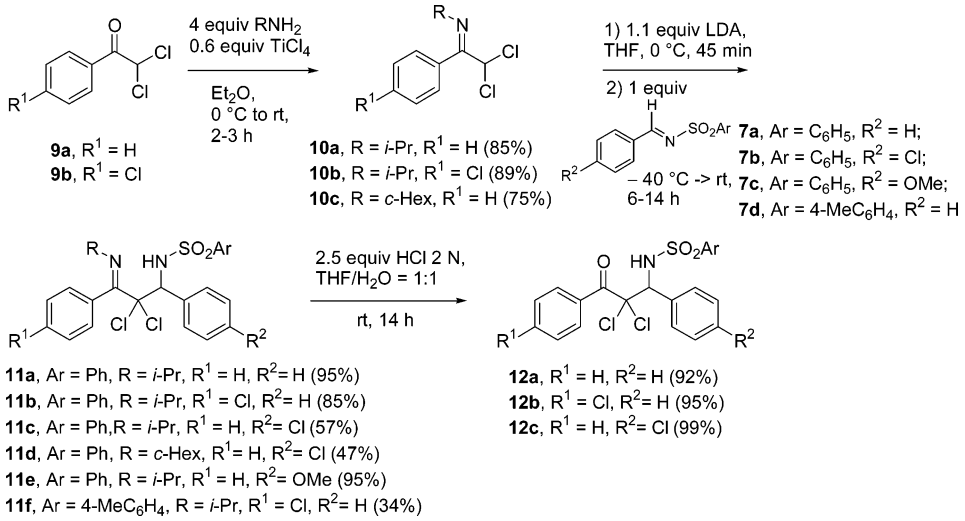
SCHEME 4



9a, R^1 = H
9b, R^1 = Cl

10a, R = *i*-Pr, R^1 = H (85%)
10b, R = *i*-Pr, R^1 = Cl (89%)
10c, R = *c*-Hex, R^1 = H (75%)

7a, Ar = C_6H_5, R^2 = H;
7b, Ar = C_6H_5, R^2 = Cl;
7c, Ar = C_6H_5, R^2 = OMe;
7d, Ar = 4-MeC_6H_4, R^2 = H

11a, Ar = Ph, R = *i*-Pr, R^1 = H, R^2= H (95%)
11b, Ar = Ph, R = *i*-Pr, R^1 = Cl, R^2= H (85%)
11c, Ar = Ph,R = *i*-Pr, R^1 = H, R^2= Cl (57%)
11d, Ar = Ph, R = *c*-Hex, R^1= H, R^2= Cl (47%)
11e, Ar = Ph, R = *i*-Pr, R^1 = H, R^2= OMe (95%)
11f, Ar = 4-MeC_6H_4, R = *i*-Pr, R^1 = Cl, R^2= H (34%)

12a, R^1 = H, R^2= H (92%)
12b, R^1 = Cl, R^2= H (95%)
12c, R^1 = H, R^2= Cl (99%)

was not yet explored (vide supra), we attempted the synthesis of 2-chloro-2-imidoylaziridines. The combination of a carbon−nitrogen double bond and a halogen atom in one molecule offers the potential to provide access to new aziridine derivatives when condensed to *N*-sulfonylaldimines, via the aza-Darzens reaction. For instance, α,α-dichloroketimines **6** can be deprotonated with strong nonnucleophilic bases and then condensed with *N*-sulfonylimines **7** giving rise to the synthesis of *β*-imidoylsulfonamides, which can be ring closed to 2-imidoylaziridine derivatives **8** (Scheme 3).

Up to now, only a few reports described the addition of an imine anion (1-azaenolate) toward an activated imine or an aldehyde, resulting in the aldol-type reaction.[32] These facts confirm that the previously designed aza-Darzens strategy is worth working out because of its synthetic potential. Natural products containing an aziridine ring have attracted much interest because the biological activity of these compounds is often attributed to the aziridine ring.[33] In the following text, the successful efforts to synthesize chlorinated *β*-imidoylsulfonamides and 2-chloro-2-imidoylaziridines in a highly stereoselective way will be highlighted.

α,α-Dichloroketimines **10a**−**c** were prepared by condensation of the corresponding α,α-dichloroketones **9** with primary amines in the presence of titanium(IV) chloride in diethyl ether (Scheme 4).[34−36] Deprotonation of α,α-dichloroimines **10a**−**c** with stoichiometric amounts of lithium diisopropylamide in THF at 0 °C gave 3,3-dichloro-1-azaallylic anions, which reacted as carbon nucleophiles with *N*-sulfonylimines **7** to afford α,α-dichloro-*β*-iminosulfonamides **11a**−**f** in 34−95% yield via an aza-aldol-type reaction (Scheme 4).

N-(2,2-Dichloro-3-iminopropyl)benzenesulfonamides **11a**−**f** represent novel structures, suitable for further elaboration. They are the aza analogues of *O*-(2,2-dichloro-3-iminopropyl)methanesulfonates, aldol adducts previously explored by our research group in the synthesis of functionalized *cis*-2,4-diaryl-3,3-dichloroazetidines.[37] Aza-aldol adducts **11a**−**f** are crystalline compounds that showed a great stability, as they can be stored for over one year in sealed bottles at −20 °C. In addition they could be produced on a multigram scale (up to 0.04 mol) without changes in the reaction yields. Mannich-type products **11a**−**c** were hydrolyzed at the imino functionality in aqueous hydrochloric acid, giving the corresponding dichlorinated *β*-aminoketone derivatives **12a**−**c** (92−99% yields) that can be considered as precursors of α-dione derivatives.[38] Finally, *β*-aminoketones **12** can be considered as a precursor of 3-amino alcohol derivatives, of which fluoxetine (antidepressant) is an example.[39]

Attempts to synthesize 2-chloroaziridines starting from *β*-ketosulfonamide **12a** by treatment with potassium hydroxide (1 equiv) in aqueous tetrahydrofuran at room temperature failed because the retro-aldol reaction was preferred over the aziridine formation. α,α-Dichloroketone **9a**, benzaldehyde **13**, and benzenesulfonamide **14** were formed in quantitative yield under these conditions (Scheme 5).

Dehalogenation of *β*-aminoketone **12b** with tributyltin hydride and a catalytic amount of 2,2′-azobisisobutyronitrile in warm carbon tetrachloride failed, and the starting material was recovered instead (Scheme 6). However, reaction of *β*-aminoketone **12b** in carbon tetrachloride−toluene (1:1) under reflux for 6 h afforded the retro-aldol-type reaction leading to α,α-dichloroketone **9b** and *N*-sulfonylimine **7a** (100% yield).

β-Aminoketimines **11a**−**d** proved to be better substrates for the synthesis of *cis*-2-chloro-2-imidoylaziridines **19** (Scheme 7) because the retro-aldol reaction was not observed anymore.

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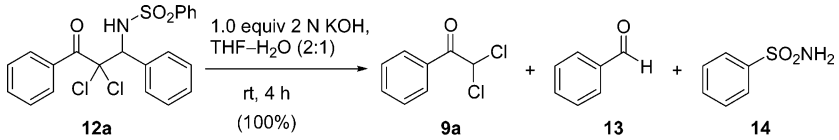
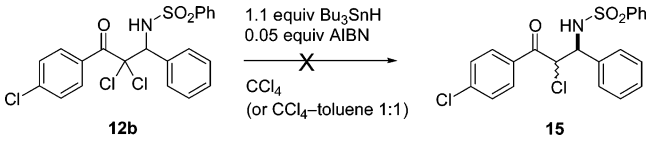
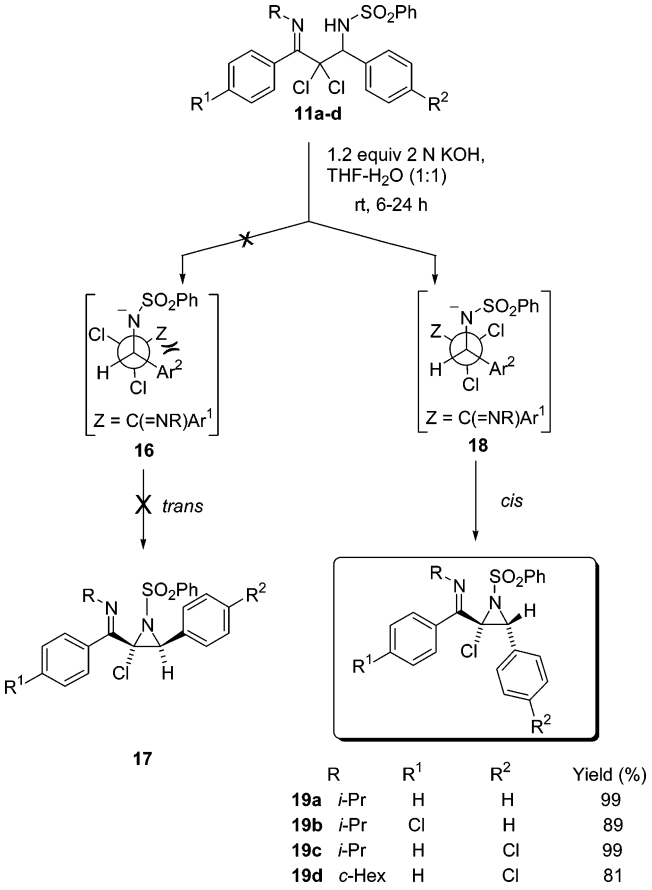
SCHEME 5



SCHEME 6



SCHEME 7



	R	R^1	R^2	Yield (%)
19a	*i*-Pr	H	H	99
19b	*i*-Pr	Cl	H	89
19c	*i*-Pr	H	Cl	99
19d	*c*-Hex	H	Cl	81

Cis-2-chloro-2-imidoylaziridines **19** are interesting chemicals difficult to access otherwise. The synthesis of ketimines derived from 2-acylaziridines cannot be performed at high temperature, i.e., in hot toluene or benzene, because intramolecular rearrangement to oxazole derivatives is in competition with the imine condensation.[40] Moreover, reactions at the carbonyl group of 2-acyl- and 2-formylaziridines are more difficult because of the inactivation caused by hyperconjugation of the adjacent aziridine ring.[41] These problems were partially overcome when a PPE−hydrolysate[42] was used in a catalytic amount during the condensation of aziridinyl ketones and tosylhydrazine.[43]

β-Imidoylsulfonamides **11a**−**d** were stirred in water−tetrahydrofuran (1:1) in the presence of 1.2 equiv of 2 N KOH at room temperature for 6−24 h, resulting in a complete diastereoselective entry to *cis*-3-aryl-2-chloro-2-imidoylaziridines **19a**−**d** in 81−99% yield after recrystallization (Scheme 7). No trans isomer **17** was found either during the analysis of the ^{1}H NMR of the crude reaction mixtures or after the purification procedure. During the course of our investigation, it was found that sodium hydroxide or organic bases (DBU, DABCO) in an organic solvent (tetrahydrofuran, acetonitrile) were not efficient reagents for the ring closure of *β*-aminoketones **11**. Moreover, no heating was allowed to prevent the retro-aldol-type reaction. The synthesis of 2-benzimidoyl-2-chloroaziridine **19d** required a longer reaction time (24 h) during the ring closure procedure (see transition state, **18d**; R = *c*-Hex), originating from the sterical hindrance exerted by the *N*-cyclohexyl substituent, without registering any significant changes in the reaction yield (81%). The latter aziridines **19** showed a great deal of conformational stability, whereas no nitrogen inversion was detected (^{1}H NMR analysis).

Finally, attempts to synthesize the aliphatic 2-acetimidoyl-2-chloroaziridine **22** were made. During the condensation of *N*-(2,2-dichloro-1-methylethylidene)isopropylamine **20** with *N*-benzenesulfonylimine **7a**, the retro-aldol reaction was faster than the ring closure, as compared to the previously studied cases. In fact, the use of analogous reaction conditions, as previously described for the synthesis of 2-benzimidoyl-2-chloroaziridines **19a**−**d**, led to the recovery of the starting material. As a result, during the reaction of *N*-(2,2-dichloro-1-methylethylidene)-isopropylamine **20** with *N*-benzenesulfonylimine **7a**, the temperature was lowered to −60° and slowly increased to −20 °C during 6 h. The reaction resulted in a crude (1:1) mixture of *cis*- and *trans*-aziridines **22**, along with unidentified reaction products, judging from the ^{1}H NMR spectrum of the crude reaction mixture (Scheme 8). The purification of the latter via flash chromatography gave a poor yield of an inseparable mixture of the corresponding hydrolyzed 2-acyl-2-chloroaziridine **23** (one isomer) along with an equal amount of the ring-opened product **24**.

As a conclusion, the aza-Darzens reaction of α,α-dichlorinated imines **10** and **20** was studied, leading to novel 2-chloro-2-imidoylaziridines **19** and **22**. In particular, the presented protocol involved the formation of stable and stereochemically defined 2-chloro-2-imidoylaziridines in preparative amounts.

Treatment of aziridines **19** with hydride reagents is of interest to produce 2-(aminomethyl)-2-chloroaziridines with three stereocenters. Previously, the diastereoselective reduction at the C═O group of aziridinyl ketones has been investigated, for

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SCHEME 8

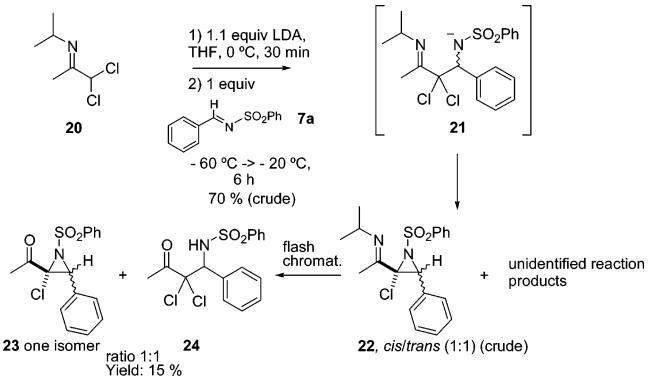
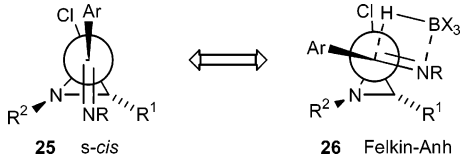


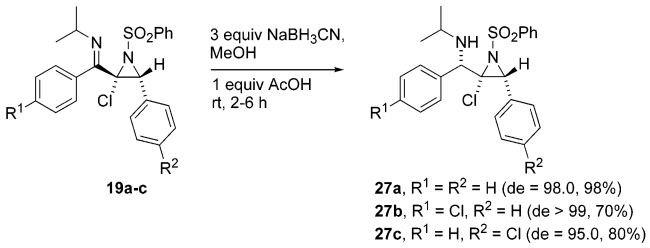
CHART 1



instance, in tetrahydrofuran with L-Selectride[44] and sodium borohydride in the presence of $ZnCl_2$ to give precursors of 1,2-amino alcohols.[45] On the other hand, only one preceding example described the reductive amination of aziridinylketimine derivatives, and this required a zinc chelate to induce a stereofacial attack.[46] The previously described 2-imidoylaziridines **19** are ideal substrates for this type of reaction, where a stereocenter can be stereoselectively created. Because of that, $NaBH_4$ was used in a mixture of 9:1 methanol−tetrahydrofuran at room temperature for the reduction of the aziridinylimine **19a**, resulting in unreacted starting product along with minor amounts of unidentified reaction products. During the course of our investigation, it was revealed that sodium cyanoborohydride in methanol was a better reagent for the reductive amination of aziridinylketimines. A nearly quantitative diastereoselective reduction of imidoylaziridines (de = 95.0−99.9%) was accomplished by the use of 3 equiv of $NaBH_3CN$ along with a stoichiometric amount of acetic acid in methanol. A Felkin−Anh model, **26**, can be recalled to explain the stereoselective reduction of the imino moiety having a neighboring aziridine ring,[45,46] considering that this model also results in better orbital overlap of the chlorine σ^*-antibonding and the C=N π-bonding (Chart 1). The borohydride adds to the C=N only from the less-hindered side, that is, from the opposite side of the sulfonyl group (**26**).

The way the acetic acid was added was important for the outcome of the reaction. When 1 equiv of acetic acid was added dropwise at 0 °C to the aziridinylketimine **19a** followed by 4 equiv of $NaBH_3CN$ and stirring was continued at room temperature for 2 h, the starting product was isolated (60%) along with a 1:1 ratio of *syn*- and *anti*-(aminomethyl)aziridines **27** (30%) and side-reaction products (10%). The addition of 1 equiv of acetic acid to the solution of the aziridine **19a** and $NaBH_3CN$ (3 equiv) in methanol gave instead the methylaminoaziridines **27a**−**c** with high diastereoselection (Scheme 9). The aziridinylketimine **19a** did not react with 2 equiv of $NaBH_4$ in ethanol at room temperature for 16 h as the starting product was recovered completely. Preliminary attempts to revert the reductive amination of 2-imidoylaziridines in favor of the anti isomer by the use of sodium borohydride (1−10 equiv) and 1 equiv of Lewis acid ($ZnCl_2$, $TiCl_4$, $CeCl_3$) failed, giving poor yields of a mixture of complex reaction products.

SCHEME 9



The reaction scale of the reductive amination of aziridine **19c** was increased to 10 mmol (compared to 1 mmol for the previous examples). Therefore, 1 equiv of acetic acid was added to a solution of the aziridine **19c** and sodium cyanoborohydride (4 equiv) in methanol at 0 °C, and then the suspension was stirred at room temperature for 6 h (Scheme 10). In that case, three compounds were isolated after flash chromatographic purification. These compounds were identified as the *syn*-methylaminoaziridine **27c**, the *anti*-aziridine **28**, existing in two invertomers, and the aziridine **29**. The stereochemistry of aziridine **29** was deduced from the coupling constant of both aziridine protons (J = 6.5 Hz; $CDCl_3$) along with NOE experiments, which revealed that the substituents at the aziridine ring adapted a cis configuration.

Also, the stereochemistry of aziridine **27c** was confirmed by NOE experiments (Chart 2). Irradiation of the proton at C-3 of the aziridine **27c** gave a NOE of 9.5% on the methine of the methylamino substituent. Vice versa, irradiating the CH proton of the methylamino substituent resulted in a NOE of 23.5% on the proton at carbon 3 of the aziridine. Normally, such a large NOE, i.e., 23.5%, is registered only between geminal and vicinal protons. From the previous NOE experiments, it can be deduced that the benzenesulfonyl group is lying on the same side of the space as the aminomethyl functionality and the aziridinyl C-3 proton, as previously described for 1-alkyl-3-aryl-2-benzoylaziridines, where the trans isomer exists in a preferred conformation with the *N*-alkyl group syn to the carbonyl.[41] Finally, the structure of 2-(aminomethyl)-2-chloroaziridine **27c** was secured by X-ray analysis.

A preceding report disclosed how the stereoselective ring opening of 3-aryl-2-(hydroxymethyl)aziridines was accomplished with aluminum hydrides, namely, $LiAlH_4$.[47] The hydride was directed toward C-2 through chelation of the nucleophile.[47] Therefore, (aminomethyl)aziridine analogues **27** could be promising reagents in the synthesis of 1,3-diaminopropane derivatives through hydride nucleophiles. The use of $NaBH_4$ in methanol or $LiAlH_4$ in dry diethyl ether resulted in the unreacted starting material, and increasing the amounts of the hydrides did not give any clean reaction mixture, as instead complex mixtures were obtained upon workup. Although this preliminary account displays a reluctant behavior of 2-(aminomethyl)-

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SCHEME 10

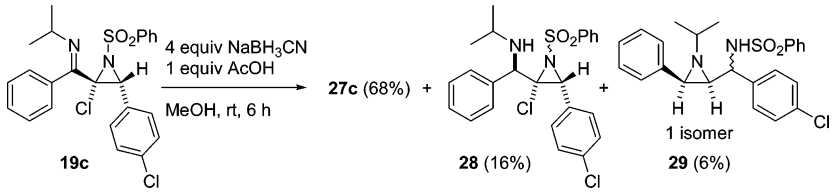
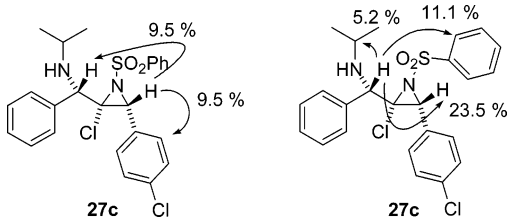


CHART 2. NOE Experiments on 2-(Aminomethyl)-2-chloroaziridine 27c



aziridines **27** to ring opening by hydride, further reactions will be reported in due course to clarify their reactivity over nucleophilic displacement.

In conclusion, 3,3-dichloro-1-azaallylic anions have been reacted with *N*-sulfonylaldimines **7** to produce the Mannich-type products *N*-[2,2-dichloro-3-(alkylimino)-1,3-diarylpropyl]-benzenesulfonamides **11**. The latter sulfonamides **11** proved to be useful reagents as they were hydrolyzed at the imino functionality to afford *N*-[2,2-dichloro-3-oxo-1,3-diarylpropyl]-arylsulfonamides **12** in excellent yields and as they were diastereoselectively ring closed to *cis*-3-aryl-2-chloro-2-imidoylaziridines **19**, which represents a novel entry to 2-chloro-2-imidoylaziridines via the aza-Darzens-type reaction. Despite the facts that a few examples which included the synthesis of 2-chloro-*N*-sulfonylaziridines started from the intramolecular substitution of *N*-(2,2-dichloro-1,2-diarylethyl)benzenesulfonamides induced by NaOH in DMF[48] and that the aza-Darzens-type reaction was successful in the synthesis of chlorinated *N*-phenylaziridines,[13,49] these syntheses did not reveal a straightforward approach to 2-chloro-2-imidoyl-1-sulfonylaziridines. The approach disclosed in the present report instead gave rise to a novel class of stable chlorinated aziridines, i.e., *cis*-3-aryl-2-chloro-2-imidoylaziridines **19**, which were elaborated to 2-(aminomethyl)-2-chloroaziridines **27** with sodium cyanoborohydride and acetic acid in methanol. The latter 2-(aminomethyl)-aziridines **27** represent stereochemically defined small azaheterocyclic rings which are scarcely represented in the literature.

Experimental Section

Synthesis of *N*-[2,2-Dichloro-3-(alkylimino)-1,3-diarylpropyl]-benzenesulfonamides 11. The synthesis of the *N*-[2,2-dichloro-3-(isopropylimino)-1,3-diphenylpropyl]benzenesulfonamide **11a** is representative. Diisopropylamine (57 mmol, 5.76 g) was placed in a 250 mL two-necked round-bottomed flask along with 10 mL of dry tetrahydrofuran, and a 2.5 N *n*-butyllithium solution in hexane (53.3 mmol, 21.32 mL) was added at 0 °C under nitrogen atmosphere. Then, α,α-dichloroimine **10a** (41 mmol, 9.39 g) was added dropwise in 10 mL of tetrahydrofuran, and the resulting red-brown solution was stirred for 30 min at 0 °C. The temperature was lowered to −40 °C, and the *N*-benzenesulfonylimine **7a** (41 mmol, 10.05 g), dissolved in 15 mL of tetrahydrofuran, was added dropwise. The resulting mixture was kept at the same temperature for 2 h and then brought to room temperature for 12 h. Upon quenching with 0.5 mL of 0.5 N NH_4Cl, the mixture was washed with an additional 100 mL of 0.5 N sodium hydroxide solution and extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over K_2CO_3−$MgSO_4$ (1:1) and evaporated to afford a red-brown residue *N*-[2,2-dichloro-3-(isopropylimino)-1,3-diphenylpropyl]benzenesulfonamide **11a** (18.50 g, 95%) that was purified by recrystallization (methanol) to afford pale yellow crystals. During the synthesis of 2,2-dichloro-3-(isopropylimino)-1,3-diarylpropylsulfonamide **11c**, after the *N*-sulfonylimine addition, the reaction mixture was stirred at −40 °C and then the temperature was increased to 0 °C over a period of 3.5 h. The reaction was quenched at 0 °C (the reaction was performed at a 5 mmol scale).

***N*-[(3*E*)-2,2-Dichloro-3-(isopropylimino)-1,3-diphenylpropyl]-phenylsulfonamide 11a.** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.16 (d, 3H, J = 6.1 Hz, CH_3), 1.09 (d, 3H, J = 6.1 Hz, CH_3), 3.26 (sept, 1H, J = 6.1 Hz, *CH*N═), 5.55 (d, 1H, J = 8.5 Hz, *CH*NH), 6.87 (brs, 1H, NH), 6.96−7.34 (m, 13H, $CH_{arom.}$), 7.57 (m, 2H, $CH_{arom.}$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.2, 23.3, 54.4, 67.9, 90.5, 127.0, 127.6, 127.8, 128.1, 128.3, 128.6, 129.0, 130.6, 132.2, 133.8, 134.9, 140.9, 165.7. IR (KBr): ν = 3262 (NH), 1642 (C═N), 1327 and 1171 (S═O). MS (ES^+): *m*/*z* (%) = 475/477/479 (MH^+, 20), 246 (100), 230/232/234 (75). Mp (MeOH) = 136.6−138.9 °C. Yield = 75%. Pale yellow crystals. Anal. Calcd for $C_{24}H_{24}Cl_2N_2O_2S$: C, 60.63; H, 5.09; N, 5.89. Found: C, 60.49; H, 5.21; N, 5.72.

Synthesis of *N*-(2,2-Dichloro-3-oxo-1,3-diarylpropyl)phenylsulfonamides 12. The synthesis of *N*-(2,2-dichloro-3-oxo-1,3-diphenylpropyl)phenylsulfonamide **12a** is representative. To *N*-[2,2-dichloro-3-(isopropylimino)-1,3-diphenylpropyl]phenylsulfonamide **11a** (0.47 g, 1 mmol) in tetrahydrofuran (15 mL) was added an equal amount of water (15 mL) and a solution of 2 N hydrogen chloride in water (0.75 mL, 1.5 mmol). After stirring for 14 h at room temperature, the reaction was neutralized with a 0.5 N aqueous sodium hydroxide solution (15 mL) and extracted with diethyl ether (15 mL × 3), then washed with brine. After drying the combined organic phases over $MgSO_4$ and removal of the solvent in vacuo, a crude solid material was obtained. Recrystallization from methanol gave pure *N*-(2,2-dichloro-3-oxo-1,3-diphenylpropyl)phenylsulfonamide **12a** as white crystals in 92% yield.

***N*-(2,2-Dichloro-3-oxo-1,3-diphenylpropyl)phenylsulfonamide 12a.** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.52 (d, 1H, J = 10.2 Hz, C*H*NH), 5.83 (d, 1H, J = 10.2 Hz, NH), 7.10−7.28 (m, 6H, $CH_{arom.}$), 7.35−7.45 (m, 3H, $CH_{arom.}$), 7.55−7.60 (m, 3H, $CH_{arom.}$), 8.99−7.02 (m, 2H, $CH_{arom.}$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 65.9, 87.9, 127.1, 128.0, 128.3, 128.7, 129.9, 130.5, 132.5, 132.5, 132.9, 133.0, 140.0, 188.6. IR (KBr): ν = 3254 (NH), 1697 (C═O), 1328 and 1164 (S═O). MS (ES^+): *m*/*z* (%) = 434/436/438 (MH^+, 8), 246 (100). Mp (MeOH) = 149.6−152.3 °C. Yield = 92%. White crystals. Anal. Calcd for $C_{21}H_{17}Cl_2NO_3S$: C, 58.07; H, 3.95; N, 3.22. Found: C, 57.98; H, 4.11; N, 3.32.

Synthesis of *N*-[(1*E*)-1-(*cis*-2-Chloro-3-aryl-1-sulfonylaziridin-2-yl)(aryl)methylidene] Alkylamines 19. The synthesis of *N*-[(1*E*)-1-(*cis*-2-chloro-3-phenyl-1-sulfonylaziridin-2-yl)(phenyl)-methylidene]-*N*-isopropylamine **19a** is representative. [2,2-Dichloro-

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3-(isopropylimino)-1,3-diphenylpropyl]benzenesulfonamide **11a** (10 mmol, 4.74 g) was dissolved in tetrahydrofuran (50 mL), and water (50 mL) was added, followed by aqueous 2 N KOH (12 mmol, 6.0 mL). The reaction was vigorously stirred at room temperature for 48 h. Upon washing with water, diethyl ether, and brine, the combined organic layers were dried ($MgSO_4$). Evaporation of the solvents in vacuo gave a crude pale yellow solid *N*-[(1*E*)-1-(*cis*-2-chloro-3-phenyl-1-sulfonylaziridin-2-yl)(phenyl)methylidene]-*N*-isopropylamine **19a** (4.38 g), which was recrystallized over MeOH to afford white crystals (4.17 g, 9.49 mmol) in 95% yield.

***N*-{(1*E*)-1-[*cis*-2-Chloro-3-phenyl-1-(phenylsulfonyl)aziridin-2-yl](phenyl)methylidene}isopropylamine 19a.** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.13 (d, 3H, J = 6.3 Hz, CH_3), 1.28 (d, 3H, J = 6.3 Hz, CH_3), 3.66 (sept, 1H, J = 6.3 Hz, *CH*N=), 4.93 (s, 1H, *CH*Ph), 7.08−7.10 (m, 2H, $CH_{arom.}$), 7.20−7.26 (m, 3H, $CH_{arom.}$), 7.42−7.52 (m, 8H, $CH_{arom.}$), 8.00 (m, 2H, $CH_{arom.}$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.9, 23.4, 50.9, 53.5, 73.4, 127.5, 128.0, 128.4, 128.5, 129.1, 131.6, 133.6, 134.8, 140.0, 159.5. IR (KBr): ν = 1638 (C=N), 1347 and 1168 (S=O). MS (ES^+): *m*/*z* (%) = 439/441 (MH^+, 20), 298/300 (100). Mp (MeOH) = 38.0−40.7 °C. Yield = 95%. White crystals. Anal. Calcd for $C_{24}H_{23}ClN_2O_2S$: C, 65.67; H, 5.28; N, 6.38. Found: C, 65.49; H, 5.40; N, 6.49.

Synthesis of 2-(Aminomethyl)aziridines 27. Aziridine **19** (1 mmol) was dissolved in 5 mL of methanol at 0 °C, and then $NaBH_3CN$ (3 mmol, 0.19 g) was added portionwise, followed by dropwise addition of acetic acid (1 mmol, 60 mg). The reaction was slowly allowed to reach room temperature and stirred up to consumption of the starting product (3−6 h, TLC, flash chromatography, petroleum ether−EtOAc 9:1). Workup was done by pouring the reaction mixture into ice-cold water (10 mL) and extraction with dichloromethane (3 × 60 mL). After drying the combined extracts with potassium carbonate and evaporation of the solvent in vacuo, the crude residue was recrystallized from methanol.

The reduction of imidoylaziridine **19c** (10 mmol, 4.72 g) gave a crude mixture which was purified by flash chromatography (petroleum ether−EtOAc 9:1), giving aziridine **27c** (68% yield) and aziridines **28** (16% yield) and **29** (6% yield).

***syn*-*N*-{1-[*cis*-2-Chloro-1-(phenylsulfonyl)-3-phenylaziridin-2-yl](phenyl)methyl}isopropylamine 27a.** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.09 (d, 3H, J = 6.3 Hz, CH_3), 1.15 (d, 3H, J = 6.3 Hz, CH_3), 2.16 (brs, 1H, CH*NH*), 2.79 (sept, 1H, J = 6.3 Hz, Me_2*CH*NH), 4.38 (s, 1H, C*CH*Ph), 4.80 (s, 1H, NH*CH*Ph), 6.69−6.71 (m, 2H, $CH_{arom.}$), 7.06−7.16 (m, 3H, $CH_{arom.}$), 7.31−7.40 (m, 3H, $CH_{arom.}$), 7.45−7.68 (m, 5H, $CH_{arom.}$), 8.06−8.08 (m, 2H, $CH_{arom.}$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.8, 24.4, 46.1, 52.4, 64.0, 76.8, 127.8, 128.2, 128.5, 128.6, 128.6, 129.3, 131.2, 134.0, 139.2, 139.6. IR (KBr): ν = 3321 (NH). MS (ES^+): *m*/*z* = 441/443 (MH^+). Mp (MeOH) = 160.0−161.8 °C. Yield = 91%. White crystals. Anal. Calcd for $C_{24}H_{25}ClN_2O_2S$: C, 65.37; H, 5.71; Cl, 8.04; N, 6.35. Found: C, 65.08; H, 5.75; N, 6.26.

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Supporting Information Available: General information, experimental procedures and data for compounds **7**, **10**, and **20**, spectroscopic data for compounds **11b**−**f**, **12b**,**c**, **19b**−**d**, **27b**,**c**, **28**, and **29**, and X-ray structure of compound **27c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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