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SHORT COMMUNICATIONS

Synthesis of 2-Substituted 5-Trifluoromethyl-1,3,4-oxadiazoles

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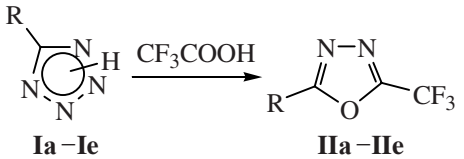
5-Substituted tetrazoles are known to be converted into 1,3,4-oxadiazoles by treating with acid anhydrides at 100–120°C [1]. The reaction is presumed to proceed through acylation of the tetrazole ring followed by thermolysis of the arising N-acyltetrazole with nitrogen elimination and the formation of an oxadiazole ring. However the fairly stringent reaction conditions result at the use of labile tetrazoles in a low yield of target products and even in a complete tarring of the initial and final compounds. We established that the efficiency of the reaction is essentially governed by the nature of the acylating agent. For instance, the employment of trifluoroacetic anhydride permits performing complete conversion of 5-substituted tetrazoles into the corresponding 2-substituted 5-trifluoromethyl-1,3,4-oxadiazoles at 20–25°C. The reaction occurred with a vigorous nitrogen evolution and without tarring. Inasmuch as the reaction proceeds at low temperature, apparently it should not be regarded as thermolysis. As expected, the trifluoroacetic anhydride does not react with unsubstituted tetrazole, and the conversion of 5-aminotetrazole stopped at the stage of amino group acylation. Yet the use of this anhydride made it possible to carry out the reaction with 5-(2-dimethylaminoethyl)tetrazole impossible at the high-temperature synthesis.



Ia–**Ie** **IIa**–**IIe**

R = $Me_2NCH_2CH_2$ (**a**), Ph (**b**), CH_2=CH (**c**), EtOOC (**d**), 2-(5-Ph-tetrazol-2-yl)ethyl (**Ie**), 2-(5-CF_3-1,3,4-oxadiazol-2-yl)ethyl (**IIe**).

2-(2-Dimethylaminoethyl)-5-trifluoromethyl-1,3,4-oxadiazole (IIa). To a dispersion of 1.0 g (7 mmol) 5-(2-dimethylaminoethyl)tetrazole (**Ia**) in 10 ml of dichloromethane was added dropwise at room temperature while stirring a solution of 1.9 g (9 mmol) of trifluoroacetic anhydride in 2 ml of dichloromethane. The reaction mixture homogenized while not getting colored. On completing the addition of the anhydride and at the end of nitrogen evolution the reaction mixture was neutralized with a saturated solution of sodium hydrogen carbonate till pH 9. The water layer was extracted with ether (3×10 ml), the combined organic solution was dried with magnesium sulfate. The solvent was distilled off, and the residue was distilled in a vacuum. Yield 1.2 g (81%), bp 66°C (10 mm Hg), n_D^{20} 1.3990. ^{1}H NMR spectrum, δ, ppm: 1.5 s (6H, $2CH_3$), 2.6 t (2H, CH_2Ht), 3 t (2H, CH_2N). ^{13}C NMR spectrum, δ, ppm: 27.4 s (1C, $\underline{C}H_2$Ht), 47.9 s (2C, $2CH_3$), 58.9 s (C, CH_2N), 120.3 q (C, CF_3, *J* 267.2 Hz), 158.5 q (C^5, Ht, *J* 43.8 Hz), 172.2 s (C^2, Ht). Mass spectrum, *m*/*z* (I_{rel}, %): 209 (0.7) $[M]^+$, 165 (2.1), 95 (2.1), 69 (16.3), 58 (100), 42 (29.8). Found, %: C 40.16; H 4.34; N 20.02. $C_7H_{10}F_3N_3O$. Calculated, %: C 40.19; H 4.78; N 20.1. *M* 209.17.

5-Trifluoromethyl-2-phenyl-1,3,4-oxadiazole (IIb) was obtained in the same way from 1 g (6.8 mmol) of 5-phenyltetrazolea (**Ib**) and 1.7 g (8.0 mmol) of trifluoroacetic anhydride in 12 ml of dichloromethane. Yield 1.3 g (89%), mp 49–50°C (EtOH). ^{1}H NMR spectrum, δ, ppm: 7.6–8.1 m (Ph). ^{13}C NMR spectrum, δ, ppm: 154.1 q (C^5, Ht, *J* 43.6 Hz), 166.1 s (C^2, Ht), 116.4 q (C, CF_3, *J* 269.5 Hz), 122.1–133.3 m (6C, Ph). Mass spectrum, *m*/*z* (I_{rel}, %): 214 (56.7) $[M]^+$, 145 (64.7), 77 (100), 68 (43.5), 118 (3.3), 195 (3.5). Found, %: C 50.39; H 2.41; N 12.92. $C_9H_5F_3N_2O$. Calculated, %: C 50.47; H 2.34; N 13.08. *M* 214.15.

2-Vinyl-5-trifluoromethyl-1,3,4-oxadiazole (IIc) was obtained in the same way from 5 g (50 mmol) of 5-vinyltetrazole (**Ic**) and 11.6 g (55 mmol) of trifluoroacetic anhydride in 115 ml of dichloromethane. Yield 6.5 g (76%), bp 40°C (15 mm Hg), n_D^{20} 1.3945, d_4^{20} 1.32. ^{1}H NMR spectrum, δ, ppm: 6.92 (1H^a, =CH), 6.45 (1H^b, =CH_2), 6.10 (1H^C, =CH_2). ^{13}C NMR spectrum, δ, ppm: 118.74 (C$^\alpha$, C=C), 128.84 (C$^\beta$, C=C), 165.26 s (C^2, Ht), 154 q (C^5, Ht,), 116.51 q (C, CF_3). Mass spectrum, *m/z* (I_{rel}, %): 164 (27.9) [*M*]$^+$, 145 (2.3), 95 (79), 69 (100). Found, %: C 36.54; H 1.45; N 17.05. $C_5H_3F_3N_2O$. Calculated, %: C 36.59; H 1.83; N 17.07. *M* 164.09.

Ethyl (5-trifluoromethyl-1,3,4-oxadiazol-2-yl)acetate (IId) was obtained in the same way from 1 g (6.4 mmol) of ethyl 5-tetrazolylacetate (**Id**) and 1.4 g (8.3 mmol) of trifluoroacetic anhydride in 15 ml of dichloromethane. Yield 0.87 g (61%), bp 91–92°C (7 mm Hg), n_D^{24} 1.3952. ^{1}H NMR spectrum, δ, ppm: 0.74 t (3H, C$\underline{H}_3$CH$_2$), 3.7 q (2H, C$\underline{H}_2$CH$_3$), 3.9 s (2H, CH_2COO). ^{13}C NMR spectrum, δ, ppm: 14.3 s (C$\underline{H}_2$COO), 32.6 s (C$\underline{H}_3$CH$_2$), 63.2 s (C$\underline{H}_2$CH$_3$), 117.6 q (CF_3, *J* 279.4 Hz), 156.9 q (C^5, Ht, *J* 45.1 Hz), 164.9 C (COO), 167.1 C (C^2, Ht). Mass spectrum, *m/z* (I_{rel}, %): 224 (0.5) [*M*]$^+$, 205 (2.3), 179 (28), 152 (85.6), 69 (100), 42 (46.5). Found, %: C 37.41; H 2.97; N 12.07. $C_7H_7F_3N_2O_3$. Calculated, %: C 37.5; H 3.13; N 12.5. *M* 224.14.

1,2-Bis(5-trifluoromethyl-1,3,4-oxadiazol-2-yl)ethane (IIe) was obtained from 1 g (4.1 mmol) of 1-(5-phenyltetrazol-2-yl)-2-(tetrazol-5-yl)ethane (**Ie**) and 1 g (5 mmol) of trifluoroacetic anhydride in 15 ml of dichloromethane. Yield 1.1 g (60%), mp 100–101°C (EtOH). ^{1}H NMR spectrum, δ, ppm: 3.0 (CH_2). ^{13}C NMR spectrum, δ, ppm: 116.1 q (C, CF_3, *J* 270.4 Hz), 21.3 s (C, CH_2), 154.1 q (C^5, Ht, *J* 43.8 Hz), 167.7 s (C^2, Ht). Mass spectrum, *m/z* (I_{rel}, %): 302 (65.1) [*M*]$^+$, 283 (47), 164 (4.2), 137 (0.9), 68 (1.9), 233 (100). Found, %: C 31.52; H 1.27; N 18.42. $C_8H_4F_6N_4O_2$. Calculated, %: C 31.79; H 1.32; N 18.54. *M* 302.14.

NMR spectra were registered on a spectrometer Varian VXR-500S at operating frequencies 500 MHz (^{1}H) and 126 MHz (^{13}C) in acetone-d_6 and DMSO-d_6. Mass spectra were measured on an Agilent 5973 N GC-6890 instrument, injector temperature 250°C, column HP-Ultra.

REFERENCES

1. Osipova, T.F., Koldobskii, G.I., and Ostrovskii, V.A., *Zh. Org. Khim.*, 1984, vol. 20, p. 2468