A new direction of ring expansion of 1,2-dialkyldiaziridines in the reactions with arylketenes

Alexander V. Shevtsov,*[a] Vera Yu. Petukhova,[a] Yurii A. Strelenko,[a] Konstantin A. Lyssenko,[b] Ivan V. Fedyanin and Nina N. Makhova[a]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 135 5328; e-mail: mnn@ioc.ac.ru*

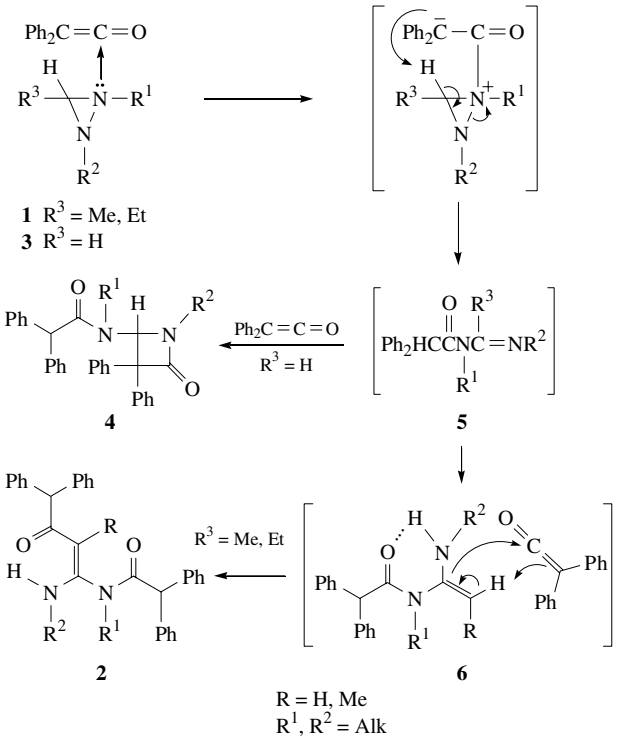
[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 135 5085; e-mail: kostya@xrlab.ineos.ac.ru*

10.1070/MC2003v013n05ABEH001844

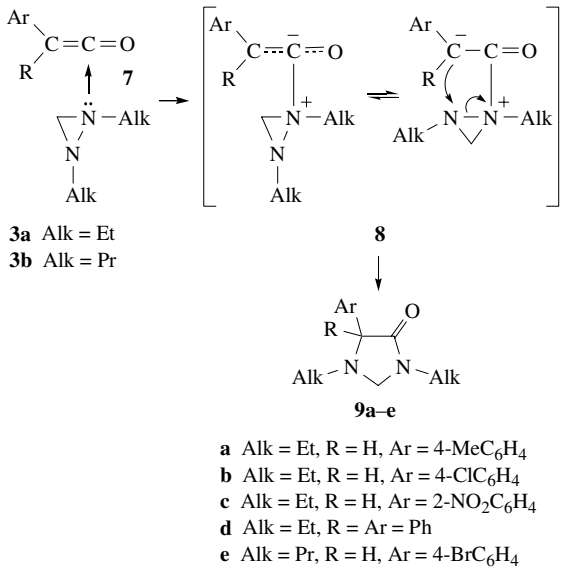
An interaction of 1,2-dialkyldiaziridines with arylketenes unexpectedly resulted in 5-aryl(5,5-diaryl)-*N*,*N*′-dialkylimidazolidin-4-ones.

Diaziridines, which are strained three-membered heterocycles, are prone to ring opening reactions with the formation of reactive intermediates.[1–4] These reactions can be initiated thermally,[5] photochemically[6] or by the action of various reagents. Diaziridine ring opening reactions under the action of electrophilic reagents are of particular interest;[7–11] in a number of cases, the mechanism of these reactions is unclear. In particular, it is of interest to study the interaction of diaziridines with ketenes.

Only few examples of diaziridine reactions with these reagents were reported.[10,11(a),(b)] The interaction of 1,2-unsubstituted diaziridines with bis(trifluoromethyl)ketene resulted in ring opening at the C–N bond with the formation of corresponding acyl hydrazones.[10] The reaction of diphenylketene with 1,2-dialkyl-substituted diaziridines in boiling benzene occurred with N–N bond cleavage and the formation of 1:2 adducts, whose structures were different depending on substitution at the carbon atom of the parent diaziridine. In the case of 3-CH_2R-substituted 1,2-dialkyldiaziridines **1**, acyclic product **2** is formed, whereas the reaction with 3-unsubstituted 1,2-dialkyldiaziridines **3** results in β-lactam derivatives **4**, which are potential biologically active compounds.[11(a)] An assumed reaction mechanism includes a nucleophilic attack of the diaziridine nitrogen atom to the central carbon atom of diphenylketene followed by detachment of the proton from the C(3) atom of the diaziridine ring and N–N bond cleavage to amidine-type intermediate **5**.



Scheme 1



Scheme 2 *Reagents and conditions*: $Ar(R)CH_2COCl$, TEA, diethyl ether, –30 °C, 2 h, then 20 °C, 15 h.

When R^3 = H, this intermediate adds a second diphenylketene molecule at the CH=N fragment with the formation of β-lactam **4**. When $R^3 = CH_2R$, the addition of the second ketene molecule occurs through aminal-type intermediate **6** and results in product **2** (Scheme 1).

In this work, we studied the reactions of 1,2-dialkyldiaziridines **3** with arylketenes in order to prepare new β-lactams **4**. 1,2-Diethyl- and 1,2-dipropyldiaziridines **3a**,**b** were taken as initial diaziridines. Arylketenes **7a–d** were generated *in situ* from arylacetic acid chlorides in the presence of TEA in dry diethyl ether at –30 °C in accordance with a standard procedure.[12] After the addition of the starting acyl chloride, the reaction mixture was allowed to stand at this temperature for 2 h and then at room temperature overnight. However, in place of expected β-lactams **4**, 1:1 adducts, 5-aryl-1,3-dialkylimidazolidin-4-ones **9a–e**,† in 40–65% yields were obtained regardless of acyl chloride:diaziridine molar ratios, which were varied from 1:2 to 2:1. Note that analogous product **9d** was obtained for diphenylacetic acid chloride. The structure of compounds was supported by a set of elemental analysis data and spectroscopic characteristics, and the structure of compound **9d** was found using X-ray diffraction analysis.

Evidently, the direction of reaction of 1,2-dialkyldiaziridines with arylketenes changed because of different process conditions. The formation of compounds **9** took place under mild temperature conditions, which are evidently insufficient for proton detachment from the carbon atom of the diaziridine ring and for the formation of intermediate **5**. Therefore, zwitterion **8** is transformed into imidazolidin-4-ones **9** (thermodynamically

controlled process) (Scheme 2). Komatsu *et al.*[11] (see Scheme 1) used previously prepared diphenylketene; this allowed them to use an elevated temperature favourable for proton detachment from the carbon atom of the diaziridine ring followed by the formation of adducts **2** and **4** (kinetically controlled process).

We found using X-ray diffraction analysis‡ that compound **9d** crystallises in centrosymmetrical space group $P2_1/n$. The conformation of the nitrogen-containing five-membered ring is an envelope with the N(4) atom projected out of the plane C(1)N(2)C(3)C(5) by 0.38 Å. The ethyl group at the N(4) atom occupies a pseudoequatorial position. The N(2) atom is flat with the sum of valence angles 359.5°. Note that the formally equivalent C(5)–C(10) and C(5)–C(16) bond lengths are somewhat different [1.531(4) and 1.517(4) Å, respectively]. This is likely due to the anomer interaction of the lone electron pair of the N(4) atom [$Lp_{N(4)}$] with the antibonding orbital of the C(5)–C(10) bond. The value of the pseudotorsion angle $Lp_{N(4)}$N(4)C(5)C(10) (155.2°) suggests the possibility of this stereoelectronic interaction.

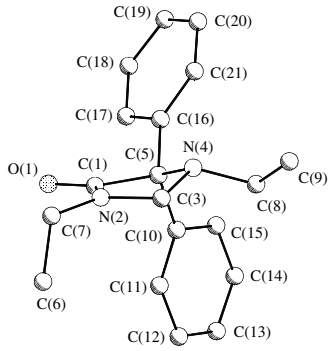


Figure 1 Molecular structure of compound **9d**. Selected bond lengths (Å) and valence angles (°): C(1)–O(1) 1.233(3), C(1)–N(2) 1.342(3), N(2)–C(3) 1.444(3), C(3)–N(4) 1.465(3), N(4)–C(5) 1.487(3), C(5)–C(16) 1.517(4), C(5)–C(10) 1.531(4), N(2)–C(7) 1.472(3), N(4)–C(8) 1.469(3); O(1)–C(1)–N(2) 126.2(2), C(1)–N(2)–C(3) 113.1(2), N(2)–C(3)–N(4) 103.5(2), C(3)–N(4)–C(5) 106.9(2), N(4)–C(5)–C(1) 101.3(2), C(5)–C(1)–N(2) 107.6(2), C(3)–N(4)–C(8) 112.8(2), N(4)–C(5)–C(16) 111.1(2).

An analysis of the crystal packing demonstrated that all intermolecular contacts correspond to ordinary van der Waals interactions.

Thus, a study of the interaction of 1,2-dialkyldiaziridines with arylketenes in diethyl ether at –30 °C allowed us to find a new unexpected direction of ring expansion of 1,2-dialkyldiaziridines with the formation of 5-aryl(5,5-diaryl)-1,3-dialkylimidazolidin-4-ones in 40–65% yields. Note that this reaction is a new, simple, and general way to the production of N-alkyl-substituted imidazolidin-4-ones; the known methods of their synthesis are based on multistage processes.[13,14]

References

1 E. Schmitz, *Adv. Heterocycl. Chem*., 1979, **24**, 63.
2 E. Schmitz, in *Comprehensive Heterocycl. Chem*., ed. W. Lwowski, Pergamon Press, Oxford, 1984, **7** (5), pp. 195–236.
3 H. W. Heine, in *Small Ring Heterocycles*, part 2, ed. A. Hassner, Wiley-Interscience, New York, 1983, ch. IV, pp. 547–629.
4 R. Kostyanovsky, R. Murugan and M. Sutharchanadevi, in *Comprehensive Heterocycl. Chem. II*, ed. A. Padwa, Pergamon Press, Oxford, 1996, **1A**, pp. 348–364.
5 A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov and R. R. Kostikov, *Synlett*., 2000, 1779.

† All new compounds exhibited satisfactory elemental analyses, and their structures were confirmed by IR, ^{1}H, ^{13}C NMR spectroscopy and mass spectrometry. IR spectra were measured on a UR-20 spectrometer in thin films of pure substances; ^{1}H and ^{13}C NMR spectra were recorded on Bruker WM-250 (230 MHz) and Bruker AM-300 (75.5 MHz) spectrometers, respectively ($CDCl_3$ was used as an internal standard). Mass spectra were measured on a Finnigan MAT INCOS-50 instrument. TLC was carried out on Silufol UV-254 plates. Isolation of new compounds was performed on Kieselgel 60 F_{254} (Merk).

1,3-Diethyl-5-(4-methylphenyl)imidazolidin-4-one **9a**: yield 40%, oil, R_f 0.4 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$) δ: 1.06 (t, 3H, $CONCH_2Me$, ^3J 7.5 Hz), 1.18 (t, 3H, $CHNCH_2Me$, ^3J 7.5 Hz), 2.33 (s, 3H, Me), 2.50 [m, 1H, CHNC*H*(H)Me], 2.76 [m, 1H, CONCH(*H*)Me], 3.41 (q, 2H, $CHNCH_2$Me, ^2J 13.8 Hz, ^3J 7.5 Hz), 3.93 [m, 2H, $NCH_a(H_b)$N and $COCH_cN$], 4.51 [d, 1H, $NCH_a(H_b)$N, ^2J 5.0 Hz], 7.12 and 7.30 (2d, both 2H, Ar, ^3J 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.83 ($CHNCH_2Me$), 12.86 ($CONCH_2Me$), 21.16 (Me), 36.23 ($CONCH_2$Me), 47.16 ($CHNCH_2$Me), 67.37 (NCH_2N), 69.89 (*C*HAr), 128.16, 129.13, 134.67, 137.58, (Ar), 171.15 (CO). IR (ν/cm^{-1}): 804, 844, 1020, 1116, 1160, 1192, 1308, 1344, 1452, 1516, 1652, 1712, 1764, 2932, 2972, 3325. MS, *m*/*z*: 232 (M^+).

5-(4-Chlorophenyl)-1,3-diethylimidazolidin-4-one **9b**: yield 57%, oil, R_f 0.45 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$) δ: 1.05 (t, 3H, $CONCH_2Me$, ^3J 7.3 Hz), 1.17 (t, 3H, $CHNCH_2Me$, ^3J 7.3 Hz), 2.52 [m, 1H, CHNC*H*(H)Me], 2.74 [m, 1H, CONCH(*H*)Me], 3.39 (q, 2H, $CHNCH_2$Me, ^2J 15.5 Hz, ^3J 7.3 Hz), 3.93 [dd, 1H, $NCH_a(H_b)$N, ^2J 4.4 Hz, $^4J_{H_bH_c}$ 2.2 Hz], 3.96 (s, 1H, $COCH_cN$), 4.50 [d, 1H, $NCH_a(H_b)$N, ^2J 4.4 Hz], 7.30 and 7.37 (2d, both 2H, Ar, ^3J 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.81 ($CHNCH_2Me$), 12.92 ($CONCH_2Me$), 36.27 ($CONCH_2$Me), 47.29 ($CHNCH_2$Me), 67.30 (NCH_2N), 69.35 (*C*HAr), 128.48, 129.41, 133.62, 136.35, (Ar), 170.34 (CO). IR (ν/cm^{-1}): 664, 764, 808, 844, 1016, 1092, 1216, 1312, 1456, 1492, 1576, 1716, 1772, 2936, 2976, 3300. MS, *m*/*z*: 253 (M^+).

1,3-Diethyl-5-(2-nitrophenyl)imidazolidin-4-one **9c**: yield 51%, oil, R_f 0.42 (eluent: hexane–ethyl acetate, 3:2). ^{1}H NMR ($CDCl_3$) δ: 1.06 (t, 3H, $CONCH_2Me$, ^3J 7.5 Hz), 1.19 (t, 3H, $CHNCH_2Me$, ^3J 7.5 Hz), 2.71 (m, 2H, $CONCH_2$Me), 3.40 (q, 2H, $CHNCH_2$Me, ^2J 14.5 Hz, ^3J 7.5 Hz), 4.00 [dd, 1H, $NCH_a(H_b)$N, ^2J 4.4 Hz, $^4J_{H_bH_c}$ 2.2 Hz], 4.06 (s, 1H, $COCH_cN$), 4.52 [d, 1H, $NCH_a(H_b)$N, ^2J 4.4 Hz], 7.39–7.72 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$) δ: 12.69 ($CHNCH_2Me$), 12.98 ($CONCH_2Me$), 36.35 ($CONCH_2$Me), 48.11 ($CHNCH_2$Me), 66.43 (NCH_2N), 67.61 (*C*HAr), 124.78, 128.61, 130.18, 132.50, 133.35, 150.13 (Ar), 169.13 (CO). IR (ν/cm^{-1}): 668, 728, 744, 788, 1160, 1256, 1308, 1356, 1456, 1528, 1648, 1708, 2820, 2936, 2976. MS, *m*/*z*: 263 (M^+).

1,3-Diethyl-5,5-diphenylimidazolidin-4-one **9d**: yield 65%, mp 127–128 °C (hexane), R_f 0.45 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$) δ: 1.15 (t, 3H, $CONCH_2Me$, ^3J 7.3 Hz), 1.30 (t, 3H, CPh_2N–CH_2Me, ^3J 7.3 Hz), 2.18 (q, 2H, CPh_2NCH_2Me, ^2J 14.5 Hz, ^3J 7.3 Hz), 3.57 (q, 2H, $CONCH_2$Me, ^2J 14.5 Hz, ^3J 7.3 Hz), 4.15 (s, 2H, NCH_2N), 7.26 (m, 10H, 2Ph). ^{13}C NMR ($CDCl_3$) δ: 13.05 (CPh_2NCH_2Me), 13.19 ($CONCH_2Me$), 36.61 ($CONCH_2$Me), 42.88 (CPh_2NCH_2Me), 65.12 (NCH_2N), 127.53, 127.88, 128.53, 128.73, 129.07, 139.15 (2Ph), 172.39 (CO). IR (ν/cm^{-1}): 632, 704, 756, 772, 904, 1052, 1172, 1196, 1312, 1448, 1700, 2764, 2820, 2950, 3056, 3400. MS, *m*/*z*: 294 (M^+).

5-(4-Bromophenyl)-1,3-dipropylimidazolidin-4-one **9e**: yield 46%, oil, R_f 0.47 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, 3H, $CONCH_2CH_2Me$, ^3J 7.5 Hz), 0.93 (t, 3H, $CHNCH_2CH_2Me$, ^3J 7.5 Hz), 1.47 (m, 2H, $CONCH_2CH_2$Me), 1.60 (m, 2H, $CHNCH_2CH_2$Me), 2.55 (m, 2H, $CHNCH_2CH_2$Me), 3.31 (t, 2H, $CONCH_2CH_2$Me, ^3J 7.5 Hz), 3.95 [d, 1H, $NCH_a(H_b)$N, ^2J 2.5 Hz], 3.98 (s, 1H, $COCH_cN$), 4.51 [d, 1H, $NCH_a(H_b)$N, ^2J 2.5 Hz], 7.33 and 7.49 (2d, both 2H, Ar, ^3J 10.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.29 ($CHNCH_2CH_2Me$), 11.64 ($CONCH_2CH_2Me$), 20.90 ($CONCH_2CH_2$Me), 21.06 ($CHNCH_2CH_2$Me), 43.16, 55.31 ($CHNCH_2CH_2$Me), 68.18 (NCH_2N), 69.62 (*C*HAr), 121.86, 129.74, 131.46, 136.95 (Ar), 170.58 (CO). IR (ν/cm^{-1}): 630, 765, 815, 913, 999, 1010, 1084, 1213, 1326, 1358, 1439, 1546, 1580, 1699, 1797, 2873, 2930, 2975. MS, *m*/*z*: 325 (M^+).

‡ *Crystallographic data for* **9d**: at 163 K, crystals of $C_{19}H_{22}N_2O$ are monoclinic, space group $P2_1/n$, a = 10.970(2) Å, b = 12.210(2) Å, c = = 12.071(2) Å, β = 95.09(3)°, V = 1610.6(6) Å^3, Z = 4, M = 294.39, d_{calc} = 1.214 g cm^{-3}, μ(MoKα) = 0.075 cm^{-1}, F(000) = 632. Intensities of 3781 reflections were measured with a Syntex $P2_1$ diffractometer at 163 K [λ(MoKα) = 0.71072 Å, $\theta/2\theta$ scans, $2\theta < 54°$], and 3431 independent reflections were used in the 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 = 0.1079 and GOF = 0.965 for all independent reflections [R_1 = 0.0608 was calculated against F for 1350 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0 on IBM PC AT.

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 223130. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2003.

6 M. Schulz, G. West, U. Muller and D. Henke, *J. Prakt. Chem*., 1976, **318**, 946.
7 H. W. Heine, R. H. Thomas, G. Paul and W. and R. Cowan Hoye, *J. Org. Chem*., 1973, **38**, 2984.
8 B. Carbony, L. Toupet and R. Carric, *Tetrahedron*, 1987, **43**, 2293.
9 E. V. Dehmlov and J. Schonefeld, *Z. Naturforsch: Anorg. Chem., Org. Chem*., 1975, **30B**, 824.
10 P. G. Kostyanovsky, K. S. Zakharov, M. Zaripova and V. F. Rudchenko, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1975, 875 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1975, **24**, 791).
11 (*a*) M. Komatsu, N. Nishikaze, M. Sakamoto, Y. Ohshiro and T. Agawa, *J. Org. Chem*., 1974, **22**, 3198; (*b*) M. Komatsu, S. Tamabuchi, S. Minakata and Y. Ohshiro, *Heterocycles*, 1999, **50**, 67.
12 L. Fieser and M. Fieser, *Reagents for Organic Synthesis*, John Wiley and Sons, New York, London, Sydney, 1968.
13 H. C. Carrington, C. H. Vasey and W. S. Waring, *J. Chem. Soc*., 1953, 3105.
14 J. T. Edward and I. Lantos, *Can. J. Chem*., 1967, **45**, 1925.

Received: 28th July 2003; Com. 03/2170