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Synthesis of 4-benzoyl-1,2,6-trialkyl-1,2,4,6-tetrazepane-5-thiones by the interaction of 1,2-dialkyldiaziridines with benzoyl isothiocyanate in ionic liquids

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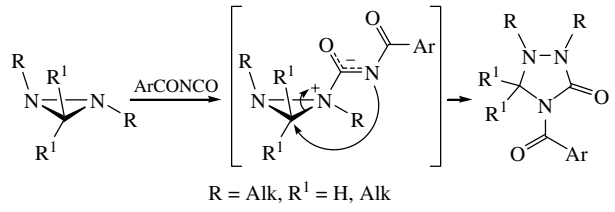
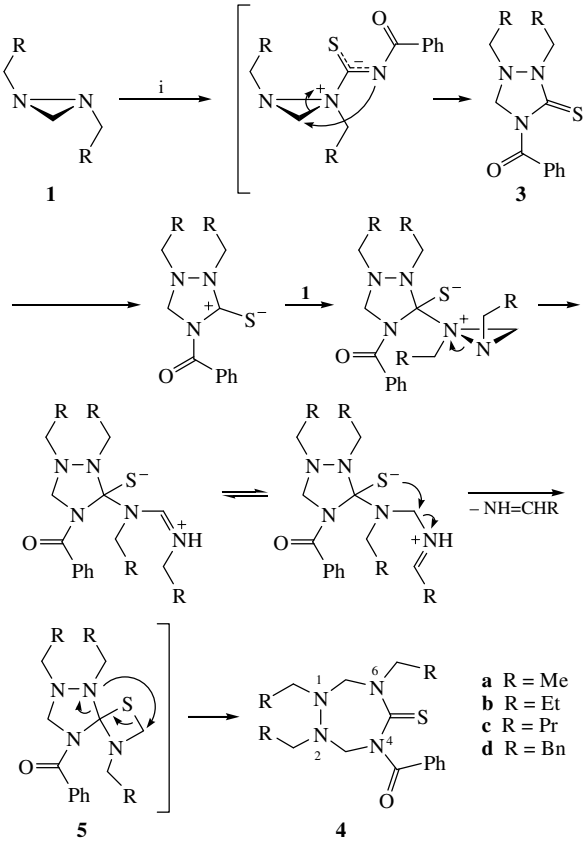
An interaction of 1,2-dialkyldiaziridines with benzoyl isothiocyanate in the room temperature ionic liquids [emim][BF_4] and [emim][PF_6] unexpectedly resulted in previously unknown 4-benzoyl-1,2,6-trialkyl-1,2,4,6-tetrazepane-5-thiones; the reaction was carried out by the cleavage of the C–N and of the N–N bonds of the diaziridine ring.

The transformation of diaziridine rings under the action of electrophilic reagents is an approach to the synthesis of nitrogen-containing heterocyclic systems.[1–3] Recently, we have shown that the diaziridine ring was cleaved on the N–N bond in the reaction of 1,2-dialkyldiaziridines with ketenes, resulting in different compounds containing the N–C–N fragment (derivatives of imidazolidin-4-one, β-lactames and 3,5-diacyl-3,5-diazahept-1-enes).[4–6] At heating, the interaction of 1,2-di-, 1,2,3-tri- and 1,2,3,3-tetraalkyldiaziridines with aroylisocyanates afforded 4-aroyl-1,2,4-triazolidin-3-one derivatives by cleavage of the C–N bond followed by cyclization of the formed zwitter-ionic intermediate (Scheme 1).[7,8]



Scheme 1

In this work, we studied the behaviour of 1,2-dialkyldiaziridines **1a–d** in the reaction with benzoylisothiocyanate **2** with the aim to synthesise 4-benzoyl-1,2,4-triazolidine-3-thiones **3**. The interaction of compounds **1** and **2** was performed both under the conditions used for the preparation of 4-aroyl-1,2,4-triazolidin-3-ones (stirring at –20 °C followed by heating in hexane) and in other solvents (chloroform, ethyl acetate and dioxane) at different temperatures (from –30 to 100 °C). However, in all cases the reaction proceeded ambiguously, with the formation of an unseparable mixture of seven to eight compounds (TLC data). Only the use of the room temperature ionic liquids [emim][BF_4] and [emim][PF_6] allowed us to perform this interaction. However, instead of the expected 4-benzoyl-1,2,4-triazolidine-3-thiones **3**, previously unknown 4-benzoyl-1,2,6-trialkyl-1,2,4,6-tetrazepane-5-thiones **4a–d** were isolated as main products (35–51%). Although fused cyclic systems containing seven-membered heterocycles with 1,2,4,6-positions of nitrogen atoms have been described in the literature,[9,10] monocyclic saturated systems **4** were synthesised for the first time.



Scheme 2 *Reagents and conditions:* i, PhCONCS **2**, [emim][BF_4] or [emim][PF_6], 20 °C, 24 h.

The assumed reaction mechanism is presented in Scheme 2. The first step of this reaction (in analogy to the interaction of 1,2-dialkyldiaziridines **1** with aroylisocyanates) is likely the formation of 4-benzoyl-1,2,4-triazolidine-3-thiones **3**. However, the reaction does not stop at this step. Evidently, the C=S unit in compounds **3** is strongly polarised due to the influence of the ionic liquids and gains capablility to interact with the second

molecule of 1,2-dialkyldiaziridine **1**, resulting in spiro compounds **5**, which then rearrange into 4-benzoyl-1,2,6-trialkyl-1,2,4,6-tetrazepane-5-thiones **4a–d** (Scheme 2). The rearrangement of similar spiro compounds into larger heterocycles is reported in the literature.[11] It is interesting to note that the first reaction step is carried out by diaziridine ring opening on the C–N bond, yet the second molecule of diaziridine **1** is built into compound **3** through the N–N bond cleavage.

The structure of the synthesised compounds **4a–d**† was established by the overall data of elemental analysis, spectral characteristics and X-ray diffraction studies of compound **4a**.

† ^{1}H and ^{13}C NMR spectra were recorded on Bruker AM-300 (300 MHz for ^{1}H and 75.5 MHz for ^{13}C) and Bruker RDX-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometers ($CDCl_3$ was used as an internal standard). Infrared spectra were determined in KBr pellets on a UR-20 spectrometer. Mass spectra were measured on a Finnigan MAT INCOS-50 instrument. TLC was carried out on ALUGRAM SIL G/UV254 plates, ALDRICH. Isolation of new compounds was performed on Kieselgel 60 F_{254} (Merck). Melting points were measured on a Gallenkamp instrument (Sanyo). Ionic liquids [emim][BF_4] and [emim][PF_6] were amiably provided by Merck KGaA. 1,2-Dialkyldiaziridines were synthesised according to the published procedure.[12]

4-Benzoyl-1,2,6-triethyl-1,2,4,6-tetrazepane-5-thione **4a**: yield 51%, white solid, mp 122–123 °C, R_f 0.33 (eluent, hexane–ethyl acetate, 10:1). ^{1}H NMR ($CDCl_3$) δ: 1.07 (t, 3H, Me, ^3J 6.87 Hz), 1.14 (t, 3H, Me, ^3J 7.33 Hz), 1.27 (t, 3H, Me, ^3J 6.87 Hz), 2.66 and 2.71 [2m, 2H, N(1)CH_2Me], 2.79 and 2.86 [2m, 2H, N(2)CH_2Me], 2.44 and 4.16 [2m, 2H, N(6)CH_2Me], 4.32 and 5.58 [2d, 2H, C(3)H_2, ^2J –14.21 Hz], 4.39 and 5.53 [2d, 2H, C(7)H_2, ^2J –14.21 Hz], 7.35 (t, 2H, Ph, ^3J 7.79 Hz), 7.44 (t, 1H, Ph, ^3J 7.33 Hz), 7.52 (d, 2H, Ph, ^3J 7.33 Hz). ^{13}C NMR ($CDCl_3$) δ: 11.37, 12.47 and 12.85 (Me), 44.68, 45.54 and 49.88 (CH_2Me), 59.46 and 67.70 [CH_2(cycl)], 128.09, 128.16, 131.22 [CH(Ph)], 135.84 [C(Ph)], 171.31 (CO), 189.13 (CS). IR (ν/cm^{-1}): 632, 668, 692, 732, 780, 792, 824, 1016, 1076, 1092, 1104, 1128, 1144, 1200, 1224, 1252, 1280, 1304, 1336, 1352, 1376, 1428, 1496, 1580, 1664, 2840, 2924, 2964, 3056. MS, *m/z*: 321 (M^+ + 1).

4-Benzoyl-1,2,6-tripropyl-1,2,4,6-tetrazepane-5-thione **4b**: yield 35%, white solid, mp 67–69 °C, R_f 0.48 (eluent, hexane–ethyl acetate, 10:1). ^{1}H NMR ($CDCl_3$) δ: 0.87 (t, 3H, Me, ^3J 6.87 Hz), 0.94 (t, 6H, 2Me, ^3J 7.33 Hz), 1.50–1.65 [m, 4H, N(1)CH_2CH_2Me and N(2)CH_2CH_2Me], 1.72 and 1.79 [2m, 2H, N(3)CH_2CH_2Me], 2.54 and 2.63 [2m, 2H, N(1)C$H_2$$CH_2$], 2.72 and 2.81 [2m, 2H, N(2)C$H_2$$CH_2$], 3.24 and 4.12 [2m, 2H, N(6)C$H_2$$CH_2$], 4.28 and 5.51 [2d, 2H, C(3)H_2, ^2J –14.21 Hz], 4.33 and 5.62 [2d, 2H, C(7)H_2, ^2J –14.21 Hz], 7.36 (t, 2H, ^3J 7.33 Hz), 7.44 (t, 1H, Ph, ^3J 7.33 Hz), 7.52 (d, 2H, Ph, ^3J 7.33 Hz). ^{13}C NMR ($CDCl_3$) δ: 11.25 and 11.73 (Me), 19.68, 20.25 and 20.47 (CH_2Me), 52.47, 53.41 and 56.88 (N$CH_2$$CH_2$), 59.19 and 68.36 [$CH_2$(cycl)], 128.06, 128.10, 131.19 [CH(Ph)], 135.87 [C(Ph)], 171.30 (CO), 189.23 (CS). IR (ν/cm^{-1}): 636, 692, 740, 796, 944, 1016, 1080, 1104, 1144, 1192, 1220, 1236, 1264, 1292, 1304, 1328, 1348, 1384, 1420, 1448, 1488, 1584, 1604, 1672, 2872, 2932, 2960, 3060. MS, *m/z*: 362 (M^+).

4-Benzoyl-1,2,6-tributyl-1,2,4,6-tetrazepane-5-thione **4c**: yield 43%, white solid, mp 75–76 °C, R_f 0.56 (eluent, hexane–ethyl acetate, 10:1). ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, 3H, Me, ^3J 7.33 Hz), 0.95 (t, 6H, 2Me, ^3J 7.33 Hz), 1.38–1.46 (m, 6H, 3CH_2CH_2Me), 1.47–1.60 [m, 4H, N(1)-CH_2CH_2Me and N(2)CH_2CH_2Me], 1.68 and 1.76 [2m, 2H N(3)CH_2-CH_2Me], 2.59 and 2.68 [2m, 2H, N(1)C$H_2$$CH_2$], 2.74 and 2.83 [2m, 2H, N(2)C$H_2$$CH_2$], 3.25 and 4.14 [2m, 2H, N(6)C$H_2$$CH_2$], 4.25 and 5.51 [2d, 2H, C(3)H_2, ^2J –14.20 Hz], 5.30 and 5.62 [2d, 2H, C(7)H_2, ^2J –14.21 Hz], 7.36 (t, 2H, Ph, ^3J 7.33 Hz), 7.53 (t, 1H, Ph, ^3J 7.33 Hz), 7.52 (d, 2H, ^3J 7.33 Hz). ^{13}C NMR ($CDCl_3$) δ: 13.71, 13.91 and 13.95 (Me), 20.18, 20.28 and 20.36 (CH_2Me), 28.34, 29.15 and 29.35 (NCH_2CH_2), 50.31, 51.22 and 55.16 (N$CH_2$$CH_2$), 59.12 and 68.23 [$CH_2$(cycl.)], 128.05, 128.12, 131.19 [CH(Ph)], 135.90 [C(Ph)], 171.28 (CO), 189.16 (CS). IR (ν/cm^{-1}): 644, 692, 752, 796, 824, 920, 948, 1020, 1028, 1088, 1100, 1152, 1180, 1212, 1224, 1248, 1264, 1292, 1336, 1352, 1368, 1424, 1484, 1560, 1584, 1600, 1668, 2860, 2872, 2932, 2956. MS, *m/z*: 405 (M^+ + 1).

4-Benzoyl-1,2,6-tris(2-phenylethyl)-1,2,4,6-tetrazepane-5-thione **4d**: yield 31%, white solid, mp 85–87 °C, R_f 0.36 (eluent, hexane–ethyl acetate, 10:1). ^{1}H NMR ($CDCl_3$) δ: 2.63–2.97 [m, 10H, CH_2Ph, N(1)-C$H_2$$CH_2$Ph and N(2)C$H_2$$CH_2$Ph], 3.02 and 3.94 [2m, 2H, N(6)C$H_2$$CH_2$], 3.96 and 5.37 [2d, 2H, C(3)H_2, ^2J –14.21 Hz], 4.37 and 5.66 [2d, 2H, C(7)H_2, ^2J –14.21 Hz], 7.12–7.58 (m, 20H, 4Ph). ^{13}C NMR ($CDCl_3$) δ: 33.61, 33.85 and 34.26 (CH_2Ph), 52.19, 53.11 and 57.32 (N$CH_2$$CH_2$), 58.99 and 69.06 [$CH_2$(cycl.)], 125.99, 126.19, 126.66, 126.84, 127.33, 128.10, 128.23, 128.38, 128.64, 128.67, 128.73, 129.00, 131.34, 131.68, 133.40, 135.75, 138.09, 138.18, 139.59, 139.64 (Ph), 171.45 (CO), 189.38 (CS). MS, *m/z*: 549 (M^+ + 1).

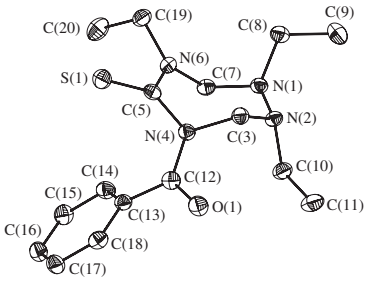


Figure 1 The general view of **4a** in the representation of atoms by thermal ellipsoids (p = 50%). Selected bond lengths (Å): S(1)–C(5) 1.656(1), N(1)–N(2) 1.437(1), N(1)–C(7) 1.437(2), N(1)–C(8) 1.461(2), N(2)–C(3) 1.442(2), N(2)–C(10) 1.470(2), C(3)–N(4) 1.485(2), N(4)–C(5) 1.420(2), N(4)–C(12) 1.396(2), C(5)–N(6) 1.340(2), N(6)–C(19) 1.477(2), N(6)–C(7) 1.493(2); bond angles (°): C(7)–N(1)–N(2) 115.7(1), C(7)–N(1)–C(8) 114.5(1), N(2)–N(1)–C(8) 111.3(1), C(3)–N(2)–N(1) 113.3(1), C(3)–N(2)–C(10) 114.6(1), N(1)–N(2)–C(10) 110.0(1), N(2)–C(3)–N(4) 115.4(1), C(12)–N(4)–C(5) 123.5(1), C(12)–N(4)–C(3) 119.1(1), C(5)–N(4)–C(3) 115.2(1), N(6)–C(5)–N(4) 111.5(1), N(6)–C(5)–S(1) 126.3(1), N(4)–C(5)–S(1) 121.9(1), C(5)–N(6)–C(19) 121.1(1), C(5)–N(6)–C(7) 120.7(1), C(19)–N(6)–C(7) 117.1(1).

According to X-ray diffraction analysis,‡ in **4a** the 1,2,4,6-tetrazepane-3-thione ring is characterised by a distorted chair conformation: the chair base is formed by C(3), N(4), C(7) and N(1) atoms (Figure 1). The N(1) and N(2) atoms are pyramidal [the bond angles are 341.5(1) and 337.9(2)°]. The ethyl groups at N(1) and N(2) are characterised by *trans*-disposition in respect to the chair base with the torsion angle C(8)N(1)N(2)C(10) equal to 144.7°.

Alternatively the atoms N(4) and N(6) are characterised by a flattened pyramidal configuration, the bond angles being 357.9(1) and 358.9(1)°. The flattening of the atoms N(4) and N(6) clearly is a consequence of the conjugation with the C=O and the C=S groups, respectively, which is clearly reflected in the shortening of the corresponding N–C bonds. The dihedral angle between N(4)C(12)O(1) and N(4)C(5)N(6)S(1) planes is 24.7°.

Thus, the interaction of 1,2-dialkyldiaziridines **1** with benzoylisothiocyanate **2** was successful only in room temperature ionic liquids and the reaction products unexpectedly appeared to be previously unknown 4-benzoyl-1,2,6-trialkyl-1,2,4,6-tetrazepane-5-thiones **4a–d**.

Note that synthesised compounds **4a–d** have a rather high configuration stability. According to the ^{1}H NMR data the geminal protons at C(3) and C(7) carbon atoms exhibit as AB systems: coalescence does not occur till 80 °C (reflux in benzene).

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‡ *Crystallographic data for* **4a**: $C_{16}H_{24}N_4OS$, M = 320.45, monoclinic, space group $P2_1/c$, at 110 K: a = 8.3152(8) Å, b = 11.0009(11) Å and c = 9.145(2) Å, β = 93.538(5)°, V = 1720.3(3) Å^3, Z = 4 (Z' = 1), d_{calc} = = 1.237 g cm^{-3}, μ(MoKα) = 1.96 cm^{-1}, F(000) = 688. Intensities of 15426 reflections were measured with a Smart 1000 CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, 2θ < 60°] and 5003 independent reflections (R_{int} = 0.0545) were used in a further refinement. The structure was solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the isotropic approximation. The refinement converged to wR_2 = 0.0805 and GOF = 0.987 for all independent reflections [R_1 = 0.0422 was calculated against F for 2930 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using the SHELXTL PLUS 5.0.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 616741. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2006.

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