Derivatives of 1-fluoroaziridine-2,2-dicarboxylic acid

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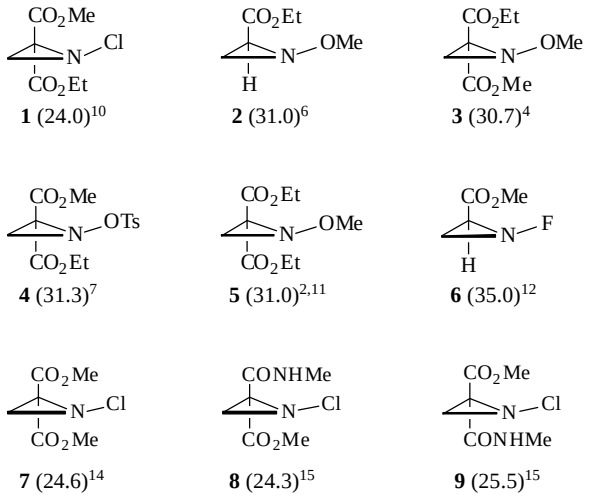
Derivatives of 1-fluoroaziridine-2,2-dicarboxylic acid **10–14** have been synthesized for the first time and characterized by spectroscopic methods; nucleophilic reactions of dimethyl 1-fluoroaziridine-2,2-dicarboxylate, such as transesterification and amidation, occur predominantly at the carboxy group *trans*-oriented with respect to the N-substituent.

Synthesis of derivatives of aziridinecarboxylic acids with electronegative N-substituents,[1–12] such as **1–6** ($G^{\#}_{inv}$/ kcal mol^{-1} in parentheses) has been developed in our laboratory in connection with the investigation of asymmetric nitrogen.



In the case of 1-alkoxyaziridines the chemistry and configurational stability were studied first on monoesters of type **2**, then diesters, *e.g.* **3** and **4**, were examined (compounds of type **4** were studied later[13]), and, finally, using diester **5**, the optical activation, complete resolution into antipodes, determination of their absolute configuration as well as reactions with retention of nitrogen atom configuration were carried out. Similarly, 1-chloro- and 1-bromo-aziridine-carboxylates were investigated.[3,4,9,10,14–19] The structure of compounds **7**,[16] **8**[17] and **9**,[15] as well as configurational stability of **1**[10] and **7–9**[14,15] were established; enzymatic resolution of 1-chloroaziridine **7**[14] was achieved, and the chiroptical properties of these types of compounds were studied.[15,18,19]

The same strategy was used for the investigation of 1-fluoroaziridinecarboxylates. Stable *cis*- and *trans*-isomers of methyl 1-fluoroaziridine-2-carboxylate were obtained recently. It was shown that aziridine **6** has a record high configurational stability.[12]

In this work, for the first time derivatives of 1-fluoro-aziridine-2,2-dicarboxylic acid **10–14** have been synthesized and studied (Scheme 1).† Compound **10** was prepared by fluorination of dimethylaziridine-2,2-dicarboxylate. 1-Fluoro-2,2-bistrifluoromethylaziridine **15** was obtained in a similar manner from 2,2-bistrifluoromethylaziridine.[20] It was synthesized earlier by another method[21] but no ^{13}C NMR spectra were reported.[22] We managed to obtain the corresponding *N*-fluoroaziridine **16** by fluorination of diisopropyl aziridine-2,3-dicarboxylate[19] but the yield was as low as 5.5%.

Fluoroaziridine **10** is quite stable; it can be distilled *in vacuo* without decomposition and does not change under boiling in a CF_3CO_2H–H_2SO_4 mixture with removal of CF_3CO_2H by distillation (under the same conditions aziridine **4** undergoes *trans*-deesterification[7]). Under prolonged boiling of **10** in [$^2H_4$]methanol stereospecific transesterification into **11** is observed, and after 10 h the ratio of signal intensities is as follows: B-MeO : A-MeO : MeOH = 2 : 1 : 1. Upon treatment with equimolar quantities of NH_3 or $MeNH_2$ *trans*-mono-amidation of **10** and formation of amides **12** and **13**, respectively, occurs on cooling. When treated with excess $MeNH_2$, diester **10** transforms into bismethylamide **14**. Therefore, in spite of the small size of the N-substituent, fluoroaziridine **10** is similar to 1-alkoxyaziridinecarbo-xylates[1–11] and 1-chloro analogue **7**,[14,15–17] in terms of its behaviour in nucleophilic reactions.

† ^{1}H NMR (400.13 MHz), ^{13}C (100.62 MHz), standard TMS, ^{19}F (376.48 MHz), standard CF_3CO_2H, δ/ppm, J/Hz.

10, yield 75%, bp 86–88°C (3 torr); ^{1}H NMR ($CDCl_3$): 2.80 dd (H_a, $^2J_{ab}$ =–5.5, $^3J_{aF}$ =29.3), 3.32 dd (H_b, $^3J_{bF}$ = 40.9), 3.80 s and 3.87 s (MeO); ^{13}C NMR ($CDCl_3$): 43.51 ddd (3-C, $^1J_{Ca}$ = 180.2, $^1J_{Cb}$ =176.6, $^2J_{CF}$ =2.9), 51.0 dt (2-C, $^2J_{CF}$ =7.3, $^2J_{Ca}$ = $^2J_{Cb}$ =3.6), 53.08q and 53.41 q (MeO, $^1J_{CH}$ = 149.0), 161.1 m (B-CO, $^3J_{CF}^{cis}$ = 8.7, $^3J_{CH}$ ~ 4.4), 164.3 hept (A-CO, $^3J_{CF}$ = $^3J_{Ca}$ = $^3J_{Cb}$ = 4.4); ^{19}F NMR (CD_3OD): 29.1 dd; mass spectrum (EI, 70 eV), *m*/*z* (%): 158 (4.6) $[M–F]^+$, 146 (4.6) $[M–MeO]^+$, 130 (2.9), 99 (2.6), 70 (2.5), 68 (3.2), 59 (29.4), 54 (11.0), 45 (100), 40 (6.4), 33 (3.6), 29 (6.1), 15 (46.0).

11 was characterized without isolation, ^{1}H NMR (CD_3OD): 2.89 dd (H_a, $^2J_{ab}$ =–5.8, $^3J_{aF}$ =30.0), 3.35 dd (H_b, $^3J_{bF}$ = 42.0), 3.35 s (MeOH), 3.78 s (B-MeO), 3.84 s (A-MeO); ratio of the intensities of signals of MeO at 3.35, 3.78 and 3.84 ppm = 1 : 2 : 1 .

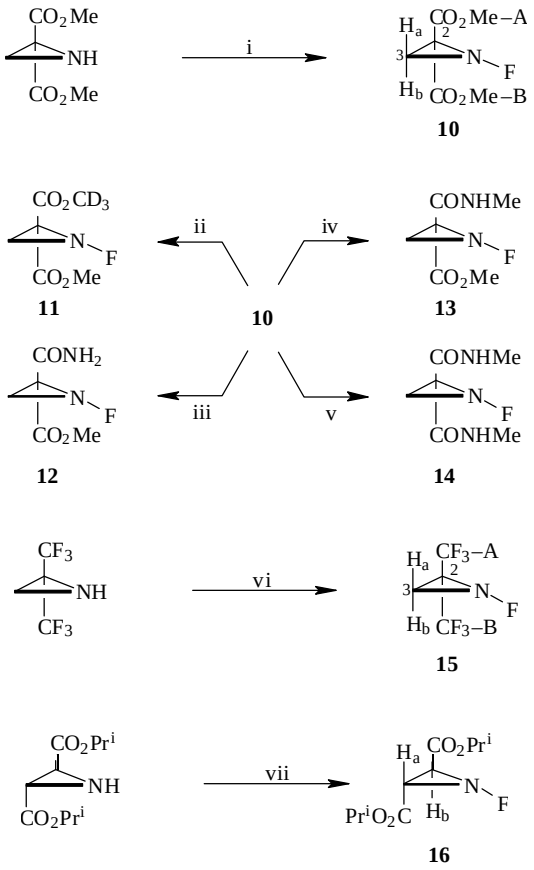
12, yield ~ 70%, oil contaminated with starting **10**; ^{1}H NMR ($CDCl_3$): 2.88 dd (H_a, $^2J_{ab}$ =–5.0, $^3J_{aF}$ =26.5), 3.47 dd (H_b, $^3J_{bF}$ =40.0), 3.9 s (MeO), 6.81 br. s (HN).

13, yield~70%, oil contaminated with starting **10**; ^{1}H NMR ($CDCl_3$): 2.81 dd (H_a, $^2J_{ab}$ = –5.8, $^3J_{aF}$ =26.6), 2.87 d (MeN, ^3J = 5.8), 3.42 dd (H_b, $^3J_{bF}$ =40.0), 3.87 s (MeO), 6.83 br. s (HN).

14, yield 80%, mp 148–150°C; ^{1}H NMR ($CDCl_3$): 2.76 dd (H_a, $^2J_{ab}$ =–5.0, $^3J_{aF}$ =26.6), 2.83 d and 2.91 d (MeN, ^3J =4.9), 3.45 dd (H_b, $^3J_{bF}$ =39.7), 6.75 br. m and 6.97 br. m (HN); ^{13}C NMR (CD_3OD): 26.51 q and 26.97q (MeN, $^1J_{CH}$ = 139.5), 43.54 ddd (3-C, $^1J_{Ca}$ =178.8, $^1J_{Cb}$ = 174.4, $^2J_{CF}$ =4.4), 54.75 dt (2-C, $^2J_{CF}$ =6.5, $^2J_{CH}$ =3.2), 163.2 m (B-CO, $^3J_{CF}$ =8.0), 166.94 m (A-CO, $^3J_{CF}$ =3.6); ^{19}F NMR (CD_3OD): 24.34 dd.

15, yield 50%, bp 65°C; ^{1}H NMR ($CDCl_3$): 2.85 ddq (H_a, $^2J_{ab}$ =–6.6, $^3J_{aF}$ = 27.2, $^4J_{B\text{-}CF_3\text{-}a}$ =2.3), 3.33 ddq (H_b, $^3J_{bF}$ = 38.9, $^4J_{A\text{-}CF_3\text{-}b}$ =1.1); ^{13}C NMR ($CDCl_3$): 39.06 td (3-C, $^1J_{CH}$ = 180.2, $^2J_{CF}$ =3.0), 47.65 hept.dt (2-C, $^2J_{CCF}$ = 37.1, $^2J_{CNF}$ =5.8, $^2J_{CH}$ = 2.9), 120.3 q (CF_3, $^1J_{CF}$ =277.6) (Commonly, chemical shifts of CF_3 group carbons in the ^{13}C NMR spectra of 2,2-bistrifluoromethylaziridines either coincide or differ slightly.[22]); ^{19}F NMR ($CDCl_3$): 6.05 ddq (A-CF_3, $^4J_{FCCCF}$ = 7.4, $^4J_{FCCNF}$ = 2.2), 8.64 br.m (FN), 13.43 ddq (B-CF_3, $^4J_{FCCNF}$ = 23.1).

16, yield 5.5%, bp 85°C (0.6 Torr), ^{1}H NMR ($CDCl_3$): 1.24 m and 1.28m (Me, ^3J = 6.1), 3.34 dd (H_a, $^3J_{HH}$ = 6.7, $^3J_{aF}$ =20.1), 3.72 dd (H_b, $^3J_{bF}$ = 33.6), 5.01 hept and 5.08 hept (HC).



Scheme 1 *Reagents and conditions*: i, F_2/N_2, 4–10 fold excess of NaF, in a mixture of freon-113–$CHCl_3$ (1:1), 3h at 0°C; ii, CD_3OD, boiling 10h; iii, equimol. quantity of dry NH_3 in abs. MeOH, 3 days at 0°C; iv, equimol. quantity of dry $MeNH_2$ in abs. MeOH, 1 day at 0°C; v, excess of dry $MeNH_2$ in abs. MeOH, 0.5 h at 0°C; vi, F_2/N_2, excess of NaF in $\{CF_3O[CF(CF_3)CF_2O]_2CF_2\}_2$ (bp 215°C); vii, under conditions i, 1.5 h at –50°C.

The authors are grateful to INTAS (grant no. 94-2839) and the Russian Foundation for Basic Research (grant no.94-03-08730) for their financial support of this work.

References

1 R. G. Kostyanovsky, A. V. Prosyanik and V. I. Markov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1974, 482 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1974, **23**, 453).
2 R. G. Kostyanovsky, V. F. Rudchenko and V. I. Markov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1975, 1685, 2621 (in Russian).
3 R. G. Kostyanovsky, A. V. Prosyanik, V. I. Markov, I. A. Zon and A. E. Polyakov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1976, 1559 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1976, **25**, 1481).
4 R. G. Kostyanovsky, V. F. Rudchenko, A. V. Prosyanik, M. D. Isobaev, I. I. Chervin and V. I. Markov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1977, 628 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1977, **26**, 565).
5 R. G. Kostyanovsky, A. V. Prosyanik, A. I. Mishchenko, G. V. Shustov, I. I. Chervin, N. L. Zaichenko, A. P. Pleshkova, P. N. Belov and V. I. Markov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 1780 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1979, **28**, 1640).
6 A. V. Prosyanik, S. V. Bondarenko, V. I. Markov, I. I. Chervin, M. D. Isobaev, S. D. Kooshch and R. G. Kostyanovsky, *Khim. Geterotsikl. Soedin.*, 1980, 212 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1980, 154].
7 G. V. Shustov, N. B. Tavakalyan, N. L. Zaichenko and R. G. Kostyanovsky, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, 2183 (in Russian).
8 A. B. Zolotoi, O. A. Diachenko, L. O. Atovmyan, V. F. Rudchenko, I. I. Chervin and R. G. Kostyanovsky, *Khim. Geterotsikl. Soedin.*, 1984, 48 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1984, 40].
9 I. I. Chervin, A. A. Fomichov, A. S. Moskalenko, N. L. Zaichenko, A. E. Alijev, A. V. Prosyanik, V. N. Voznesensky and R. G. Kostyanovsky, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, 1110 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37**, 972).
10 A. S. Moskalenko, I. I. Chervin, A. V. Prosyanik and R. G. Kostyanovsky, *Khim. Geterotsikl. Soedin.*, 1988, 324 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1988, 264].
11 V. F. Rudchenko, O. A. Dyachenko, A. B. Zolotoi, L. O. Atovmyan, I. I. Chervin and R. G. Kostyanovsky, *Tetrahedron*, 1982, **38**, 961.
12 R. G. Kostyanovsky, A. G. Korepin, P. V. Galkin, Yu. I. El'natanov, G. K. Kadorkina, I. I. Chervin and V. R. Kostyanovsky, *Mendeleev Commun.*, 1995, 216.
13 J. Perrocheau, R. Carrie and J.-P. Fleury, *Can. J. Chem.*, 1994, **72**, 2458.
14 M. Bucciarelli, A. Forni, I. Moretti and F. Prati, *Tetrahedron: Asymmetry*, 1990, **1**, 5.
15 L. Antolini, M. Bucciarelli, A. Forni, I. Moretti, F. Prati and G. Torre, *J. Chem. Soc., Perkin Trans. 2*, 1992, 959.
16 L. Antolini, A. Forni, I. Moretti, L. Schenetti and F. Prati, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1541.
17 L. Antolini, M. Bucciarelli, A. Forni, I. Moretti and F. Prati, *J. Chem. Soc., Chem. Commun.*, 1991, 538.
18 G. V. Shustov, G. K. Kadorkina, R. G. Kostyanovsky and A. Rauk, *J. Am. Chem. Soc.*, 1988, **110**, 1719.
19 G. V. Shustov, A. V. Kachanov, V. A. Korneev, R. G. Kostyanovsky and A. Rauk, *J. Am. Chem. Soc.*, 1993, **115**, 10267.
20 I. L. Knunyantz and Yu. V. Zeifman, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1967, 711 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1967, **16**, 695).
21 R. G. Kostyanovsky, I. I. Chervin, A. A. Fomichov, Z. E. Samojlova, K. N. Makarov, Yu. V. Zeifman and B. L. Dyatkin, *Tetrahedron Lett.*, 1969, 4021.
22 R. G. Kostyanovsky, G. K. Kadorkina, I. I. Chervin and I. K. A. Romero Maldonado, *Khim. Geterotsikl. Soedin.*, 1988, 757 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1988, 616].

Received: Moscow, 2nd August 1996
Cambridge, 20th September 1996; Com. 6/05683I