



Pergamon

Tetrahedron Letters 41 (2000) 313–316

TETRAHEDRON
LETTERS

Arylation of polyamines by perfluoroarenes

Irina P. Beletskaya,^{a,*} Galina A. Artamkina,^a Vasyli A. Ivushkin^a and Roger Guillard^{b,*}

^aDepartment of Chemistry, Moscow State University, Vorobyevy Gory, Moscow, 119899, Russia

^bLaboratoire d'Ingénierie Moléculaire pour la Séparation et les Applications des Gaz (LIMSAG),
Université de Bourgogne/CNRS, Faculté des Sciences Gabriel, 6, Boulevard Gabriel, 21100 Dijon, France

Received 11 September 1999; accepted 29 October 1999

Abstract

The conditions of selective mono- and diarylation of diamines, and di- and triarylation of triamines by perfluoroarenes are described. The introduction of four perfluoroaryl groups in cyclam and two groups in dioxocyclam has been carried out. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: arylation; perfluoroaryl compounds; polyamines (polyaza-alkanes/cycloalkanes); regioselective reaction.

In previous papers we have studied the arylation of polyamines by nonactivated aryl halides catalysed by palladium complexes.^{1,2} Moreover, many researches have been devoted to the study of the perfluorylation of amines.³ Herein we report on the selective arylation of polyamines including cyclic polyamines by activated aryl halides.

The reactions of perfluoroarenes with polyamines are not known, the only exception being the monoarylation of 1,2-diaminoethane by hexafluorobenzene⁴ and 4-azidoperfluoropyridine.⁵ Meanwhile, fluoroarylamines are an important class of biologically active compounds.⁶

We have studied the reactions of 1,2-diaminoethane, 1,3-diaminopropane, *N*-(3-aminopropyl)-1,3-diaminopropane, 1,4,8,11-tetraazacyclotetradecane (cyclam), 1,4,8,11-tetraazacyclotetradecane-5,12-dione (dioxocyclam) with perfluoropyridine, perfluorobenzene and perfluorotoluene. Thus, we determined the conditions for selective introduction of one or two aryl groups in diamines, two or three aryl groups in triamines and four groups in cyclam, and two groups in its dioxo derivative (Table 1).⁷ The reactions with both perfluoropyridine and perfluorotoluene proceed selectively at the *para* position.

Monoarylation of 1,3-diaminopropane was performed in THF at 0°C for C₅F₅N and C₆F₅CF₃ or in DMF at 100°C in the case of the less active C₆F₆ (entries 1–3 in Table 1) using an amine:arene ratio of 2:1 because the amine served also as a base. All products were obtained in high yields. The only exception was the monoarylation by hexafluorobenzene (entry 1 in Table 1). Due to its lower reactivity, the reaction required prolonged heating and as a result of competing processes double arylation and cyclisation occurred.

* Corresponding authors. Fax: 7 095 938 18 44 (I.P.B.); fax: 33 3 80 39 61 17 (R.G.); e-mail: beletska@org.chem.msu.ru (I. P. Beletskaya), roger.guillard@u-bourgogne.fr (R. Guillard)

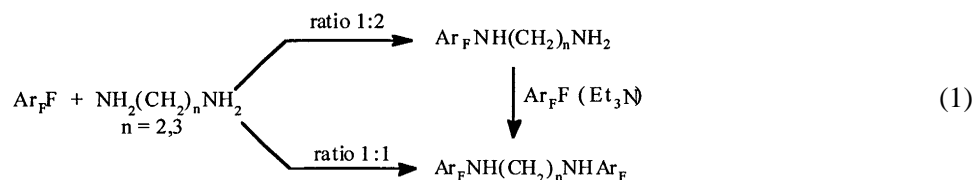
Table 1
Reaction conditions and yields

Entry	Starting amine	Perfluoro-arene	Molar ratio amine /arene	Solvent	Conditions	Product	Yield (%) ^b
1		C ₆ F ₆	2:1	DMF	100 °C, 7 h		42
2	"	C ₆ F ₅ CF ₃	"	THF	0 °C, 1 h		91
3	"	C ₃ F ₅ N	"	"	0 °C, 0.5-1 h		85
4	"	C ₆ F ₆	1:1	DMF	90-100 °C, 6 h		80
5 ^a		"	"	"	100 °C, 7 h	"	70
6		C ₆ F ₅ CF ₃	"	THF	70 °C, 3.5 h		77
7	"	"	"	DMF	80 °C, 1-1.5 h	"	98
8		C ₃ F ₅ N	"	THF	20 °C, 0.5 h		86
9		"	"	"	20 °C, 0.5 h		98
10		"	"	"	20 °C, 1 h		93
11 ^a		"	"	"	70 °C, 4 h		93
12 ^a		"	1:4	DMF	90-100 °C, 13 h		94
13 ^a		"	1:2	"	110 °C, 13 h		85

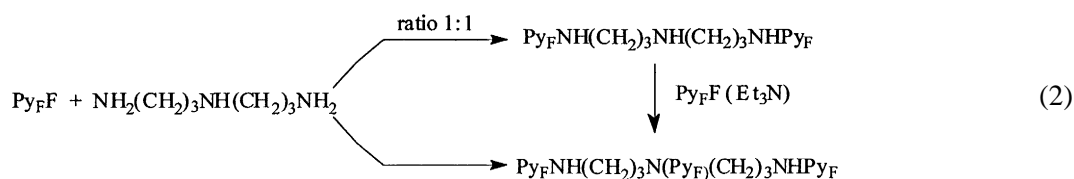
^aTriethylamine (1 equiv.) was used as base.

^bYields were calculated according to the perfluoroarene.

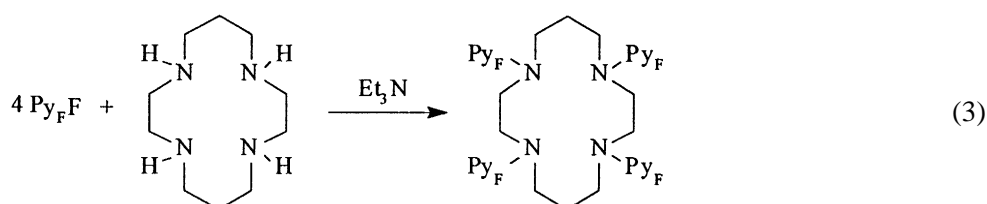
Heating the reaction mixture up to 70–80 °C for C₆F₅CF₃, up to 90–100 °C for C₆F₆ and up to 20 °C for C₅F₅N led to disubstituted products (entries 4, 6–9 in Table 1). Moreover, the yield in DMF is higher than in THF (entries 6 and 7 in Table 1).



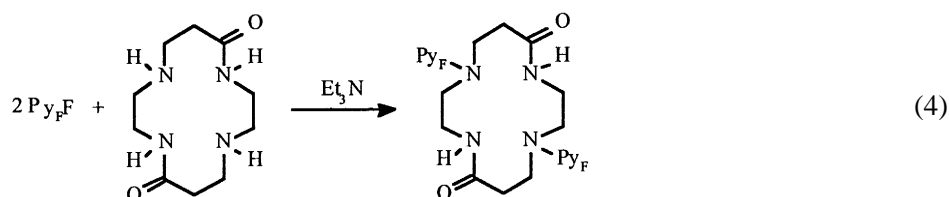
Diarylation of a triamine by perfluoropyridine at both primary amino end groups proceeded easily at room temperature in THF (entry 10 in Table 1). Further heating of the reaction mixture in the presence of Et₃N as a base gave the trisubstituted product (entry 11 in Table 1).



The reaction of cyclam with perfluoropyridine in DMF at 90–100°C in the presence of Et₃N (entry 12 in Table 1) gave the tetraarylated product in quantitative yield.



The same reaction carried out with 5,12-dioxocyclam instead of cyclam led to the 1,8-disubstituted compound since the carbonyl groups can be easily reduced,⁸ reaction 4 represents a new approach to obtain 1,8-diarylated cyclam.



All compounds were isolated in high yield and characterised by elemental analysis and ¹H, ¹⁹F NMR spectroscopy.

Acknowledgements

We are grateful to INTAS (grant no. 97-0791) for financial support.

References

1. Beletskaya, I. P.; Bessmertnykh, A. G.; Guilard, R. *Tetrahedron Lett.* **1997**, 38, 2287.
2. Beletskaya, I. P.; Bessmertnykh, A. G.; Mishechkin, R. A.; Guilard, R. *Russ. Chem. Bull.* **1998**, 1416–1417.
3. *Fluorine Chemistry Reviews*; Tarrant, P., Ed.; Marcel Dekker: New York, 1974; p. 1.
4. Abezgauz, F. I.; Sokolov, S. V. *Zh. Obshch. Khim.* **1968**, 38, 2502.
5. Nungaray, J.; Meziane-Cheref, D.; Le Goffic, F. *Synth. Commun.* **1996**, 26, 1273.
6. *Fluorine compounds. Synthesis and application*; Ishikawa, N., Ed.; Mir: Moscow, 1990 (Russian translation).
7. Typical experimental procedures: (a) Diarylation of diamines. A solution made of 0.120 g (4 mmol) of 1,2-diaminoethane in 1 ml THF was added to 0.68 g (4 mmol) of C₅F₅N in 5 ml THF. The mixture was stirred for 0.5 h, before the THF was evaporated in vacuum. The residue was treated with water, filtrated and recrystallised from hexane:benzene (1:1). The yield of *N,N'*-bis(4-tetrafluoropyridil)-1,2-diaminoethane was 0.62 g (86%). M.p. 170°C. (b) Monoarylation of diamines. A solution

of 0.83 g (3.5 mmol) of perfluorotoluene in 7 ml THF was slowly added dropwise to the solution of 0.510 g (7 mmol) 1,3-diaminopropane in 20 ml THF at 0°C. After 0.5 h of stirring, THF was removed and the residue was stirred with water for 0.5 h. The product was extracted with ether and the ethereal extract was dried over MgSO₄. After evaporation of the solvent, 0.930 g (91%) of [3-(4-perfluorotolylamino)propyl]amine was isolated. M.p. 40°C (low temperature crystallisation from hexane).

8. Brandes, S.; Denat, F.; Lacour, S.; Rabiet, F.; Barbette, F.; Pullumbi, P.; Guillard, R. *Eur. J. Org. Chem.* **1998**, 2349.