The synthesis of alkyl aryl nitriles from *N*-(1-arylalkylidene)-cyanomethylamines. Part 2. Mechanism

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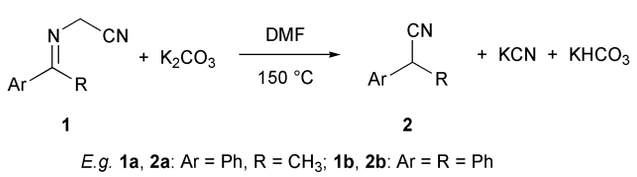
The mechanism of the rearrangement of *N*-(1-arylalkylidene)cyanomethylamines ArC(=NCH_2CN)R **1** to the corresponding nitriles ArCH(CN)R **2** (in DMF, at 150 °C, with K_2CO_3) is described. Reaction **1** ⟶ **2** was investigated for different types of imine **1**, and it was found that with a leaving group other than CN^- the reaction does not proceed to yield the nitrile, whereas imines such as PhC(=NCH_2CN)H, prepared starting from aldehydes rather than ketones, yield the expected phenylacetonitrile even at temperatures as low as 120 °C. Evidence for the mechanism comes from a study of the reactivity of the postulated intermediates: 2-cyano-3-phenylaziridine **4c**, and 2,2-diphenyl-2*H*-azirine **5b**. The route involving aziridine **4c** is ruled out, since this compound does not react at all under the investigated conditions. The 2*H*-azirine **5b** instead, yields the corresponding diphenylacetonitrile in DMF with K_2CO_3, at 150 °C. The transformation seems to involve an initial deprotonation, followed by an intramolecular ring closure–CN elimination step, which yields the 2*H*-azirine. The azirine then isomerizes to the nitrile. Additional evidence for the intermediacy of the 2*H*-azirine, based on ^{1}H NMR monitoring of the reaction **1** ⟶ **2**, is described. Finally, the results of a simple isotope exchange experiment provide a rationale for the previously observed scrambling of labels, and further confirm the proposed mechanism.

Introduction

We have recently reported a new reaction of *N*-(1-arylalkylidene)cyanomethylamines ArC(=NCH_2CN)R **1**:[1] when **1** is heated in DMF in the presence of potassium carbonate, it undergoes a clean rearrangement to alkyl aryl nitriles [ArCH(CN)R, **2**] (Scheme 1). The reaction proceeds only at relatively

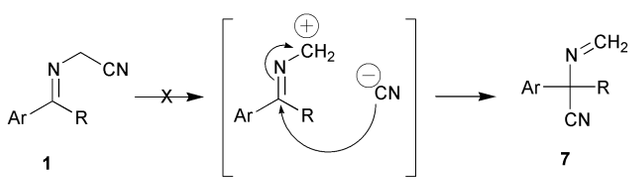


Scheme 1 Rearrangement of *N*-(1-arylalkylidene)cyanomethylamines to alkyl aryl nitriles.

high temperatures ($T \geq 150$ °C), through the formal loss of HCN, and both alkyl aryl-, substituted alkyl aryl-, and diarylimines **1** can be used as reagents.[2]

In a previous paper on the mechanism of the **1** ⟶ **2** rearrangement, some unequivocal mechanistic evidence was collected through the investigation of the reaction kinetics and through the study of the reactivity of *N*-alkylformimidoyl cyanides [ArCH(N=CHCN)R],[3] and of labeled imines [ArC(=$NCH_2{}^{13}CN$)R (***1**) and ArC(=$^{14}NCH_2CN$)R (**1***)].[4] In particular, it was concluded that:

(1) the first, and rate-determining step of the mechanism was deprotonation at the methylene of imines **1** to yield **1**$^-$. This was derived from the Hammett free-energy relationship obtained from the reactions of different *p*-substituted *N*-(1-arylethylidene)cyanomethylamines **1** (Ar = *p*-BrC_6H_4-, *p*-ClC_6H_4-, *p*-$CH_3C_6H_4$- and *p*-$CH_3OC_6H_4$-; R = CH_3). The reaction was first order and fitted the Hammett equation ($\log k/k_o = \sigma\rho$), giving a ρ value of 1.86, consistent with the fact that an electron withdrawing group (EWG) on the aryl ring stabilizes the developing negative charge in **1**$^-$. This observation rules out any mechanisms initiated by an S_N1' or S_N2' isomerization, such as the one depicted in Scheme 2.



Scheme 2

In compound **7**, the aryl ring is not conjugated to the reactive site, a fact not compatible with the large positive ρ value obtained by the Hammett treatment. In addition, when imine **1** (with R = Ar = Ph) was deprotonated with *n*-BuLi in THF at −90 °C, and then heated at the reflux temperature of THF (67 °C), no reaction was observed. However, when THF was replaced with DMF, and the solution refluxed at 150 °C, the usual clean rearrangement to nitrile $Ph_2CH(CN)$ **2** was observed.

(2) The cyano group of ArC(=NCH_2CN)R acted as the leaving group. In fact cyanide was titrated at the end of the reaction, and when it was replaced with other substituents (*e.g.* phenyl), reaction **1** ⟶ **2** did not take place.

(3) The process was mainly intramolecular and the cyano functionality of nitriles **2** derived primarily from the methylene-imino (=NCH_2–) fragment of **1**. This was inferred by running a series of reactions using isotopically labeled PhC(=$NCH_2{}^{13}CN$)CH_3, and PhC(=$^{15}NCH_2CN$)CH_3, under the conditions of Scheme 1. The isotope distribution in the two products [PhCH(CH_3)^{13}CN] and [PhCH(CH_3)C^{15}N] showed enrichments of 32 and 57%, respectively.

Accordingly, two possible reaction pathways were proposed (Scheme 3). They involved the common initial formation of an aziridine ring system, either followed by expulsion of CN^- to give a 2*H*-azirine, and isomerization to the nitrile (path a); or by loss of cyanide through a symmetrical intermediate, and rearrangement to the nitrile (path b).[4] Although path a appeared more elegant and would somewhat account for the predominant source of CN^-, the experimental evidence was not conclusive in its favor. In the present work the proposed

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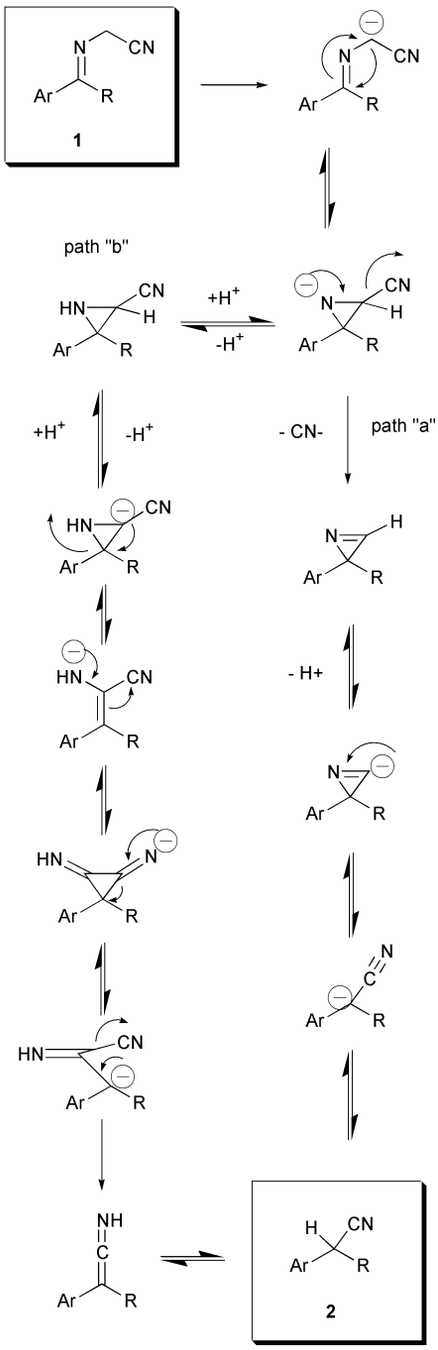


Scheme 3 Two possible pathways for the **1** ⟶ **2** rearrangement.

intermediacy of an azirine in the mechanism of the reaction **1** ⟶ **2**, was tested and the results are reported. The behavior of representative examples of the proposed intermediates, synthesized independently by other routes, is described. The outcome of the reaction on substrates with different leaving groups (other than cyano), as well as extension of the process to aldehyde derivatives [PhC(=NCH_2CN)H] will be discussed. Finally, a new experiment is described to explain the observed isotope scrambling.

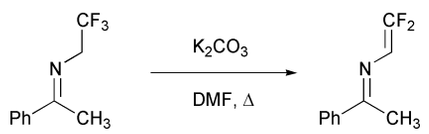
Results and discussion

Before exploring the reactivity of aziridines and azirines—the proposed intermediates—attention was focused on determining how general the examined reaction could be. Thus, functionalized imines of general formula PhC(=NCH_2X)R were considered. To understand whether nitriles would still be observable as products and consequently, whether azirines were possible intermediates for such compounds, different X groups, as well as an aldehyde derivative, PhC(=NCH_2CN)H, were investigated.

Alternative X groups

In view of the proposed mechanism, whereby the CN moiety of the reagent ArC(=NCH_2CN)R **1** is expelled during the reaction, other groups able to stabilize the negative charge on the methylene were considered in place of CN. Compounds PhC(=NCH_2X)Me (X = CO_2Me,[1] **3a**; CF_3, **3b**) were prepared by condensation of acetophenone with hydrochloride salts of glycine methyl ester and of 2,2,2-trifluoroethylamine,† respectively. The synthesis of the mesyl (X = Ms), tosyl (X = Ts), and oxazole derivatives was attempted, with no success as of yet.‡

Imines **3a**,**b** were made to react under the conditions of Scheme 1, and would have been expected to yield the corresponding nitrile PhCH(CN)CH_3 **2a**. Compound **3a** proved to be completely unreactive: it was recovered unchanged without any other reaction having taken place: a result likely due to the poor leaving group ability of the –$COOCH_3$ group.[5] Compound **3b**, possessing an electron withdrawing CF_3 group able to promote deprotonation and perhaps to act as a leaving group,[6] did not yield the expected nitrile **2a** either; however, it did undergo base-promoted HF elimination to the corresponding conjugated product [eqn. (1)].



Under the same reaction conditions, a similar product was observed for PhCH(Me)N=$CHCCl_3$ (**3f**).§ In this case, compound **3f** underwent a 1,4-elimination of HCl to yield PhC(=NCH=CCl_2)Me (**3g**) as the product; behavior analogous to that of base-promoted reactions of 7α-amino-1-oxacephems.[7]

On the whole, since no other groups but cyano were suitable for this reaction, it appeared that the presence of electron withdrawing groups capable of negative charge stabilization was not enough to promote the examined reaction: the X group must also have leaving group ability. This dual behavior of CN as (a) negative charge stabilizer and (b) leaving group, has an analogy in the benzoin condensation, where cyanide first promotes α-deprotonation, and then acts as a leaving group.[8]

Imines derived from aldehydes

In order to investigate the possible effect of the alkyl group (R) on the iminic carbon, analogs of imines **1** were considered. Specifically, PhC(=NCH_2CN)H **1c** (R = H) was prepared starting from benzaldehyde following the usual procedure.[1] When reacted under the conditions of Scheme 1, compound **1c** proved much more reactive than methyl aryl imines **1**, and it was converted very quickly (10 min) into phenylacetonitrile **2c** (66%). The double bond isomer of the reagent $PhCH_2N$=CHCN **1c**$_i$ (24%) appeared as a by-product, implying that the isomerization **1c** ⟶ **1c**$_i$—forbidden for ketone derivatives—took place in this case. However, the rearrangement of **1c** to **2c** proved feasible at a lower temperature (80 °C instead of 150 °C; conversion: 84%; **2c**: 78%, after 180 min), thereby drastically decreasing **1c**$_i$ formation (6%).

† Compounds **3a** and **3b** were prepared by the same general procedure used for **1**.[1]

‡ The syntheses of PhC(=NCH_2X)Me (X = LG) were carried out analogously to the above imines, starting from a ketone and the appropriate amine. However, attempts to synthesize H_2NCH_2X·HCl (X = Ms, Ts, oxazole) proved fruitless.

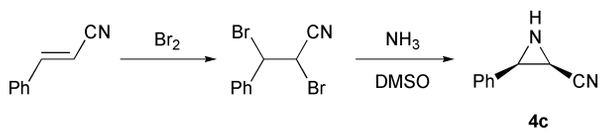
§ PhCH(Me)N=$CHCCl_3$ was prepared, rather than its isomer PhC(=NCH_2CCl_3)Me, since its synthesis is easier and since it is known that under the conditions of Scheme 1, R_2CHN=CHCN undergoes isomerization to yield R_2C=NCH_2CN.[3]

Aziridines 4 and azirines 5

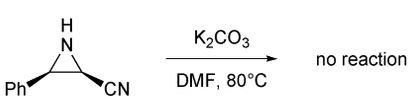
Direct and indirect methods were used to probe the intermediacy of the three-membered heterocycles postulated for both pathways a and b in the mechanism of Scheme 3. The following section describes how the search for evidence of the mechanism was approached through the study of these compounds. Indirect tests were carried out by investigating the reactivity of compounds **4** and **5** under the conditions of Scheme 1. Direct evidence of an intermediate was sought through NMR analysis of the reaction **1** ⟶ **2**.

Reaction of aziridines

For the synthesis of an intermediate in the mechanism shown in Scheme 3, two general considerations led to the choice of 2-cyano-3-phenylaziridine **4c** (Scheme 4), as a model compound: (i) as described above, the rearrangement **1** ⟶ **2** occurs more readily on the benzaldehyde-derived imine PhC(=NCH_2-CN)H **1c** with respect to ketone-derived imines; (ii) both reaction pathways (a and b) of compounds **1** in Scheme 3, require an aziridine as a common precursor, and **4c** was one of the more readily accessible synthetically.[9] Thus 2-cyano-3-phenylaziridine was obtained in the *cis* configuration by a literature method,[9] by reacting α,β-dibromocinnamonitrile with dry ammonia. Once prepared, the aziridine **4c** was made to react under the same conditions as for **1c**. No reaction whatsoever occurred [eqn. (2)] and the reagent was recovered unchanged. This observation allowed us to rule out path b of Scheme 3.

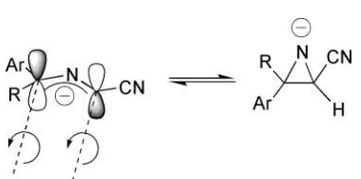


Scheme 4 Synthesis of 2-cyano-3-phenylaziridine **4c**.



(2)

Path a of Scheme 3 implies the initial deprotonation of the reactant imine **1**, followed by ring closure and CN^- expulsion. The proposed ring closure is thermal, 4-electron, conrotatory, and allowed by the Woodward–Hoffmann rules.[10] Scheme 5 shows the allylic anion type HOMO of $\mathbf{1}^-$, which controls the course of the reaction, and its conrotatory closure to the intermediate cyclized anion. In this case, the subsequent step of cyanide elimination (path a of Scheme 3), to give the 2*H*-azirine, must necessarily be favored over protonation at the nitrogen under the investigated conditions, to avoid the bottleneck posed by the aziridine of path b. The mechanistic analogy is again with the benzoin condensation,[8] where the intermediate, with a negative charge on a heteroatom in the α position with respect to the CN, prefers to eliminate cyanide, rather than to protonate at the oxygen (Fig. 1). To test this hypothesis the synthesis of an appropriate 2*H*-azirine was undertaken.



Scheme 5 Electrocyclic ring closure of $\mathbf{1}^-$.

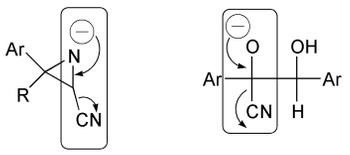
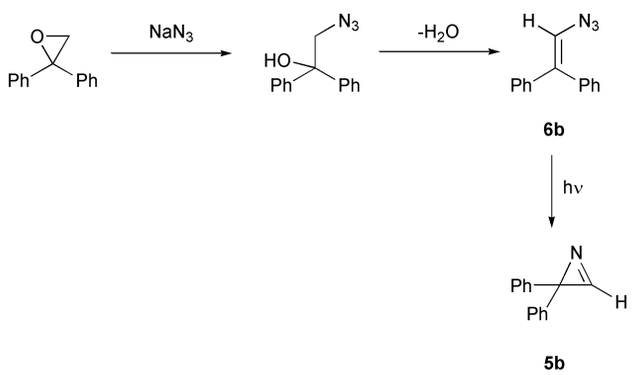


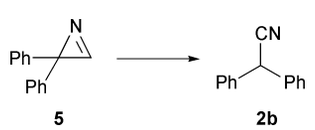
Fig. 1 Comparison between Scheme 4 and the benzoin condensation.

Reaction of 2*H*-azirine

2,2-Diphenyl-2*H*-azirine **5b**—the proposed intermediate for the rearrangement of PhC(=NCH_2CN)Ph **1b** to diphenylacetonitrile **2b**—was synthesized,[6,11] as shown in Scheme 6, by irradiation of diphenylvinyl azide **6b**. Since 2*H*-azirines are quite air sensitive, once a 37% yield was reached,¶ the solvent ($CDCl_3$) was immediately removed with a stream of nitrogen, and the mixture containing **5b** was set to react at 150 °C with K_2CO_3 in DMF. Rewardingly, the reaction yielded predominantly diphenylacetonitrile **2b** [85%, eqn. (3)] along with 15% phenylindole, known to derive from the thermal treatment of **6b**.[6] This result supported the mechanism delineated in path a of Scheme 3 for the transformation **1** ⟶ **2**, although some doubt still persisted as to whether the vinyl azide **6b**, present in the reaction mixture, might itself have generated diphenylacetonitrile **2b** under the same conditions. This hypothesis was ruled out by treating compound **6b** at 150 °C with K_2CO_3 in DMF: benzophenone (74%) and phenylindole (23%) were the only products.



Scheme 6 Synthesis of 2,2-diphenyl-2*H*-azirine **5b**.



(3)

Having established that nitriles **2** can originate from azirines **5**, direct evidence for the intermediacy of azirines **5** in the overall rearrangement of Scheme 1 was sought. This was done by ^{1}H NMR monitoring of the reaction of *N*-(diphenylmethylene)-cyanomethylamine [PhC(=NCH_2CN)Ph, **1b**] at 150 °C, in DMF-d_7, and with K_2CO_3. The reaction proceeded as expected, with the disappearance of the 2H methylene singlet of **1b** (4.5 ppm) and the appearance of the 1H singlet of diphenylacetonitrile **2b** (6.0 ppm). The signal at 10.7 ppm—ascribable to the 2*H*-azirine **5b**—was detected, and remained at a constant intensity with respect to the starting material PhC(=NCH_2CN)-Ph, **1b** until the reaction was over (Fig. 2).

From a mechanistic standpoint, the general scenario appeared clear: path a of Scheme 3, shown in Scheme 4, was

¶ Yield calculated by acquiring a ^{1}H NMR spectrum of the reaction mixture, and by integrating the peak of the proton in the 2-position of the 2*H*-azirine **5b** (10.2 ppm),[13] relative to that of the vinyl proton of **6b** (6.7 ppm). This experiment also provided direct confirmation of the NMR resonance frequency of the azirine proton, which is reported in the literature, but with some ambiguity on the synthetic procedure.

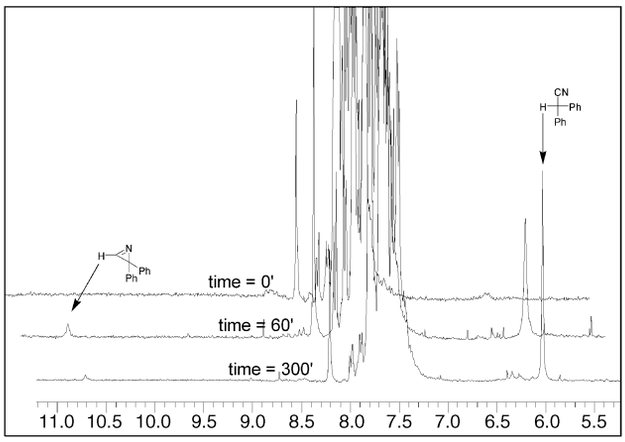


Fig. 2 ^{1}H NMR of reaction PhC(=NCH$_2$CN)Ph, **1b** ⟶ Ph$_2$CH(CN) **2b**, collected at time intervals.

validated experimentally and offered a plausible pattern for the rearrangement **1** ⟶ **2**. However, for a definitive explanation, one question remained to be answered. The intramolecular reaction shown in path a implied that the cyano group of the product nitrile **2** had to originate exclusively from the imine fragment (=N–CH$_2$–) of the reactant. By contrast, as determined by the isotope labeling experiments carried out with PhC(=NCH$_2$^{13}CN)Me (**1a***),[4] a fraction (32%) of the CN incorporated in the nitrile **2a** resulted from the starting nitrile functionality of **1a*** [eqn. (4)]. This isotope distribution (not explainable by path a, but partially accounted for by path b), was rationalized by means of a simple cross-over experiment.

Reaction of phenylacetonitrile 2c with ^{13}CN$^-$

A cross-over experiment had been previously reported by us,[4] and it had shown that under the conditions of Scheme 1, the reaction of **1a** in the presence ^{13}C-labeled sodium cyanide, yielded product PhCH(Me)^{13}CN **2a*** with 15% ^{13}C enrichment. Although this result did not exclude an intermolecular attack of ^{13}CN on the reagent, the existing evidence for the intramolecular character of the reaction **1** ⟶ **2**, strongly suggested that the isotope scrambling occurred on the product nitrile **2**, after the imine had reacted. A more in-depth review of the literature, supported this hypothesis.[12]

When phenylacetonitrile **2c** was allowed to react directly with ^{13}C-labeled sodium cyanide under the conditions of Scheme 1, a significant isotopic enrichment (25%) of the product nitrile **2c** was observed. Therefore, since the CN scrambling was the final, independent step, from the preceding ones involving imines **1**, the intramolecular mechanism of Scheme 4 appeared compatible with the results also obtained for the ^{13}C-labeled imine [**1a***, eqn. (4)]. The CN$^-$ released from the reaction of imines **1** accounted for the observed scrambling.[4]

Conclusions

The results presented allow an overall mechanism for the transformation **1** ⟶ **2**, under the conditions of Scheme 1, to be proposed, such as the one shown in path a of Scheme 3. It involves a thermal electrocyclic 4-electron reaction followed by a CN elimination step. While it is observed that the aziridine **3** does not react at all, and therefore cannot be an intermediate, direct and indirect evidence supports the intermediacy of a 2*H*-azirine, which does give the expected nitrile under the conditions investigated.

The reaction is very sensitive to the nature of the reacting imines. Imines derived from aldehydes react much faster than those prepared from ketones, indicating that the proposed intramolecular ring closure is influenced by steric factors. However, even the sterically undemanding methyl group in the α position of imine **1** disfavors the intramolecular ring closure to give the 2*H*-azirine ring, presumably by electron donating effects.

The data available to date seem to indicate that leaving groups other than CN$^-$ inhibit the reaction. Current efforts are aimed at extending its scope to other substrates, and some preliminary data indicate that compounds such as PhC(=NCH$_2$CO$_2$CH$_3$)H, derived from aldehydes, do in fact undergo the same rearrangement to yield phenylacetonitrile. This observation may open the way to a more general application of the reaction, and to its use with reagents possessing poorer leaving groups. To this end, there are significant challenges in the syntheses of imines **1** with such characteristics, which may follow the same rearrangement mechanism, thereby paving the way to new synthetic applications.

Experimental

Imine PhC(=NCH$_2$CF$_3$)Me (**3b**) was obtained through the condensation of acetophenone (2 g, 16.7 mmol) with 2,2,2-trifluoroethylamine hydrochloride salt (CF$_3$CH$_2$NH$_2$·HCl).[1,10] Yield of distilled product (bp = 65 °C/0.8 mmHg): 1.8 g (54%). ^{1}H NMR (CDCl$_3$) δ 7.87–7.83 and 7.45–7.35 (m, 4 H, Ph), 4.00 (qq, 2H, J = 9.6 Hz, J' = 0.98 Hz), 2.28 (t, 3H, CH$_3$, J' = 0.98 Hz). Mass spectrum (70 eV) *m*/*z* (relative intensity): 201 (M$^+$, 30%), 200 (32), 187 (10), 186 (M$^+$ − CH$_3$, 100), 132 (M$^+$ − CF$_3$, 5), 124 (18), 104 (24), 103 [PhC(Me)=N$^+$, 10], 91 (26), 83 (10), 77 (18), 51 (10).

Compound **3b** (0.2 g, 0.99 mmol) was made to react under the conditions of Scheme 1, during which elimination of HF took place. After 310 min in refluxing DMF, the conversion was 54% (by GC) and a mixture of *E*/*Z* isomers [PhC(=NCH=CF$_2$)Me: **3e** (45%) and **3e′** (3%)] was obtained. Structures were assigned by GC–MS. Mass spectrum (70 eV) *m*/*z* (relative intensity): **3e**, 181 (M$^+$, 47%), 166 (M$^+$ − Me, 100), 154 (15), 104 (25), 103 (12), 77 (38), 51 (13); **3e′**, 181 (M$^+$, 37%), 104 (M$^+$ − NCH=CF$_2$, 10), 103 (100), 77 (25), 51 (11).

Imine PhCH(Me)N=CHCCl$_3$ (**3f**) was obtained through the condensation of α-methylbenzylamine (0.5 g, 4.1 mmol) with 2,2,2-trichloroacetaldehyde.[12] Yield of distilled product (bp = 62–65 °C/0.4 mmHg): 0.73 g (70%). ^{1}H NMR (CDCl$_3$) δ 7.77 (s, 1H, CH=), 7.37–7.32 (m, 4 H, Ph), 4.68 (q, 1H, J = 6.7 Hz), 1.59 (d, 3H, CH$_3$, J = 6.7 Hz). Mass spectrum (70 eV) *m*/*z* (relative intensity): 249 (M$^+$, <1%), 132 (M$^+$ − CCl$_3$, 7), 106 (11), 105 (100), 77 (14), 51 (10).

Compound **3f** (0.2 g, 0.80 mmol) was made to react under the conditions of Scheme 1. As already reported for similar conditions,[12] elimination of HCl took place. After 90 min in refluxing DMF, the conversion was 64% (by GC) and a mixture of *E*/*Z* isomers [PhC(=NCH=CCl$_2$)Me **3g** (41%) and **3g′** (20%)] was obtained. Structures were assigned by GC–MS. Mass spectrum (70 eV) *m*/*z* (relative intensity): **3g**, 215 (M$^+$ + 2, 33), 213 (M$^+$, 50%), 202 (11), 200 (66), 199 (11), 198 (M$^+$ − CH$_3$, 100), 180 (11), 178 (33), 138 (11), 136 (17), 104 (63), 103 (22), 102 (16), 77 (45), 51 (32); **3g′**, 213 (M$^+$, <1%), 164 (2), 106 (10), 105 (100), 103 (10), 77 (15).

Imine PhC(=NCH$_2$CN)H **1c** was obtained through the condensation of benzaldehyde (1.0 g, 9.4 mmol) with aminoacetonitrile hydrochloride.[1] Yield of distilled product (bp = 110 °C/0.7 mmHg, lit.,[13] 92–93 °C/0.1 mmHg): 0.60 g (44%). Characterization data of **1c** are in ref. 14.

cis-2-Cyano-3-phenylaziridine (4c)[9]

4c was obtained by saturating a solution of α,β-dibromocinnamonitrile (650 mg, 2.14 mmol) solution of α,β-dibromocin-

namonitrile in DMSO (20 ml) with dry ammonia gas for one hour. The mixture was stirred overnight at room temperature, poured into brine, and extracted with dichloromethane. The organic layer was washed twice with 50 ml of water, dried over sodium sulfate and evaporated to dryness. The product solidified (55% yield) upon standing. ^{1}H NMR ($CDCl_3$) δ 7.5–7.3 (m, 5H), 3.56 and 3.02 (AB systems, J_1 = 5.9 Hz, J_2 = 9.7 Hz, *cis*-aziridine ring protons‖), 1.72 (t, 1H, J = 9.7 Hz).

2-Azido-1,1-diphenylethylene (6b)

Compound **6b** was prepared following known methods starting from diphenylethylene oxide, *via* 1,1-diphenyl-2-azidoethanol.[6] Dehydration of the latter was conducted by the following procedure, adapted from the literature:[15] 1,1-diphenyl-2-azidoethanol (1 g, 4.2 mmol) was dissolved in 7 ml of dry DMF, 3.0 ml of pyridine were added, and the mixture was cooled to 15 °C in an ice bath. In a separate flask, SO_2, obtained by the dropwise addition of sulfuric acid to Na_2SO_3, was bubbled through 10 ml of methanesulfonyl chloride (MsCl, Aldrich reagent), until a 5% wt solution of SO_2 in MsCl was obtained. An aliquot (2 ml, corresponding to 26 mmol of MsCl) of MsCl–SO_2 was added to the 2-azido-1,1-diphenylethylene solution over 15 min, maintaining the temperature of the mixture below 15 °C, during which the solution turned deep red. It was allowed to stir overnight at room temperature. Work-up consisted of the dropwise addition of 3 ml water, followed by a large excess (15 ml), and extraction of the mixture with methylene chloride (15 ml). The organic phase was washed successively with saturated brine, half saturated brine, and water, and dried over Na_2SO_4. It was then filtered, and evaporated to dryness at reduced pressure. Purification was carried out by flash chromatography eluting with a 1 : 1 mixture of toluene and petroleum ether (R_f = 0.55). Yield 300 mg (35%). ^{1}H NMR ($CDCl_3$) δ 7.4–7.2 (m, 10H), 6.7 (s, 1H). IR ν_{max}(neat)/cm^{-1} 2102 (N_3), 1612 (C=C). Mass spectrum (70 eV) *m*/*z* (relative intensity): 193 ($M^+ - N_2$, 100), 165 (42), 139 (7).

2,2-Diphenyl-2*H*-azirine (5b) and its reaction under the conditions of Scheme 1

2-Azido-1,1-diphenylethylene (200 mg, 0.9 mmol) was dissolved in 10 ml $CDCl_3$ in a nitrogen atmosphere in a Pyrex jacketed reactor maintained at −20 °C by circulating ethanol. The solution was irradiated with a medium pressure Hg lamp (filter cut-off λ < 350 nm). The tendency of atmospheric humidity to condense on the reactor was controlled by means of a nitrogen flow over the part exposed to the lamp. After 90 minutes, a portion of the solution was analyzed by ^{1}H NMR which showed the presence of 37% of the desired 2*H*-azirine **5b**, the remaining being substrate **6b**, indicating that the reaction had proceeded cleanly. **5b**: ^{1}H NMR ($CDCl_3$) δ 10.2 (s, 1H), 7.4–7.2 (m, 10H).

‖ Aziridine *cis*-protons are known to have larger coupling constants and larger chemical shifts with respect to protons in the *trans*-configuration; in the latter case the signals of the protons should therefore be broad, while in the former two AB systems would be expected. The observed AB systems (J_1 = 5.9 Hz, J_2 = 9.7 Hz) are therefore consistent with an aziridine in the *cis*-configuration.[9]

After removal of the $CDCl_3$ with a stream of nitrogen (at 0 °C), the residue containing 2,2-diphenyl-2*H*-azirine **5b** was transferred to a 10 ml flask containing 150 mg (1.1 mmol) of K_2CO_3, using 5 ml of dry DMF. The mixture was heated under nitrogen at 120 °C for 2 hours, and then analyzed by GC–MS. Along with **6b**, the mixture showed the presence of diphenylacetonitrile **2b** (85%) and a small amount of phenylindole (15%), all recognized by comparison with authentic samples. Diphenylvinyl azide **6b** was made to react under the same conditions as **5b**. After 2 hours at 150 °C, at complete conversion, 74% of benzophenone, 23% of phenylindole and <3% of **2b** were observed.

Reaction of phenylacetonitrile 2c with $^{13}CN^-$

Phenylacetonitrile (50 mg, 0.43 mmol) was set to react at 120 °C in a nitrogen atmosphere, with an equimolar amount of $Na^{13}CN$ in the presence of K_2CO_3 (90 mg, 0.65 mmol) in 5 ml of dry DMF. After 1 hour the mixture was analyzed by GC–MS, and the phenylacetonitrile showed a 25% isotope enrichment of ^{13}C.

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References

1 M. Selva, C. A. Marques and P. Tundo, *Synth. Commun.*, 1995, **25**, 369.
2 M. Selva, A. Bomben and P. Tundo, *Synth. Commun.*, 1999, **29**, 1561.
3 A. Perosa, M. Selva and P. Tundo, *Tetrahedron Lett.*, 1999, **40**, 7573.
4 A. Perosa, M. Selva and P. Tundo, *J. Chem. Soc., Perkin Trans. 2*, 1999, 2485.
5 R. G. Pearson, H. Sobel and J. Songstad, *J. Am. Chem. Soc.*, 1968, **90**, 319.
6 W. Tumas, R. F. Foster and J. Brauman, *J. Am. Chem. Soc.*, 1988, **110**, 2714.
7 T. Aoki, N. Haga, Y. Sendo, T. Konoike, M. Yoshioka and W. Nagata, *Tetrahedron Lett.*, 1985, **26**, 339.
8 M. B. Smith and J. March, in *March's Advanced Organic Chemistry*, 5th edn., J. Wiley & Sons, New York, 2001, p. 1243.
9 A. I. Ayi and R. Guedj, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2045.
10 R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, 1965, **87**, 395; H. C. Longuet-Higgins and E. W. Abrahamson, *J. Am. Chem. Soc.*, 1965, **87**, 2045; R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, 1965, **87**, 2046.
11 K. Isomura, M. Okada and H. Taniguchi, *Tetrahedron Lett.*, 1969, **46**, 4073; K. Isomura, H. Taniguchi, M. Mishima, M. Fujio and Y. Tsuno, *Org. Magn. Reson.*, 1977, **9**, 559.
12 M. Jay, W. J. Layton and G. A. Digenis, *Tetrahedron Lett.*, 1980, **21**, 2621.
13 A. C. Davis and A. L. Levy, *J. Chem. Soc.*, 1951, 3479.
14 O. Tsuge, K. Ueno, S. Kanemasa and K. Yorozu, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 1809.
15 G. G. Hazen and D. W. Rosenburg, *J. Org. Chem.*, 1964, **29**, 1931.