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SYNTHESIS OF 3-R-6,7,8,9,10,11-HEXAHYDRO-5H-5,9:7,11-DIMETHANO[1,2,4]TRIAZOLO[4,3-*a*]AZOCINES

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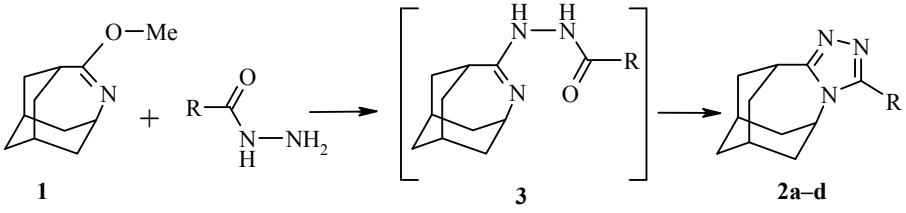
Keywords: 3-R-6,7,8,9,10,11-hexahydro-5H-5,9:7,11-dimethano[1,2,4]triazolo[4,3-*a*]azocines, lactim ethers, 5-methoxy-4-azatricyclo[4,3,1,$1^{3,8}$]undec-4-ene.

Lactim ethers of monocyclic lactams react with hydrazides to give amidrazones but 1,2,4-triazoles only upon prolonged heating [1, 2]. We have found that treatment of 5-methoxy-4-azatricyclo[4.3.1.$1^{3,8}$]undec-4-ene (**1**) with acid hydrazides gives the substituted triazoles **2a-d**, even at room temperature. The ease of the cyclization can be due to the lowering of resonance delocalization of the unshared electron pair of the endocyclic nitrogen atom in the intermediately formed amidrazone **3**. This is confirmed by the ability of 4-azatricycl[4.3.1.$1^{3,8}$]undecan-5-one to form a stable hydrochloride [3].



1 **3** **2a–d**

a R = CF_3, **b** R = Ph, **c** R = 3-Py, **d** R = Ad

IR spectra were taken on a Shimadzu FTIR-8400S spectrometer for KBr tablets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer (400 and 100 MHz respectively) using $CDCl_3$. Mass spectra were obtained on a Finnigan Trace DSQ chromato-mass spectrometer with an ionization energy of 70 eV. Elemental analysis was carried out on a Euro Vector EA-3000 automatic CHNS analyzer.

5-Methoxy-4-azatricyclo[4.3.1.$1^{3,8}$]undec-4-ene (1) was prepared by a known method [4].

3-Trifluoromethyl-6,7,8,9,10,11-hexahydro-5H-5,9:7,11-dimethano[1,2,4]triazolo[4,3-*a*]azocine (2a). A mixture of compound **1** (1 g, 5.6 mmol) and trifluoroacetic acid hydrazide (5.7 mmol) in methanol (6 ml) was held for 1 day at room temperature. The precipitate formed was filtered off and recrystallized from *o*-xylene. Yield 0.63 g (44%) as white crystals with mp 136-138ºC. IR spectrum, ν, cm^{-1}: 2923, 1639, 1504, 1442, 1353, 1245, 1184, 1141, 1118, 1002. ^{1}H NMR spectrum, δ, ppm: 4.58-4.59 (1H, m, H-1); 3.62-3.63 (1H, m,

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H-7); 1.75-2.28 (12H, m, H-8 to H-14). Mass spectrum, *m/z* (I_{rel}, %): 257 $[M]^+$ (100), 214 (14), 188 (25), 164 (33), 91 (14), 79 (15), 53 (11). Found, %: C 56.15; H 5.41; N 16.38. $C_{12}H_{14}F_3N_3$. Calculated, %: C 56.03; H 5.49; N 16.33.

3-Phenyl-6,7,8,9,10,11-hexahydro-5H-5,9:7,11-dimethano[1,2,4]triazolo[4,3-*a*]azocine (2b) was prepared similarly to compound **2a**. Yield 40% as white crystals with mp 178-181ºC (toluene). IR spectrum, ν, cm^{-1}: 2920, 1639, 1477, 1446, 1253, 1215, 1091, 771, 698. ^{1}H NMR spectrum, δ, ppm: 7.48-7.56 (5H, m, Ph); 4.47-4.48 (1H, m, H-1); 3.61-3.63; (1H, m, H-7); 1.79-2.24 (12H, m, H-8 to H-14). Mass spectrum, *m/z* (I_{rel}, %): 265 $[M]^+$ (100), 196 (12), 172 (34), 159 (7), 104 (12), 91 (13), 77 (23). Found, %: C 76.89; H 7.31; N 15.80. $C_{17}H_{19}N_3$. Calculated, %: C 76.95; H 7.22; N 15.84.

3-(3-Pyridyl)-6,7,8,9,10,11-hexahydro-5H-5,9:7,11-dimethano[1,2,4]triazolo[4,3-*a*]azocine (2c) was prepared similarly to compound **2a**. Yield 22% as white crystals with mp 172-174ºC (acetonitrile). IR spectrum, ν, cm^{-1}: 2916, 1593, 1469, 1442, 1384, 1253, 1087, 817, 717. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.62-8.66 (2H, m, H-2",6"); 7.81-7.84 (1H, dt, ^1J = 7.5, ^2J = 1.8, H-4"); 7.37 (1H, dd, ^1J = 7.5, ^2J = 5.5, H-5"); 4.39-4.41 (1H, m, H-1); 3.61-3.63 (1H, m, H-7); 1.70-2.25 (12H, m, H-8 to H-14). ^{13}C NMR spectrum, δ, ppm: 160.3, 151.1, 150.8, 149.4, 136.8, 124.0, 123.8, 49.5, 35.0, 34.5, 32.7, 30.1, 26.7. Mass spectrum, m/z (I_{rel}, %): 265 $[M]^+$ (100), 173 (46), 105 (19), 93 (20), 77 (23). Found, %: C 72.23; H 6.92; N 20.85. $C_{16}H_{18}N_4$. Calculated, %: C 72.15; H 6.81; N 21.04

3-(1-Adamantyl)-6,7,8,9,10,11-hexahydro-5H-5,9:7,11-dimethano[1,2,4]triazolo[4,3-*a*]azocine (2d) was prepared similarly to compound **2a**. Yield 44% as white crystals with mp 313-314ºC (*o*-xylene). IR spectrum, ν, cm^{-1}: 2904, 1635, 1596, 1512, 1446, 1373, 1253, 1103. ^{1}H NMR spectrum, δ, ppm: 4.82-4.83 (1H, m, H-1); 3.54-3.55 (1H, m, H-7); 1.76-2.26 (27H, m, H-8 to H-14, H-Ad). ^{13}C NMR spectrum, δ, ppm: 160.5, 142.5, 50.0, 36.5, 35.2, 34.6, 32.6, 30.7, 29.6, 27.0, 26.6. Mass spectrum, *m/z* (I_{rel}, %): 324 $[M]^+$ (100), 267 (28), 228 (13), 91 (10), 79 (13). Found, %: C 78.08; H 8.99; N 12.93. $C_{21}H_{29}N_3$. Calculated, %: C 77.97; H 9.04; N 12.99.

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