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Phototransformations of aziridin-1-yl enones and aziridin-1-yl fumarates substituted by a trifluoromethyl group in various positions

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Summary — 1-Vinylaziridines substituted by a trifluoromethyl group in various positions undergo photochemical rearrangement. From trifluoromethylated aziridin-1-yl enones, heterocyclic compounds are obtained. Regioselectivity of the cyclization of the ylide is observed when the trifluoromethyl group is bonded to the aziridine ring.

trifluoromethylaziridine / photochemistry / azomethine ylide / trifluoromethylpyrrole / trifluoromethylindole

Résumé — Phototransformation d'aziridin-1-yl énones et d'aziridin-1-yl fumarates substitués par un groupement trifluorométhyle dans différentes positions. *Un réarrangement photochimique est observé pour des 1-vinylaziridines substituées dans diverses positions par un groupement trifluorométhyle. Des composés hétérocycliques sont obtenus à partir d'aziridin-1-yl énones trifluorométhylées. La régiosélectivité de la cyclisation de l'ylure apparaît quand le groupement trifluorométhyle est directement lié au noyau aziridine.*

trifluorométhylaziridine / photochimie / ylure d'azométhine / trifluorométhylpyrrole / trifluorométhylindole

Introduction

Investigations of the photochemistry of the aziridine ring have shown that this system is exceptionally reactive under the influence of UV light [1]: irradiation may lead to geometrical isomerization, rearrangement, internal hydrogen abstraction, photofragmentation, or photochemical valence tautomerization. In those cases that have been fully investigated it has usually been found that the photolysis can best be described by a cleavage of the C–C bond of the aziridine ring followed by a multitude of possible second steps. The data obtained indicate that the chemical fate of the electronically excited aziridine is particularly sensitive to the nature of the substituent groups on the nitrogen or on the ring. A lot of results have shown facile dipolar additions of ylides obtained by photolysis or thermolysis to a dipolarophile to form five-membered heterocycles [2]. Intramolecular cyclization of the ylide obtained by photolysis or thermolysis is well documented when a vinylic functional group is bonded to a carbon of the ring [3], but few results are known when an activated vinylic system such as enone or fumarate is bonded to the nitrogen atom [4, 5]. Moreover, it is well known that a trifluoromethyl group can drastically change the reactivity of a molecule [6]. We therefore decided to investigate the phototransformation of some diphenylaziridines substituted by a trifluoromethyl group bonded to the enone function or to the ring [7].

Results and discussion

Irradiations were carried out in acetonitrile using a high pressure mercury lamp. The photochemical rearrangements of 1,1,1-trifluoro-4-(*cis*-2,3-diphenylaziridin-1-yl)-4-phenylbut-3-en-2-one **1a** (R = H) gave exclusively the (trifluoromethyl) pyrrole **6a** (23%) and the (trifluoromethyl) indole **7a** (46%) (scheme 1). Similarly, the irradiation of **1b** (R = CH_3) gave the 2,5-dihydro-1*H*-pyrrol-2-ols (*cis-trans*) **8b** (58%).

The formation of the various products in the photolysis of **1a,b** can be understood in terms of the pathway shown in scheme 1. In general, these substrates undergo electrocyclic ring-opening reactions involving C–C bond cleavage to give an azomethine ylide **2** [1, 8]. The ylide undergoes a 3-*exo*trig cyclization to form the aziridinium **3** leading to the Schiff base **4**. The fact that a Schiff base could be isolated from another reaction (vide infra **14c**, scheme 3) supports this assumption. The isomerization of an ylide to a Schiff base has been described [9, 10] as a Stevens rearrangement, which is known as a radical [11] or a cationic migration [12] in the solvent cage. The structure of the nitrogen substituent of the ylide **2** must be favorable to a 3-*exo*trig cyclization to form the aziridinium **3** rather than undergoing an ionic or a radical process. As a retention of configuration occurs during the Stevens rearrangement, and the cyclization on the carbon C4 of the enone function corresponds to a Michael reaction, it may be pos-

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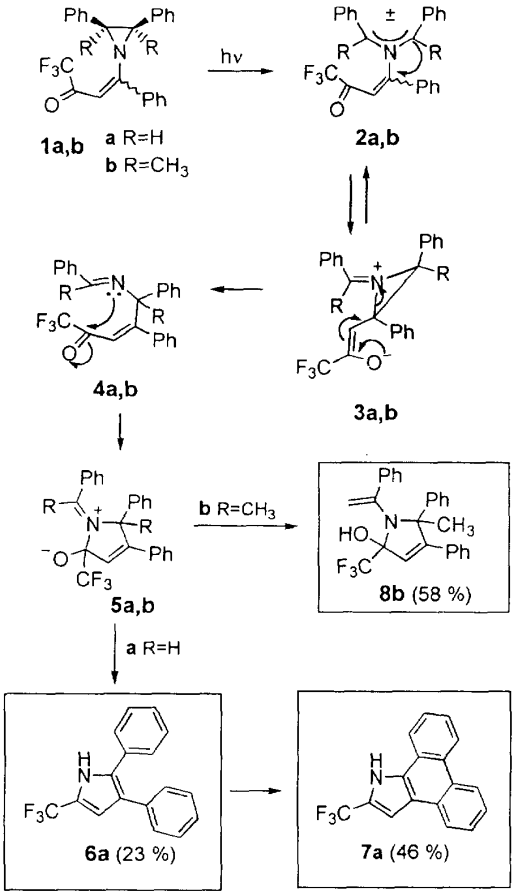
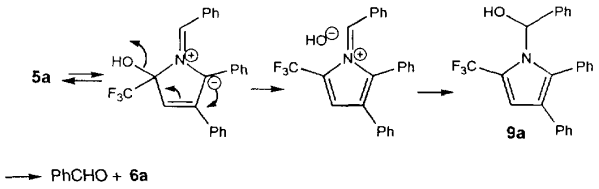


Scheme 1

tulated that the formation of the aziridinium **3** is in agreement with an orbital control reaction [13]. Subsequent transformations of **4** could lead to the cyclized intermediates **5** which are the precursors of the isolated compounds **6a** and **8b**. When the substituents R are hydrogens (scheme 2), **5a** is isomerized to the hemiaminal **9a** which eliminates benzaldehyde and leads to **6a** (benzaldehyde was detected).

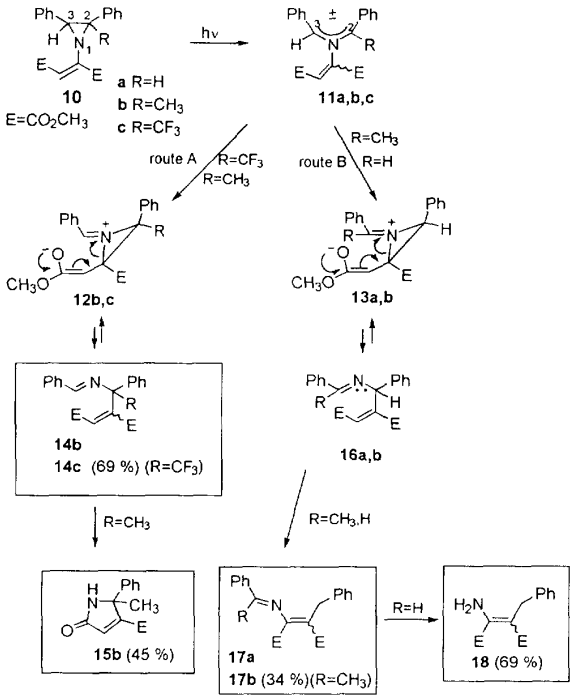
It is well known that azomethine ylides are also obtained by thermolysis [1]. By gas chromatography mass spectrometry analysis of aziridine **1a**, it was possible to detect thermolysis compounds formed in the injector: ions from pyrrole **6a** were observed. Moreover, we observed that independent photolysis of pyrrole **6a** gave the dibenzoindole **7a** (88%). It may be mentioned in this connection that some dibenzopyrroles are reported to undergo similar rearrangements [14].



Scheme 2

Subsequent transformations of **5b** (R = CH_3) lead to the pyrroline **8b** (58%); deprotonation of the methyl group by the alcoholate anion of the iminium **5b** may explain the formation of the stereoisomeric compounds **8b**. The proof of the structure of **8b** was established not only by ^1H, ^{19}F and ^{13}C NMR but also by its fragmentation in mass spectrometry: ion m/z: 215 (CH_2=CPh–N=C(OH)CF_3)$^{+\cdot}$ is in agreement with the structure suggested for the heterocyclic compound **8b**.

Irradiation of a dimethyl aziridin-1-yl fumarate, with a trifluoromethyl group bonded to the ring, must yield a dissymmetric ylide whose reactivity has not been described (scheme 3). We therefore studied the photochemistry of the aziridine **10c**; photolysis of **10c** (R = CF_3) gave exclusively the imine (*Z*,*E*)-**14c**. The starting material was the *Z* isomer; of course, during the photolysis, the isomerization of the fumarate to the maleate moiety was observed (after photolysis of **10c** for 0.25 h, a mixture of **14c** (25%), (*E*)-**10c** (60%) and (*Z*)-**10c** (15%) was recovered).



Scheme 3

Photolysis of (*Z*)-**10c** for 1.5 h produced the imine **14c** (69%) as a *Z*/*E* (85:15) mixture. Photolysis for 6 h or thermolysis (6 h in xylene) did not transform the imine **14c** into a pyrrolinone. It is noteworthy that **14c** did not cyclize into the corresponding pyrrolinone **15c** (R = CF_3) because recently Das et al [5] obtained some imines **14** (R = H, CH_2Ph) which did give the corresponding pyrrolinone **15**, as we observed with **14b** (R = CH_3) (vide infra). The cyclization of the dissymmetrical ylide **11c** (R = CF_3) to the aziridinium **12c** is regiospecific (only the route A is observed); it is the most unencumbered carbon of the ylide which reacts to form an aziridinium. This must result from a large

difference in amplitude between the orbitals of the two carbons of the ylide or the two Lewis structures. We therefore studied the regioselectivity of this 'concerted Stevens rearrangement' and examined the photolysis of the aziridine **10b** (R = CH_3) to try to observe the formation of the two aziridiniums **12b** and **13b**. The photolysis of the aziridine **10b** (R = CH_3) produced 1*H*-pyrrol-2(5*H*)-one **15b** (yield 45%) and azadiene **17b** (34%). These results agree with the formation of the two aziridiniums **12b** and **13b**. The aziridinium **12b** undergoes a ring-opening reaction to form the imine **14b**, which cyclized (via an aminal) into 1*H*-pyrrol-2(5*H*)-one **15b** (yield 45%) as observed by Das and George [5] in the quoted aziridine. The other aziridinium **13b** is transformed, via the imine **16b**, to the azadiene **17b** (34%). Transformation of the imine **16b** to the isolated isomeric compound **17b** could result from a series of rearrangements.

Isolation of the azadiene **17b** seems to be in disagreement with results published by Das et al [5]. These authors observed that photolysis of the aziridine **10a** (R = H) gave a 1*H*-pyrrol-2(5*H*)-one, like **15** (H instead of CH_3); they explain the formation of this compound by several chemical rearrangements of the imine **16a** (R = H). However they carried out the steady state isomerization of **10a** by irradiation at 290 nm using the output from a medium pressure mercury lamp coupled with a monochromator; benzene was used as solvent. We repeated the photolysis of the aziridine **10a** under our experimental conditions (a high pressure mercury lamp and acetonitrile as solvent). Under these conditions, **10a** (R = H) gave exclusively the enaminoester **18** (69%), in agreement with the formation of **17a** of course; the difference between these results must arise from the irradiation conditions (high pressure mercury lamp vs medium pressure mercury lamp coupled with a monochromator).

Conclusion

Under our experimental conditions, photochemistry of aziridines always produced an ylide, which underwent a Stevens rearrangement to form a Schiff base **4** or **14**. The Schiff base **4** cyclized to various pyrroles and pyrroline derivatives; the Schiff base **14c** is stable. It is noteworthy that the trifluoromethyl group from **10c** induces a regiospecific cyclization of the ylide **11c**, in contrast to the methyl group of the ylide **11b**.

Experimental section

^1H, ^{13}C and ^{19}F NMR spectra were measured on a solution in $CDCl_3$ with a Bruker AM 200 instrument (200 MHz) using TMS or $CFCl_3$ as internal standards. Mass spectra were obtained on a Nermag R10-105 via GC–MS at 70 eV. Melting points are uncorrected. Column chromatography was performed with gel 60 (230–400 mesh, Merck).

Materials

Starting materials **1a,b**, **10a,b,c** were prepared according to literature procedures [5, 7]. Photolyses were performed with acetonitrile (Aldrich), dried over 3 Å molecular sieves prior to use.

General procedure for the photolysis

A solution (0.2 mmol) of the appropriate 1-vinylaziridine in dry MeCN (20 mL) under nitrogen was irradiated (lamp Philips, HPK 125 high pressure) for between 45 min and 1.5 h in a quartz cell. The irradiation was repeated several times to photolyze, in total, 0.8 mmol of 1-vinylaziridine. Removal of the solvent under reduced pressure gave a residue, which was chromatographed on silica gel.

Irradiation of **1a** for 1 h gave:

- *2,3-Diphenyl-5-(trifluoromethyl)pyrrole* **6a**

Colorless crystals; 53 mg (23%); mp 184–185 °C (light petroleum) [eluent: light petroleum/CH_2Cl_2 (1:1)].

^1H NMR: δ 6.76 (q, 1H, =CH, $^4J_{HF}$ = 1.3 Hz), 7.20–7.36 (m, 10H, Ph), 8.46 (s, 1H, NH).

^{19}F NMR: δ −60.04 (s, CF_3).

^{13}C NMR: δ 108.6 (=*C*H), 123.9 (*C*F_3, q, $^1J_{CF}$ = 267.8 Hz), 124.6, 126.1, 127.3, 127.8, 128.4, 129.1, 134.5, 137.5 (Ph).

MS (*m/z*) (relative intensity): 387 ($M^{+\cdot}$, 100%), 286 (10), 272 (6), 268 (7), 266 (14), 218 (19), 217 (41), 216 (6), 189 (9), 108 (7).

Anal calc for $C_{17}H_{12}F_3N$, 287.27: C, 71.07; H, 4.21; N, 4.87. Found: C, 71.21; H, 4.30; N, 4.80.

- *2-(Trifluoromethyl)-1*H*-dibenzo[eg]indole* **7a**

Colorless crystals; 105 mg (46%); mp 199–200 °C ($CHCl_3$) (eluent: CH_2Cl_2).

^1H NMR: δ 7.41 (q, 1H, =CH, $^4J_{HF}$ = 1.1 Hz), 7.52–7.67 (m, 4H, Ar), 7.95–8.00 (m, 1H, Ar), 8.14–8.18 (m, 1H, Ar), 8.61–8.71 (m, 2H, Ar), 9.13 (s, 1H, NH).

^{19}F NMR: δ −59.9 (s, CF_3).

^{13}C NMR : δ 104.1 (q, =CH, $^4J_{CF}$ = 3.5 Hz), 121.7 (q, *C*F_3, $^1J_{CF}$ = 266.9 Hz), 123.3 (q, *C*-CF_3, $^2J_{CF}$ = 39.4 Hz), 120.9, 123.3, 123.5, 123.9, 124.8, 125.9, 126.9, 127.2 (*C*H, Ar), 120.0, 123.0, 127.4, 128.2, 129.4, 130.5 (*C*q, Ar).

MS (*m/z*): 285 ($M^{+\cdot}$, 100%), 284 (5), 266 (7), 265 (12), 264 (6), 245 (18), 187 (5), 142 (6), 132 (5), 94 (9).

Anal calc for $C_{17}H_{10}F_3N$, 285.25: C, 71.58; H, 3.53; N, 4.91. Found: C, 71.52; H, 3.58; N, 4.94.

Irradiation of **1b** for 0.5 h gave a mixture *cis/trans* (40:60) of 4,5-diphenyl-5-methyl-1-(1-phenylethenyl)-2-(trifluoromethyl)-2,5-dihydro-1H-pyrrol-2-ol **8b**

Colorless crystals; 195 mg (58%); mp 61–66 °C (light petroleum) [eluent: light petroleum/CH_2Cl_2 (1:1)].

- *Major isomer* **8b**

^1H NMR: δ 1.41 (s, 3H, CH_3), 4.90 (s, 1H, =CH_2), 4.96 (s, 1H, =CH_2), 6.25 (s, 1H, =CH), 6.85–7.59 (m, 15H, Ph).

^{19}F NMR: δ −79.3 (s, CF_3).

^{13}C NMR: δ 24.8 (*C*H_3), 114.1 (=*C*H_2), 117.3 (q, *C*F_3, $^1J_{CF}$ = 312 Hz), 120.3 (=CH) and 126.9–145.6 (*C*-Ph, *C*-CF_3).

MS (*m/z*): 403 ($M^{+\cdot}$-H_2O, 100%), 402 (23), 400 (25), 216 (15), 214 (25), 77 (10), 18 (12).

- *Minor isomer* **8b**

^1H NMR: δ 1.25 (s, 3H, CH_3), 5.10 (s, 1H, =CH_2), 5.26 (s, 1H, =CH_2), 6.35 (s, 1H, =CH), 6.85–7.59 (m, 15H, Ph).

^{19}F NMR: −77.9 (s, CF_3).

^{13}C NMR: δ 24.2 (*C*H_3), 112.5 (=*C*H_2), 120.0 (=*C*H), 116.2 (q, CF_3, $^1J_{CF}$ = 310 Hz) and 126.9–145.6 (*C*-Ph, *C*-CF_3).

Mass spectrum is comparable to that of the major isomer, **8b**.

Irradiation of **10a** for 45 min gave dimethyl 2-amino-3-benzylbut-2-enedioate **18**

138 mg (69%); viscous oil; [eluent: light petroleum/CH_2Cl_2 (1:2)].

^{1}H NMR: δ 3.01 (s, 2H, CH_2-Ph), 3.64 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 7.39 (s, 5H, Ph).

^{13}C NMR: δ 34.0 (CH_2-Ph), 50.9 (OCH_3), 51.6 (OCH_3), 89.1 (=Cq), 127.5, 128.7, 129,3 (Ph), 137.8 (Ph), 160.9 (=Cq), 170.4 (C=O), 173.9 (C=O).

MS (m/z) (relative intensity): 249 ($M^{+\cdot}$, 20), 190 (100), 158 (31), 130 (20), 104 (58), 77 (15), 55 (26).

Irradiation of **10b** for 1 h gave:

• *Methyl 2-methyl-5-oxo-2-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate* **15b**

Colorless crystals; 83 mg (45%); mp 148–150 °C (light petroleum); [eluent: light petroleum/CH_2Cl_2 (4:1)].

^{1}H NMR: δ 1.98 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 6.68 (s, 1H, =CH), 7.25–7.40 (m, 5H, Ph), 7.82 (s, 1H, NH).

^{13}C NMR: δ 23.6 (CH_3), 52.2 (OCH_3), 66.0 (Cq), 127.4 (=CH), 125.9, 128.1, 128.3, 128.6, 132.1 (Ph), 138.4 (Cq, Ph), 155.6 (=C), 161.8 (C=O), 170.8 (C=O).

MS (m/z) (relative intensity): 231 ($M^{+\cdot}$, 44), 216 (83), 172 (100), 144 (23), 104 (20), 77 (32), 53 (31), 51 (34), 42 (27).

• *Dimethyl 2-benzyl-3-[(1-phenylethylidene)amino]-but-2-enedioate* **17b**

Viscous oil; 96 mg (34%) [eluent: high petroleum/CH_2Cl_2 (2:1)]. Mixture of two stereoisomers (58:42) (unstable compound).

■ *Major isomer* **17b**

^{1}H NMR: δ 2.24 (s, 3H, CH_3), 3.31 (s, 2H, CH_2-Ph), 3.53 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 7.33–7.49 (m, 8H, Ph), 7.85–7.91 (m, 2H, *o*-Ph).

■ *Minor isomer* **17b**

^{1}H NMR: δ 2.34 (s, 3H, CH_3), 3.34 (s, 2H, CH_2-Ph), 3.64 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 7.33–7.49 (m, 8H, Ph), 7.85–7.91 (m, 2H, *o*-Ph).

Irradiation of **10c** for 1.5 h gave a mixture *Z/E* (85:15) of dimethyl 2-(1-benzylideneamino-2,2,2-trifluoro-1-phenylethyl)but-2-enedioate **14c**

Viscous oil; 224 mg (69%); eluent: light petroleum/CH_2Cl_2 (2:1).

• *Major isomer (Z)-***14c**

^{1}H NMR: δ 3.38 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 7.04 (s, 1H, =CH), 7.40–7.46 (m, 8H, Ph), 7.70–7.74 (m, 2H, *o*-Ph), 7.90 (s, 1H, CH=N).

^{19}F NMR: δ −68.7 (s, CF_3).

^{13}C NMR: δ 52.0 (OCH_3), 52.6 (OCH_3), 76.5 (q, C–CF_3, $^2J_{CF}$ = 30.9 Hz), 124.4 (q, CF_3, $^1J_{CF}$ = 287.7 Hz), 132.0 (=CH), 136.9 (=Cq), 165.9 (C=O), 166.7 (HC=N) and C-Ph (for mixture of isomers).

MS (m/z) (relative intensity): 405 ($M^{+\cdot}$, 33), 346 (48), 326 (100), 314 (26), 211 (18), 193 (22), 183 (27), 181 (39), 89 (28), 77 (41), 59 (66).

• *Minor isomer (E)-***14c**

^{1}H NMR: δ 3.71 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 7.25 (s, 1H, =CH), 7.40–7.46 (m, 8H, Ph), 7.78–7.82 (m, 2H, *o*-Ph), 8.09 (s, 1H, CH=N).

^{19}F NMR ($CDCl_3$): δ −69.9 (s, CF_3).

^{13}C NMR ($CDCl_3$): δ 52.2 (OCH_3), 52.3 (OCH_3), 77.2 (q, C-CF_3, $^2J_{CF}$ = 31.0 Hz), 124.5 (q, CF_3, $^1J_{CF}$ = 231.8 Hz), 133.5 (=CH), 138.3 (=Cq), 166.2 (C=O), 166.5 (CH=N).

MS (m/z) (relative intensity): 405 ($M^{+\cdot}$, 40), 346 (49), 326 (100), 314 (27), 211 (26), 193 (32), 183 (30), 181 (47), 89 (41), 77 (56), 59 (79).

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