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ADDITION OF 2-SILYLAZOLES TO HETEROARYL CATIONS. SYNTHESIS OF UNSYMMETRICAL AZADIARYLS

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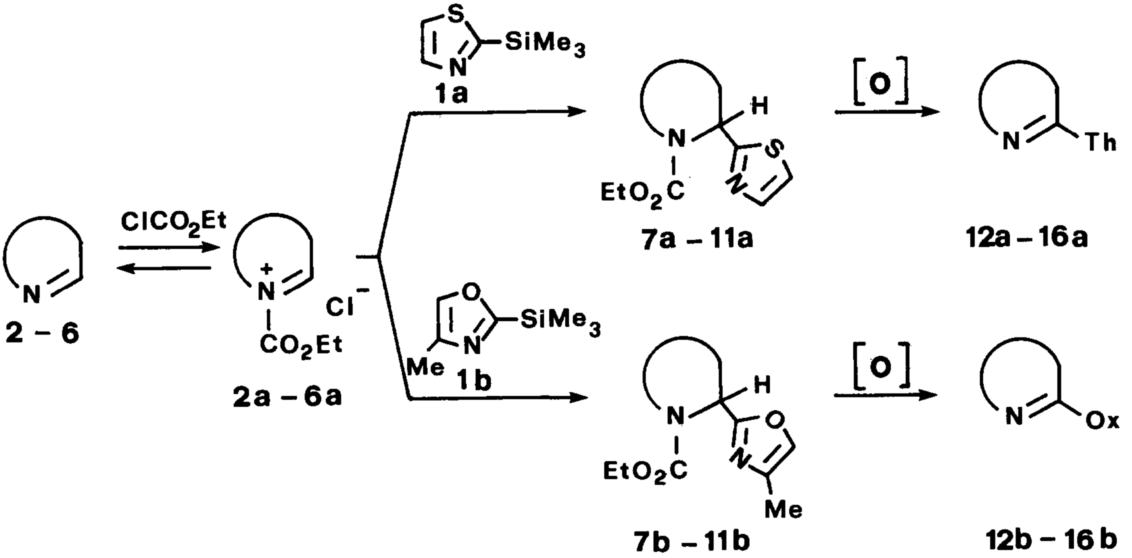
Summary : Thiazole, pyridine and some of their benzoderivatives react *via* their *N*-ethoxycarbonyl chlorides with 2-trimethylsilylthiazole (**1a**) and 4-methyl-2-trimethylsilyloxazole (**1b**) to give the corresponding adducts at C_α which by oxidative deacylation afford azadiaryls.

Diheteroaryl systems are potential building blocks for the synthesis of molecules with biological activity.[1] They are prepared mainly by two methods, *viz*. homolytic substitutions[2] and cyclization reactions,[3] which however suffer from some disadvantages since the latter are scarcely selective and the former require properly tailored intermediates.

We[4] and others[5] have recently observed that azaryls such as thiazole, pyri-

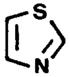
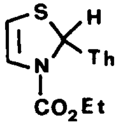
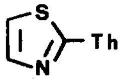
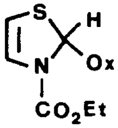
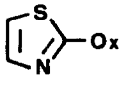
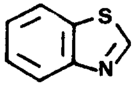
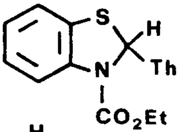
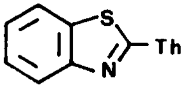
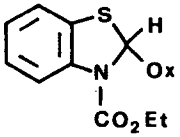
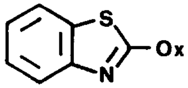
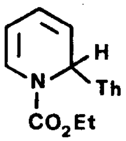
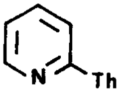
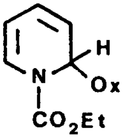
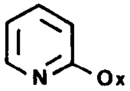
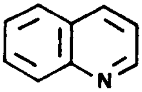
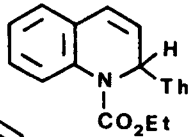
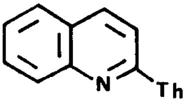
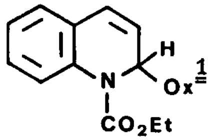
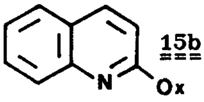
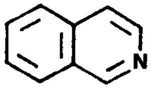
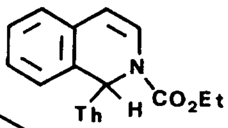
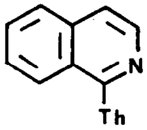
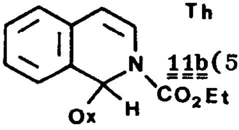
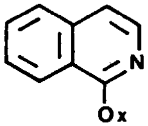


dine, and isoquinoline react with C-nucleophiles *via* their N-ethoxycarbonyl salts to give the corresponding addition products in good yields. We have also described the preparation of 2-trimethylsilylthiazole (**1a**)[6] and 4-methyl-2-trimethylsilyloxazole (**1b**)[7] and their reactivity as masked and stable thiazol-2-yl and oxazol-2-yl carbanions. We report here the reactions of the silylated heterocycles **1** with the N-ethoxycarbonyl salts of selected azaryls, namely thiazole, pyridine and some of their benzoderivatives **2** - **6** which afforded the corresponding adducts **7** - **11**; the oxidative deacylation of the latter gave the diheteroaryl compounds **12** - **16** (Table 1).

A general procedure follows. To a solution of the selected nitrogen heterocycle **2** - **6** (2 mmol) in methylene dichloride (30 mL) at 0°C was added 1 equiv. of ethyl chloroformate in 5 mL of the same solvent. After 30 min., a solution of the 2-silylazole **1** (1 equiv.) in methylene dichloride (10 mL) was added. The reaction mixture was stirred for an appropriate time (Table 1) and the solvent evaporated under vacuum. Flash chromatography (silica, CH_2Cl_2 - Et_2O 9:1) of the crude reaction mixture gave the adducts **7** - **11**. Treatment of **7** - **11** (2 mmol) in benzene with o-chloranyl (1.1 equiv.), heating at solvent reflux for 1 - 3 h and work-up (NaOH 5%, flash chromatography) of the reaction mixture, gave products **12** - **16**.

The results of Table 1 shows that the addition of **1** to the heteroaryl cations **2a** - **6a** occurs regioselectively at C_2 even when another position is equally activated such as in the pyridinium **4a** and quinolinium salts **5a** and **6a**. The only by product isolated was the thiazol-2-yl thiazoline (**7a**) arising from the competitive attack of **1a** on its quaternary salt.[8] In every case the reaction of the silylthiazole **1a** appeared to be faster than that of the silyloxazole **1b**.[9] Some of the adducts **7** - **11** were isolated in modest yields but all these compounds were deacylated to the corresponding azadiaryls **12** - **16** in good yields. Therefore the overall process appears to be a convenient method for the introduction of the thiazol-2-yl and oxazol-2-yl nuclei in nitrogen heterocycles. This enlarges the scope of the 2-silylazoles **1a** and **1b** as stable synthetic equivalents of the C_2 anion of thiazole and oxazole respectively. In fact it is well known that lithium oxazole prefers to react with electrophiles in the form of its open-chain isomer, the α-isocyano enolate;[7] moreover we have observed that

TABLE 1. Reaction of 2-Silylazoles 1a and 1b with Nitrogen Heterocycles 2 - 6 *via* their *N*-Ethoxycarbonyl Salts.

Compound	Reagent	Time (h)	Adduct[a] (yield %)	Product[a] (yield %)	m.p. (°C)
 2	1a	1	7a(56) 	12a(95) 	100-102
	1b	3	 7b(35)	 12b(77)[b]	86-88
 3	1a	24	8a(26) 	13a(70) 	145-148
	1b	24	 8b(35)	 13b(66)	88-90
 4	1a	2	9a(42) 	14a(53) 	62-63
	1b	5	 9b(18)	 14b(72)	-
 5	1a	3	10a(25) 	15a(55) 	112-113
	1b	5	 10b(43)	 15b(44)	106-109
 6	1a	1	11a(70) 	16a(94) 	73-75
	1b	1	 11b(57)	 16b(98)	62-66

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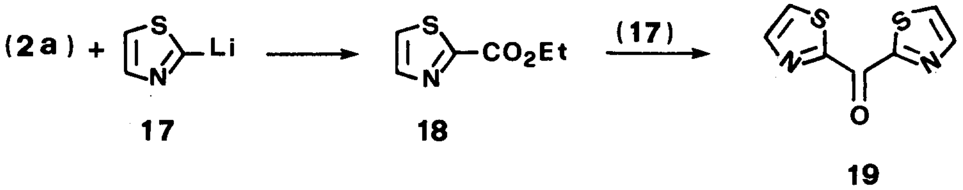
[a] Th = 1,3-thiazol-2-yl; Ox = 4-methyl-1,3-oxazol-2-yl. All adducts 7 - 11 and their oxidation products 12 - 16 gave satisfactory elemental analyses and consistent spectroscopic data (IR, NMR, MS). [b] Obtained at r. t. (5h).

lithium thiazole (17) reacts with N-ethoxycarbonylthiazolium chloride (2a) to give 2,2'-dithiazolylketone (19)[11] probably via ethyl thiazol-2-yl-carboxylate (18) formed by attack at the carbonyl carbon instead at C_2 of 2a.



References and Notes

1. For selected references see: B. W. Bycroft, and M. S. Gowland, J. Chem. Soc. Chem. Commun., 256 (1978). Y. Aoyagi, K. Katano, H. Suguna, J. Primeau, Li-Ho Chang, and S. M. Hecht, J. Am. Chem. Soc., 104, 5537 (1982). C. M. Ireland, A. R. Durso Jr., R. A. Newman, and M. P. Hacker, J. Org. Chem., 47, 1807 (1982). S. Halazy, and P. Magnus, Tetrahedron Lett., 25, 1421 (1984).
2. G. Vernin, M. A. Lebreton, H. J. M. Dou, and J. Metzger, Tetrahedron, 30, 4171 (1974).
3. T. Rinderspacher, and B. Prijs, Helv. Chim. Acta, 43, 1522 (1960).
4. A. Dondoni, T. Dall'Occo, G. Fantin, M. Fogagnolo, and A. Medici, preceding paper.
5. K. Akiba, K. Araki, M. Nakatani, and M. Wada, Tetrahedron Lett., 22, 4961 (1981). K. Akiba, Y. Iseki, and M. Wada, ibid., 23, 429 (1982). K. Akiba, Y. Nishihara, and M. Wada, ibid., 24, 5269 (1983). D. L. Comins, ibid., 24, 2807 (1983). D. L. Comins, and N. B. Mantlo, ibid., 24, 3683 (1983).
6. a) A. Medici, P. Pedrini, and A. Dondoni, J. Chem. Soc. Chem. Commun., 655 (1981). b) A. Medici, G. Fantin, M. Fogagnolo, ans A. Dondoni, Tetrahedron Lett., 24, 2901 (1983).
7. A. Dondoni, T. Dall'Occo, G. Fantin, M. Fogagnolo, A. Medici, and P. Pedrini, J. Chem. Soc. Chem. Commun., 258 (1984).
8. Another nucleophile which in principle can attack the quaternary salt of 1a to give 7a is the N-ethoxycarbonylthiazolium ylide (see ref. 6b).
9. A ratio 11a : 11b of ca. 10 was obtained after 15 min. reaction, on treating an equimolar mixture of 1a and 1b (2 mmol.) with isoquinoline (40 mmol.)and ethylchloroformate (10 mmol.) in methylene dichloride (20 mL, 0°C).
10. R. Schroder, U. Schollkopf, E. Blume, and I. Hoppe, Justus Liebigs Ann. Chem., 533 (1975).
11. 19:(yield 18%); m.p. 140°-141°C (dec.) (from n-hexane); IR (KBr) 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.87 (d, 2H, J = 3 Hz), 8.27 (d, 2H, J = 3 Hz).

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