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An unexpected transformation of 1,2-dialkyldiaziridines into *N*-{[acetyl(alkyl)amino]methyl}-*N*-(alken-1-yl)acetamide under the action of the parent ketene

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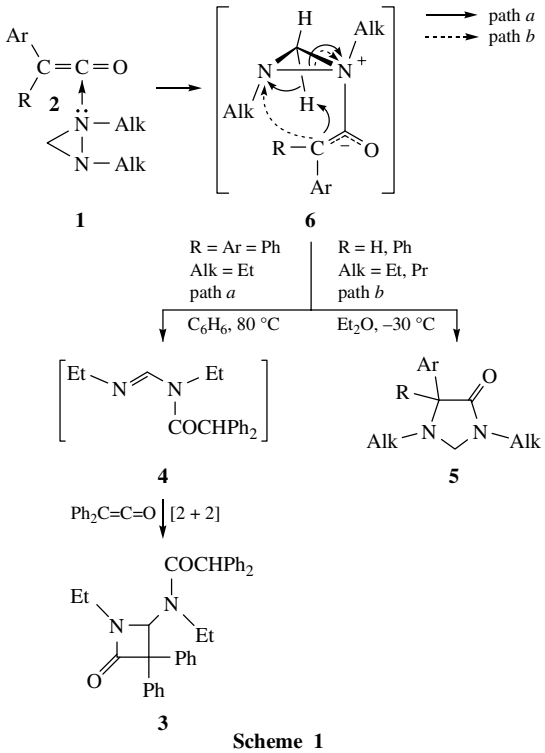
The interaction of 1,2-dialkyldiaziridines with the parent ketene unexpectedly resulted in *N*-{[acetyl(alkyl)amino]methyl}-*N*-(alken-1-yl)acetamides; the mechanism of this transformation was offered.

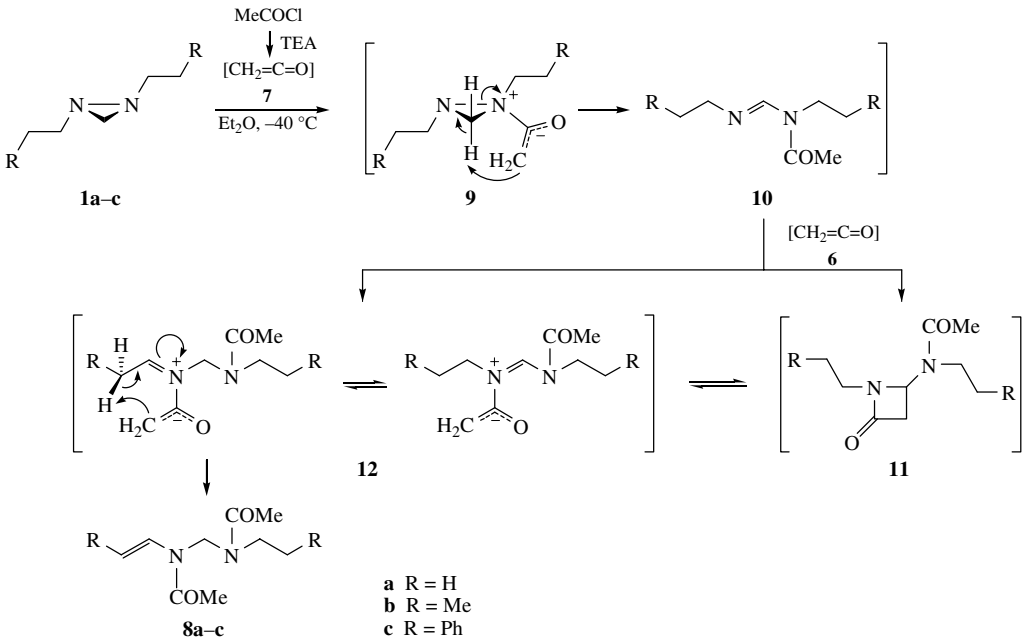
Previously,[1] we studied the interaction of 1,2-dialkyldiaziridines **1** with *in situ* generated arylketenes (arylacetic acid chlorides, TEA, –30 °C, diethyl ether) in order to prepare new 1:2 adducts, β-lactams **3**, by analogy with a reaction of compounds **1** with diphenylketene in refluxing benzene.[2] In our opinion, a possible mechanism of this reaction involved a nucleophilic attack of the nitrogen atom of a diaziridine to the central carbon atom of a cumulative bond of the diphenylketene followed by proton transfer from the C(3) atom of the diaziridine ring and a break of the N–N bond leading to amidine-type intermediate **4**. The following [2 + 2]-cycloaddition of a second diphenylketene molecule to the CH=N fragment of intermediate **4** resulted in β-lactam **3** (path *a*). The structure of β-lactam **3** was proposed on the basis of elemental analysis data, spectral characteristics and reactivity (Scheme 1).[2] However, instead of β-lactams **3**, we obtained 1:1 adducts, 5-aryl-1,3-dialkylimidazolidin-4-ones **5**, in 40–65% yields independently of the chloranhydride–diaziridine ratio, which was verified from 1:2 to 2:1 (path *b*) (Scheme 1). The reaction found is an example of the reactions of 1,2-dialkyldiaziridine ring expansion under the action of electrophilic reagents,[3–5] which carry out with N–N bond break.



Scheme 1

It was supposed[1] that a change of the reaction direction of 1,2-dialkyldiaziridines **1** with arylketenes **2** in comparison with an earlier described reaction[2] was connected with different conditions of the process. The formation of compounds **5** under mild temperature conditions, which evidently are insufficient for a tearing of a proton from a carbon atom of the diaziridine ring which could give 1:2 adducts, β-lactams **3**. In this case, zwitter-ions **6** formed at the first step of reaction transformed to imidazolidin-4-ones **5**.

In this work, the interaction of 1,2-dialkyldiaziridines **1** with parent ketene **7** has been investigated. The ketene was also generated *in situ* from acetyl chloride in dry ether in the presence of TEA at –40 °C. It could be expected that, in spite of mild conditions for performance of reaction, a negative charge formed on a carbon atom of a zwitter-ion will be more active owing to



Scheme 2 *Reagents and conditions*: MeCOCl, TEA, diethyl ether, –40 °C, 3 h, then 20 °C, 15 h.

the absence of stabilization by a conjugate with an aromatic ring and so will be capable to tear off the proton from a carbon atom of the diaziridine ring with the formation of corresponding β-lactams. However, the possibility of formation of 1,3-dialkylimidazolidin-4-ones unsubstituted at the 5-position cannot be excluded.

1,2-Diethyl-, 1,2-dipropyl- and 1,2-bis(2-phenylethyl)diaziridines **1a–c** were used as initial compounds. By their interaction with parent ketene **7**, in all cases, new compounds as base products were obtained instead of the expected β-lactam or imidazolidin-4-one derivatives. Their spectral data were significantly different from those of expected structures. In the ^{1}H NMR spectra of the compounds, the complex multiplets of diastereotopic protons of CH_2 fragments, connected with a cyclic nitrogen atom of the β-lactams, as well as protons of cyclic CH and CH_2 groups, were absent. The chemical shifts of protons in ^{1}H NMR spectra were significantly different from the expected chemical shifts of corresponding imidazolidin-4-ones.[1] Opposite signals of olefin protons appeared in spectra, in particular, a vinyl fragment appeared in the spectra of diaziridine **1a** reaction product. In addition, in the ^{1}H NMR spectra† of all the new compounds, one alkyl fragment, a singlet of N–CH_2–N fragments in a rather weak field (5.1–5.7 ppm) and two methyl groups, which could be attributed to N–COMe groups, potential products of a transformation of unsubstituted ketene, were present. All fragments corresponding to the ^{1}H NMR spectra were present in the ^{13}C NMR spectra; however, only one carbonyl group was found. The situation was not cleared using COSY and NOESY methods. The signals of both acetyl groups were only shown when ^{13}C NMR spectra were detected at –30 °C, their chemical shifts being minimal differs. This difference was only 0.07 ppm for the product of a transformation of diaziridine **1a** and 0.7–0.8 ppm for the products of a transformation of diaziridines **1b**,**c**. Once more peculiarity of NMR spectra (mainly, ^{1}H NMR spectra) of the condensation products of diaziridines **1** and ketene **7** was a duplication of signals composition of one of olefin proton, a singlet of N–CH_2–N fragment and, in some cases, of NCH_2 and solvents owing to the structure fragment 'amide nitrogen atom, connected with *sp*^{2}-C atom of olefin substituent' and, as a consequence, slowed down rotation around

† 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 AM300 (300 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).

1,2-Bis(2-phenylethyl)diaziridine **1c**: yield 47%, oil, R_f 0.6 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$) δ: 2.46 (s, 2H, NCH_2N), 2.58 and 2.82 (2m, 2H, NCH_2CH_2), 2.98 (t, 3H, $PhCH_2$, ^3J 7.6 Hz), 7.25–7.32 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$) δ: 35.31 (CH_2Ph), 57.01 (NCH_2N), 62.66 (NCH_2CH_2), 126.11, 128.38, 128.72, 139.71 (Ph).

N-*{[Acetyl(ethyl)amino]methyl}*-N-*vinylacetamide* **8a**: yield 33%, mp 26–28 °C, R_f 0.26 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$, –30 °C) δ: 1.18 (t, 3H, CH_2Me, ^3J 7.4 Hz), 2.14 (s, 3H, $MeCH_2NCOMe$), 2.31 (s, 3H, CH_2=CHNCO*Me*), 3.19 and 3.28 (10:1) (q, 2H, CH_2Me, ^3J 7.4 Hz), 4.40 and 4.56 (10:1) (d, 1H, NCH_a=CH_aH_b, $^3J_{H_aH_a}$ 9.6 Hz), 4.92 (d, 1H, NCH_a=CH_aH_b, $^3J_{H_aH_b}$ 15.0 Hz), 5.16 and 5.46 (10:1) (s, 2H, NCH_2N), 6.66 and 7.07 (10:1) (dd, 1H, CH=, $^3J_{H_aH_a}$ 9.6 Hz, $^3J_{H_aH_b}$ 15.0 Hz). ^{13}C NMR ($CDCl_3$, –30 °C) δ: 13.45 (NCH_2Me), 21.66 ($MeCH_2NCOMe$), 22.83 (CH_2=CHNCO*Me*), 40.14 (CH_2Me), 47.61 (NCH_2N), 96.82 (CH=CH_2), 130.79 (*C*H=CH_2), 171.03 (CH_2CH_2NCO), 171.10 (CH_2=CHN*C*O). IR (ν/cm^{-1}): 628, 780, 800, 864, 912, 968, 996, 1036, 1104, 1164, 1204, 1240, 1288, 1340, 1368, 1392, 1424, 1460, 1632, 1668, 2924, 2976. MS, *m*/*z*: 184 (M^+).

N-*({Acetyl[(1E)-prop-1-enyl]amino}methyl)*-N-*propylacetamide* **8b**: yield 36%, oil, R_f 0.29 (eluent: hexane–ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, 3H, CH_2Me, ^3J 7.2 Hz), 1.59 (m, 2H, $MeCH_2CH_2$), 1.68 (d, 3H, Me, ^3J 6.6 Hz), 2.09 (s, 3H, CH_2CH_2NCOMe), 2.19 (s, 3H, CH=CHNCO*Me*), 3.11 and 3.22 (8:1) (q, 2H, NCH_2, ^3J 7.2 Hz), 5.06 and 5.35 (8:1) (s, 2H, NCH_2N), 5.42 (m, 1H, NCH_a=CH_bMe), 6.14 and 6.28 (8:1) (d, 1H, NCH_a=CH_bMe, $^3J_{H_aH_b}$ 13.8 Hz). ^{13}C NMR ($CDCl_3$, –30 °C) δ: 11.39 (CH_2Me), 16.16 ($CHMe$), 21.49 (CH_2CH_2NCOMe), 21.50 ($MeCH_2CH_2$), 22.99 (CH=CHNCO*Me*), 47.12 (CH_2CH_2N), 49.00 (NCH_2N), 110.20 (CH=*C*HMe), 125.87 (*C*H=CHMe), 170.71 (CH_2CH_2NCO), 171.01 (CH=CHN*C*O). IR (ν/cm^{-1}): 620, 664, 736, 796, 824, 896, 960, 1000, 1036, 1076, 1108, 1160, 1200, 1232, 1264, 1288, 1352, 1376, 1400, 1428, 1656, 1680, 2876, 2932, 2964. MS, *m*/*z*: 212 (M^+).

N-*{[Acetyl(2-phenylethyl)amino]methyl}*-N-*[(*E*)-2-phenylvinyl]acetamide* **8c**: yield 44%, mp 110–111 °C, R_f 0.34 (eluent: hexane–ethyl acetate, 3:2). ^{1}H NMR ($CDCl_3$) δ: 2.01 (s, 3H, CH_2CH_2NCOMe), 2.38 (s, 3H, CH=CHNCO*Me*), 2.92 (t, 2H, CH_2Ph, ^3J 7.3 Hz), 3.41 and 3.56 (7:1) (t, 2H, NCH_2CH_2, ^3J 7.3 Hz), 5.12 and 5.65 (7:1) (s, 2H, NCH_2N), 6.45 (d, 1H, NCH_a=CH_bPh, $^3J_{H_aH_b}$ 14.0 Hz), 6.90 and 7.01 (7:1) (d, 1H, NCH_a=CH_bPh, $^3J_{H_aH_b}$ 14.0 Hz), 7.21–7.36 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$, –30 °C) δ: 21.42 (CH_2CH_2NCOMe), 22.68 (CH=CHNCO*Me*), 34.95 (CH_2CH_2N), 47.79 (CH_2CH_2N), 49.75 (NCH_2N), 114.95 (CH=*C*HPh), 126.31 (*C*H=CHPh), 125.62, 125.81, 125.99, 126.70, 126.87, 128.47, 128.69, 128.74, 128.90, 129.02, 136.31, 138.10 (2Ph), 170.99 (CH_2CH_2NCO), 171.14 (CH=CHN*C*O). IR (ν/cm^{-1}): 572, 612, 692, 704, 752, 956, 996, 1032, 1076, 1164, 1200, 1240, 1268, 1336, 1396, 1424, 1492, 1576, 1600, 1636, 1640, 1668, 3000, 3024. MS, *m*/*z*: 336 (M^+).

the N–Ac bond. In the mass spectra of compounds prepared, the maximal ions corresponded to the molecular ions of 1:2 adducts. Therefore, according to the total spectra characteristics and elemental analysis data, it can be confirmed that the new compounds are *N*-{[acetyl(alkyl)amino]methyl}-*N*-(alken-1-yl)acetamides **8**.

A proposed mechanism for the formation of compounds **8** is presented in Scheme 2. The first step of this reaction analogously to the interaction of 1,2-dialkyldiaziridines **1** with arylketenes **2**, is the attack of one of nitrogen atoms of the diaziridine ring on the central carbon atom of ketene **7** with formation of zwitter-ionic intermediate **9**. Then, as expected, one of hydrogen atoms connected with a carbon atom of the diaziridine ring was removed under the action of a negative charge of zwitter-ion **9** and after a break of the N–N bond intermediate azometine **10** is formed. The following step of reaction is the [2+2]-cycloaddition of the second molecule of ketene **7** on the double bond of azometine **10** with the formation of β-lactam **11** because the interaction of azometines with ketenes is a general method for the preparation of β-lactams.[6] It is known,[6,7] however, that β-lactams without substituents at the 3-position can open ring to dipolar intermediates stabilising as linear products. Their structure is determined by the substituents at other atoms of the four-membered ring. In our case, β-lactam **11** evidently is opened with formation of new intermediate **12**, which is stabilised as linear structures, *N*-{[acetyl(alkyl)amino]methyl}-*N*-(alken-1-yl)-acetamides **8**. However, it is impossible to exclude that intermediate **12** can be formed not through β-lactam **11** but by the acylation of the nitrogen atom of azometine **10** under the action of ketene **7** (Scheme 2).

Therefore, the interaction of 1,2-dialkyldiaziridines **1** with parent ketene **7** occurs through N–N bond rupture. However, in this case, a new kind of structures, *N*-{[acetyl(alkyl)-amino]methyl}-*N*-(alken-1-yl)acetamides **8**, are formed instead of β-lactams.

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