Ring Transformation of 1,5-Diazabicyclo[3.1.0]hexanes Under the Action of Arylketenes

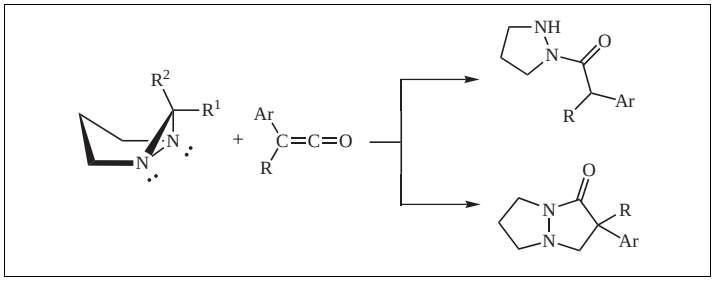
Alexander V. Shevtsov, Vladimir V. Kuznetsov, Alexander A. Kislukhin, Vera Yu. Petukhova, Yu. A. Strelenko, Nina N. Makhova*

N. D. Zelinsky Institute of Organic Chemistry of Russian Academy of Sciences,
47 Leninsky pr., 119991 Moscow, Russia; e-mail: mnn@ioc.ac.ru

and Konstantin A. Lyssenko

A. N. Nesmeyanov Institute of Organoelement Compounds of
Russian Academy of Sciences,
Vavilova str., 28, 119991, Moscow, Russia

Received August 22, 2005



The reactions of 1,5-diazabicyclo[3.1.0]hexanes **8** with arylketenes **1** have been studied in different conditions. The 1-(arylacethyl)pyrazolidines **11** were obtained at -30 °C in ether and at 20 °C in benzene instead of the expected bicyclic systems 1,5-diazabicyclo[3.2.1]octan-6-one **9** and 3-aryl-1,5-diazabicyclo[3.3.0]octane-2-one **10**. The synthesis of two representatives of bicycles **10** (**10a,b**) proceeded in the reaction of unsubstituted 1,5-diazabicycle[3.1.0]hexane **8a**, accordingly, with diphenylketene **1a** in benzene at 20 °C and with 4-chlorophenylketene **1b** in toluene at 60-110 °C. Mechanisms of the studied transformations were offered.

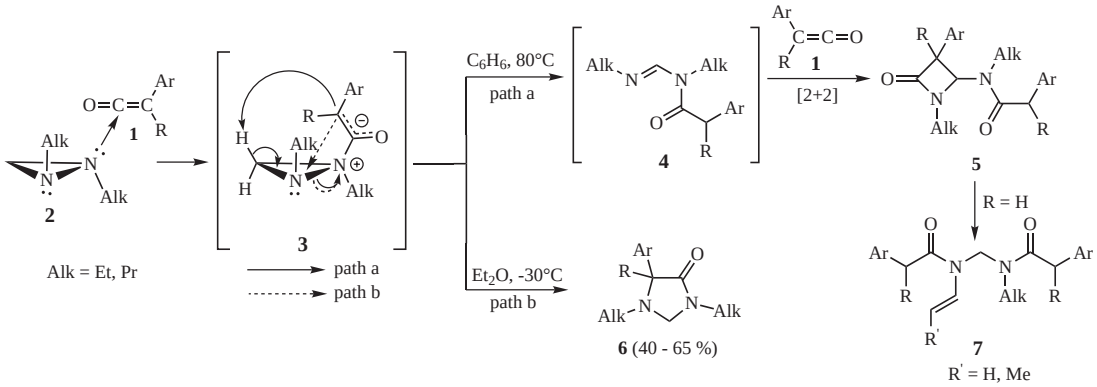
J. Heterocyclic Chem., **43**, 881 (2006).

Introduction.

Diaziridines, being strained three-membered heterocycles, tend to the 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 a few examples of diaziridine reactions with these reagents were reported [10,11a,b]. The interaction of 1,2-unsubstituted diaziridines with bis-(trifluoromethyl)ketene resulted in the ring opening at the C-N bond with the formation of corresponding acyl hydrazones [10]. The reaction of diphenylketene **1a** with 1,2-dialkyldiaziridines **2** in boiling benzene proceeded with the N-N bond cleavage and the generation of 1:2 adducts - β-lactam derivatives **5** [11a], which are potential biologically active compounds. The assumed reaction mechanism includes a nucleophilic attack of the diaziridine nitrogen atom at the central carbon atom of diphenylketene **1a** with the formation of zwitterion **3** followed by the detachment of the proton from the C(3) atom of the diaziridine ring and the N-N bond cleavage to the amidine-type intermediate **4**, which adds the second diphenylketene molecule at the CH=N fragment ([2+2]-cycloaddition) with the formation of β-lactams **5** (Scheme 1, path a).

To prepare new the β-lactams **5** we have recently studied in detail the interaction of the 1,2-dialkyl-diaziridines **2** with different kinds of ketenes (arylketenes [12a,b] and parent ketene [12c]). Arylketenes **1** (including diphenylketene **1a**) were generated *in situ* from corresponding arylacetyl chloride derivatives in the presence of TEA in dry diethyl ether or benzene in accordance with the standard procedure [13]. It was found that the reaction of 1,2-dialkyldiaziridines **2** with arylketenes **1**, depending on the conditions, apart from β-lactams **5** resulted in two new kinds of structures containing the N-C-N fragment: 5-aryl(5,5-diaryl)-1,3-dialkylimidazolidin-4-ones **6** and alkenylacetamides **7** (Scheme 1).

Scheme 1



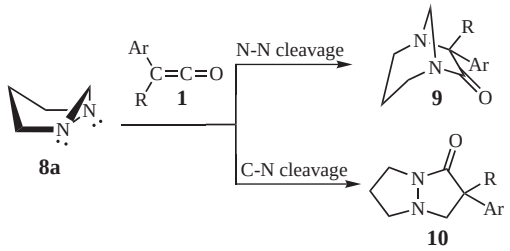
5-Aryl(5,5-diaryl)-1,3-dialkylimidazolidin-2-ones **6** are formed in ether at -30 °C in 40-65% yields. These conditions were evidently inadequate for the proton detachment from the carbon atom of the diaziridine ring in zwitterion **3**, therefore the latter transformed into compounds **6** through the concerted mechanism **(**path **b**, a kinetics-controlled process). The realization of the analogous reaction at higher temperature (benzene, 80 °C, working conditions [11a]) promoted the proton detachment from the carbon atom of the diaziridine ring in zwitterion **3** (path **a**, thermodynamics-controlled process) resulting in the formation of alkenylacetamides **7**. It was assumed and proved in one experiment that alkenylacetamides **7** were actually formed *via* the formation of corresponding β-lactams **5**, which are unstable where they contained hydrogen atoms in position 3 of the formed azetidine ring [14]. We managed to prepare stable β-lactams **5** using diphenylketene **1a** (Scheme 1).

Results and Discussion.

In this work, the interaction of arylketenes **1** with 1,5-diazabicyclo[3.1.0]hexanes **8** (cyclic analogs of 1,2-dialkyldiaziridines **2**) was investigated. Such reactions have not been studied earlier.

The structural feature of 1,5-diazabicyclo[3.1.0]-hexanes **8** is the *cis*-position of lone electron pairs at nitrogen atoms [15], in contrast to the *trans*-position in 1,2-dialkyldiaziridines **2** [16]. Unsubstituted 1,5-diazabicyclo[3.1.0]hexane **8a** was chosen as the initial target for investigating the interaction with arylketenes **1**. In this case, the formation of two isomeric bicyclic systems could be expected: bicycles **9** may be formed if the ring transformation of **8a** under the action of arylketenes **1** would proceed with the N-N bond cleavage and bicycles **10** may be obtained as reaction products if the C-N bond cleavage would occur (Scheme 2).

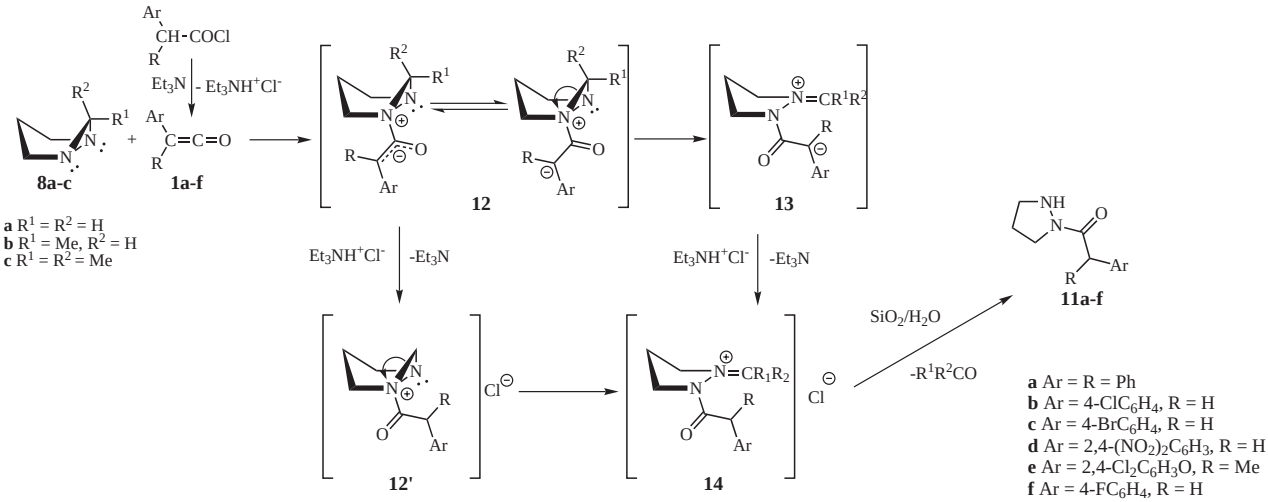
Scheme 2



The interaction of 1,5-diazabicyclo[3.1.0]hexane **8a** with arylketenes **1b-d** was studied both at -30 °C in ether and at 20 °C in benzene. However, in both cases, instead of expected bicycles **9** or **10**, monocyclic products – arylacetyl pyrazolidines **11b-d** were isolated in 15-20% yields by column chromatography on SiO_2. In addition, the behavior of 6-methyl- and 6,6-dimethyl-1,5-diazabicyclo[3.1.0]hexanes **8b,c** in the reaction with arylketenes **1a,b,e** was studied using the same conditions. The formation of monocyclic arylacetyl pyrazolidines **11** was also observed with both sorts of compounds (Scheme 3).

It is interesting to note that the yields of compounds **11** obtained from compounds **8b,c** were higher (45-48%) than in the reactions with compound **8a**. The optimized general procedure for the preparation of compounds **11** is specified in Experimental. The structure of synthesized pyrazolidines **11** was established by the elemental analysis and standard spectroscopy characterization (IR, ^{1}H, ^{13}C NMR and mass spectra) and for compound **11a** it was supplemented by the X-ray diffraction study (Figure 1).

Scheme 3



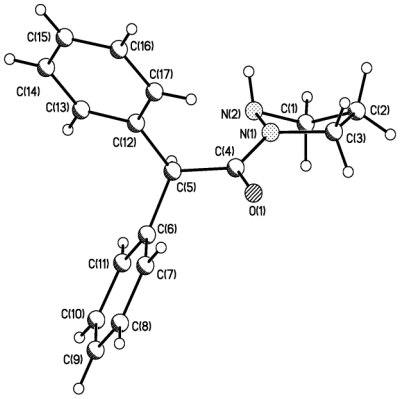


Figure 1. The general view of molecule **11a** with numerating of the atoms.

The 5-membered ring in compound **11a** is characteristic of the envelope conformation - the deviation of the C(1) atom from the plane of N(1), N(2)C(2), C(3) atoms is 0.54Å. The conjugation of the N(1) atom with the C=O group leads to the significant shortening of the N(1)-C(4) bond down to 1.347(2)Å and to its flattening (the sum of bond angles for N(1) and N(2) atoms is 356.3 and 319.6º, correspondingly). In crystal, molecules are assembled into infinite chains by N(2)-H(2N)…O(1) (-x+2, y-1/2, -z+1/2) H-bond (N(2)…O(1) 2.967(2)Å. Selected geometrical parameters for the investigated crystal structure **11a** taken from the X-ray analysis are given in Table 1 and Table 2.

The following mechanism of this unexpected reaction is offered. At the first stage (similar to the transformation of *trans*-diaziridines **2**), a nucleophilic attack of one of the nitrogen atoms of 1,5-diazabicyclo[3.1.0]hexanes **8** at the central carbon atom of the C=C=O fragment of arylketenes is carried out

Table 1

Selected bond lengths [Å] (**11a**) taken from X-ray analysis.

Selected bond	Lengths [Å]
N1-C4	1.347(2)
N1-N2	1.433(2)
N1-C3	1.480(2)
N2-C1	1.468(2)
O1-C4	1.234(2)

Table 2

Selected bond angles [°] (**11a**) taken from X-ray analysis.

Selected bond	Angles [°]	Selected bond	Angles [°]
C4-N1-N2	121.9(1)	C3-C2-C1	102.8(1)
C4-N1-C3	122.0(1)	N1-C3-C2	103.2(1)
N2-N1-C3	112.4(1)	O1-C4-N1	120.9(2)
N1-N2-C1	102.4(1)	O1-C4-C5	122.7(2)
N2-C1-C2	105.2(1)	N1-C4-C5	116.3(1)

resulting in zwitterion **12**. But as lone electron pairs in initial compounds **8a-c** are in the *cis*-position, an attack of formed enolate ion in the intermediate **12** on the second nitrogen atom (like path **b**, Scheme 1) with the formation of bicycles **9** is impossible. So in this case the cleavage of the C-N bond instead of the N-N bond is performed with the formation of another zwitterion intermediate **13**. The enolate ion in this intermediate is a rather strong base, which can remove the HCl molecule from triethylammonium chloride giving salt **14** – an analog of α-halogen alkylamines [17]. The latter are hydrolysed to corresponding pyrazolidines **11** and carbonyl compounds at contacting with water (Scheme 3). It is however impossible to exclude a

possibility of enolate ion blocking with triethylammmonium chloride (the formation of intermediate **12**′) before the diaziridine ring cleavage. Higher yields of compounds **11** in the reaction of 1,5-diazabicyclo-[3.1.0]hexanes **8b,c** may be explained by the stabilization of the iminium cation in intermediate **13** with electron-donating methyl groups.

Thus, the interaction of 1,5-diazabicyclo[3.1.0]hexanes **8a-c** with arylketenes **1** resulted in monocyclic products **11** instead of expected bicyclic systems **9** or **10**. As we proposed earlier, the formation of bicycle **9** is impossible due to the *cis*-position of lone electron pairs of initial 1,5-diazabicyclo[3.1.0]hexanes **8**. But why the cyclization of intermediate **13** to bicyclic system **10** does not occur? According to Baldwin's rules [18], this cyclization (*endo-trig* process) is disfavored because the attack of the nucleophylic enolate ion should be carried out from above or below of the R^1R^2C=N plane, which is hard to achieve in intermediate **13**. To overcome this prohibition we proposed the following conditions: proper stabilization of the enolate ion in zwitterion intermediate **13**, absence of substituents at position 6 of 1,5-diazabicyclo[3.1.0]hexane **8** and the temperature not lower than 20 °C. These conditions could be provided by using 1,5-diazabicyclo[3.1.0]hexane **8a** and diphenylketene **1a**. The absence of substituents at position 6 of **8a** was expected to decrease a steric disfavor for the ring closure and the presence of two phenyl groups - to stabilize of the enolate ion.

Taking into account these factors we carried out an interaction of 1,5-diazabicyclo[3.1.0]hexane **8a** with diphenylketene **1a** at 20 °C in benzene and obtained the expected bicyclic product 3,5-diphenyl-1,5-diaza-bicylo[3.3.0]octan-2-one **10a** together with a small amount of pyrazolidine **11a**. The cyclization can proceed both by a concerted and by a two-step mechanism *via* intermediates **12**″ and **13**″ (Scheme 4).

The structure of synthesized compound **10a** was established by spectral methods and X-ray diffraction study (Figure 2). 5-Membered rings in **10a** have an envelope conformation where the deviation of C(3) and C(6) atoms deviate from the planes of N(1), N(2), C(1), C(2) and N(1), N(2), C(4), C(5) atoms, respectively, by 0.55 and 0.65Å. The geometry of the nitrogen-containing ring in **10a** is close to **11a**, in particular N(1)-N(2) bond lengths in this structures are 1.446(4) and 1.433(2)Å. Selected geometrical parameters for the investigated crystal structure **10a** taken from the X-ray analysis are given in Table 3 and Table 4.

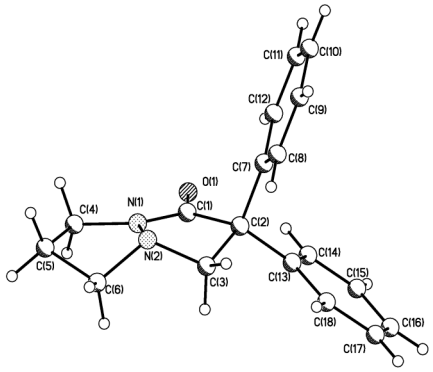


Figure 2. The general view of molecule **10a** with numerating of the atoms.

Table 3

Selected bond lengths [Å] (**10a**) taken from X-ray analysis.

Selected bond	Lengths [Å]
N1-C4	1.457(4)
N1-N2	1.446(4)
N2-C3	1.428(3)
N2-C6	1.470(9)
C1-N1	1.328(3)

Scheme 4

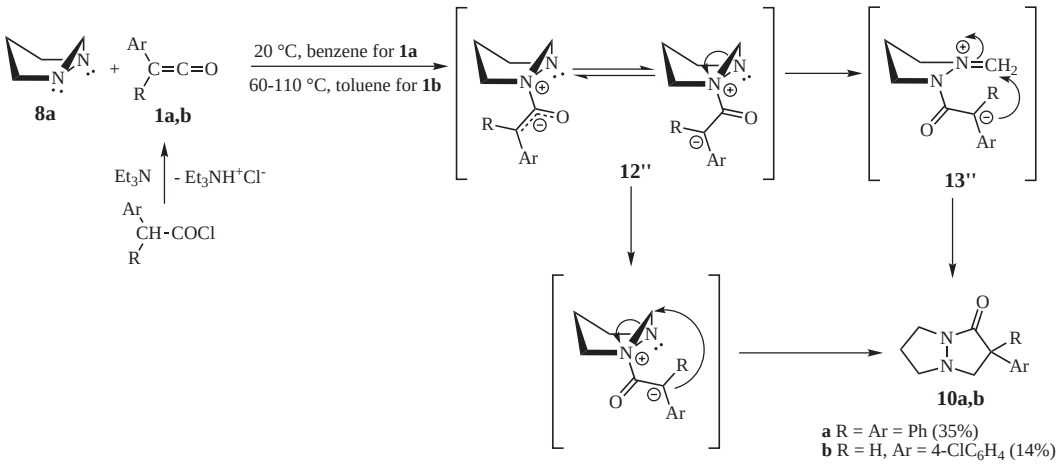


Table 4

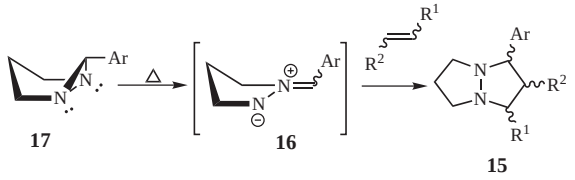
Selected bond angles [°] (**10a**) taken from X-ray analysis.

Selected bond	Angles [°]
O1-C1-N1	124.8(2)
O1-C1-C2	129.7(2)
N1-C1-C2	105.4(2)
C1-N1-N2	114.9(2)
C1-N1-C4	132.1(3)
N2-N1-C4	112.9(2)
C3-N2-N1	101.1(2)
C3-N2-C6	117.8(3)
N1-N2-C6	101.3(4)

It is evident that the cyclization of intermediates **12′′** or **13′′** into bicycle **10a** is a thermodynamics-controlled process, so it might be possible to prepare bicycles **10** from 1,5-diazabicyclo[3.1.0]hexane **8a** and other arylketenes **1** using higher temperature. This assumption was implemented for the interaction of compound **8a** and arylketene **1b**. Bicycle **10b** was prepared in 14% yield at temperature 60-110 °C.

The heterocyclic system 1,5-diazabicylo[3.3.0]-octane has been described in literature. It was prepared through the 1,3-dipolar cycloaddition of azomethinimines to different dipolarophiles [19-21]. Azomethinimines are unstable compounds and they are generated in the presence of dipolarophiles. One of the methods for the synthesis of 1,5-diazabicylo-[3.3.0]octane derivatives **15** is to produce azometinimines **16** by the thermolysis of 6-aryl-1,5-diazabicylo[3.1.0]hexanes **17** (reflux in toluene) in the presence of different alkenes [20,21] (Scheme 5).

Scheme 5



17 **16** **15**

The mechanism of the formation of bicycles **10** from 1,5-diazabicylo[3.1.0]hexane **8a** is different. A driving force of this process is the emergence of the positive charge on the nitrogen atom of initial strained bicyclic system **8a** after the interaction with arylketenes **1** (see Scheme 4).

Note that synthesized bicyclic compounds **10** are structural analogs of γ-lactams that possess a wide scope of antibacterial activity [22,23] 1-Acylpyrazolidenes **11** are applied as initial compounds in the synthesis of biologically active substances [24-26]. The method for the preparation of 1-acylpyrazolidenes **11** developed in this work is an important asset in the preparation of these useful compounds.

Thus the transformation of 1,5-diazabicyclo[3.1.0]-hexanes **8** under the action of arylketenes **1** has been studied in detail. It was found that, depending on the conditions and structure of the initial substances, this reaction resulted in two kinds of compounds: 1-(aryl-acethyl)pyrazolidines **11** and 3-aryl(3,3-diaryl)-1,5-diaza-bicyclo[3.3.0]octan-2-ones **10**.

Acknowledgements.

The authors thank the Russian Foundation for Basic Research (grant N 04-03-32799) for financial support of this work.

EXPERIMENTAL

All of the melting points were determined using a Gallenkamp melting-point apparatus and are uncorrected. Elemental analysis was performed by the CHN Analyzer Perkin-Elmer 2400. The IR spectra were measured using a UR-20 spectrometer in KBr pellets. Mass spectra were measured using a Finnigan MAT INCOS-50 instrument. All of the nmr spectra were recorded using a Bruker AM-300 spectrometer at 300 MHz for ^{1}H and 75.47 MHz for ^{13}C Spectra in $CDCl_3$. The chemical shifts are shown in δ and are expressed relative to the chemical shifts for the deuteriochloroform (7.27 ppm and 77.08 ppm for ^{1}H and ^{13}C nmr, respectively). Analytical thin-layer chromatography (TLC) was conducted on precoated silica gel plates (Silufol UV-254). New compounds were isolated on Kieselgel 60 F_{254} (Merk).

X-Ray diffraction experiments were carried out with a Bruker SMART 1000 CCD area detector, using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å, ω-scans with a 0.3° step in ω and 10 s per frame exposure) at 110 K. Low temperature of the crystals was maintained with a Cryostream (Oxford Cryosystems) open-flow N_2 gas cryostat. Reflection intensities were integrated using SAINT software [27] and absorption correction was applied semi-empirically using the SADABS program [28]. The structures were solved by a direct method and refined by the full-matrix least-squares against F^2 in the anisotropic approximation for no-hydrogen atoms. The analysis of the Fourier electron density synthesis in **10a** has revealed that the bicyclic fragment, namely atoms N(1), N(2), C(4), C(5) and C(6), were disordered by two positions with occupancies 0.8 and 0.2. The crystal data and structure refinement parameters for **10a** and **11a** are given in Table 5. All calculations were performed using the SHELXTL software [29].

The crystallographic data have been deposited with the Cambridge Crystallographic Data Center, CCDC 277464 for **10a** and CCDC 277463 for **11a**. Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Table 5.

Crystallographic data for compounds **10a** and **11a**

Properties	**10a**	**11a**
Molecular formula	$C_{18}H_{18}N_2O$	$C_{17}H_{18}N_2O$
Formula weight	278.34	266.33
Crystal system	Monoclinic	Orthorhombic
Space group	Cc	$P2_12_12_1$
Temperature (K)	120(2)	120(2)
a (Å)	15.900(5)	9.179(1)
b (Å)	6.5348(18)	10.181(2)
c (Å)	15.946(5)	14.923(2)
(°)	119.819(11)	
V (Å^3)	1437.4(8)	1394.6(4)
Z (Z')	4 (1)	4(1)
F (000)	592	568
ρ_{calc} (gcm^{-1})	1.286	1.268
Linear absorption, μ (cm^{-1})	0.81	0.80
$2\theta_{max}$ (°)	54	60
Measured (Rint)	5060 (0.0259)	11013 (0.0288)
Unique	2608	4029
With [I>2σ(I)]	2431	3265
Parameters	236	185
Final R(F_{hkl}): R_1	0.0484	0.0481
wR_2	0.1183	0.1082
GOF	0.9824	1.057
ρ_{max}/ρ_{min} (eÅ^{-3})	0.322/-0.316	0.274/-0.233

Optimal General Procedure for the Synthesis of 1-Acylpyrazolidines (**11**) by Interaction of 1,5-Diazabicyclo[3.1.0]hexanes (**8**) with Arylketenes **(1**).

The reactions were carried out in dry conditions under argon atmosphere. Solution of acylchloride (10 mmol) in 10 ml of benzene was slowly added dropwise to a solution of 1,5-diazabicyclo[3.1.0]hexanes (**8**) (10 mmol) and triethylamine (TEA) (13 mmol) in 50 ml of dry benzene at room temperature and intense stirring. The resulting suspension was stirred for 5 hours at room temperature followed by addition of a few drops of water. The precipitated triethylammonium chloride was filtered off and washed twice with 10 ml of benzene. The combined filtrate was evaporated under reduced pressure. The resulting oil was purified by column chromatography eluted with hexanes/ethyl acetate 1:1 to 0:1 followed by crystallization from hexanes to give **11a-e**.

1-(Diphenylacetyl)pyrazolidine (**11a**).

Yield 46%, 6-methyl-1,5-diazabicyclo[3.1.0]hexane (**8b**) and arylketene (**1a**) were used as starting materials.

The compound was obtained as an off-white solid, mp 146-147°; R_f: 0.54 (ethyl acetate:*n*-heptane 1:1 (v/v)); ir: 3232, 1624, 1600, 1492, 1416, 1124, 748, 704 cm^{-1}; ^{1}H nmr: δ 2.05 (m, 2H, CCH_2C), 2.93 (m, 2H, $HNCH_2$), 3.59 (t, 2H, $CONCH_2$, ^3J = 9.0 Hz), 3.76 (br.s, 1H, NH), 5.88 (s 1H, $CHPh_2$), 7.19-7.46 (m, 10H, 2Ph); ^{13}C nmr: δ 27.42 (CCH_2C), 44.35, 48.15 (CH_2), 54.45 (*C*HPh), 126.67, 128.37, 129.09 (CH of Ph-group), 140.18 (C of Ph-group), 171.99 (CO). ms: m/z 266 (M+).

Anal. Calcd for $C_{17}H_{18}N_2O$ (266.34): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.82; H, 6.90; N, 10.21.

X-ray quality crystals of the compound **11a** were grown by slow evaporation of a saturated hexanes/ethyl acetate 1:1 solution at room temperature.

1-[(4-Chlorophenyl)acetyl]pyrazolidine (**11b**).

Yield 40%, 6-methyl-1,5-diazabicyclo[3.1.0]hexane (**8b**) and arylketene (**1b**) were used as starting materials.

The compound was obtained as a white solid, mp 104-105°; R_f: 0.34 (ethyl acetate:*n*-heptane 1:1 (v/v)); ir: 2928, 1652, 1600, 1492, 1432, 1092, 808, 752 cm^{-1}; ^{1}H nmr: δ 2.04 (m, 2H, CCH_2C), 2.96 (m, 2H, $HNCH_2$), 3.53 (t, 2H, $CONCH_2$, ^3J = 7.3 Hz), 3.80 (br.s, 1H, NH), 3.85 (s, 2H, CH_2Ar), 7.27 (s, 4H, Ar); ^{13}C nmr: δ 27.55 (CCH_2C), 40.58, 44.23, 48.17 (CH_2), 128.52, 130.64 (CH of Ar-group), 132.31, 134.46 (C of Ar-group), 171.25 (CO). ms: m/z 225 (M+).

Anal. Calcd for $C_{11}H_{13}ClN_2O$ (224.69): C, 58.80; H, 5.83; Cl, 15.78; N, 12.47. Found: C, 59.01; H, 5.97; Cl, 15.52; N, 12.28.

1-[(4-Bromophenyl)acetyl]pyrazolidine (**11c**).

Yield 40%, 6,6-dimethyl-1,5-diazabicyclo[3.1.0]hexane **(8c**) and arylketene (**1c**) were used as starting materials.

The compound was obtained as a light brown solid, mp 102-104 °C; R_f: 0.37 (ethyl acetate:*n*-heptane 1:1 (v/v)); ir: 3204, 1620, 1588, 1508, 1436, 1012, 808, 748 cm^{-1}; ^{1}H nmr: δ 2.03 (m, 2H, CCH_2C), 2.95 (t, 2H, $HNCH_2$, ^3J = 6.5 Hz), 3.51 (t, 2H, $CONCH_2$, ^3J = 7.9 Hz), 3.80 (br.s, 1H, NH), 3.82 (s, 2H, CH_2Ar), 7.21 and 7.41 (both d, 4H, CH(Ar), ^3J = 7.9 Hz); ^{13}C nmr: δ 27.50 (CCH_2C), 40.60, 44.23, 48.17 (CH_2), 131.11, 131.49 (CH of Ar-group), 120.41, 135.14 (C of Ar-group), 171.13 (CO). ms: m/z 269 (M+).

Anal. Calcd for $C_{11}H_{13}BrN_2O$ (269.14): C, 49.09; H, 4.87; Br, 29.69; N, 10.41. Found: C, 49.35; H, 5.16; Br, 29.25; N, 10.18.

1-[(2,4-Dinitrophenyl)acetyl]pyrazolidine (**11d**).

Yield 20%, 1,5-diazabicyclo[3.1.0]hexane (**8a**) and arylketene (**1d**) were used as starting materials.

The compound was obtained as an orange-brown solid, mp 119-125° (decomp.); R_f: 0.21 (ethyl acetate:*n*-heptane 1:1 (v/v)); ir: 3312, 3220, 2968, 1628, 1604, 1528, 1480, 1424, 1348, 1260, 1054, 840, 804, 724 cm-1; ^{1}H nmr: δ 2.12 (m, 2H, CCH_2C), 3.08 (m, 2H, $HNCH_2$), 3.56 (t, 2H, $CONCH_2$, 3J = 7.5 Hz), 4.05 (br.s, 1H, NH), 4.39 (s, 2H, CH_2Ar), 7.61 and 8.40 (both d, 2H, CH(Ar), ^3J = 7.9 Hz), 8.89 (s, 1H, CH(Ar)); ^{13}C nmr: δ 27.54 (CCH2C), 39.38, 44.48, 48.19 (CH_2), 120.39, 127.02, 134.75 (CH of Ar-group), 125.22, 138.75; 149.42 (C of Ar-group), 168.77 (CO). ms: m/z 280 (M+).

Anal. Calcd for $C_{11}H_{12}N_4O_5$ (280.24): C, 47.15; H, 4.32; N, 19.99. Found: C, 47.19; H, 4.46; N, 19.76.

1-[2-(2,4-Dichlorophenoxy)propanoyl]pyrazolidine (**11e**).

Yield 48%, 6-methyl-1,5-diazabicyclo[3.1.0]hexane **(8b**) arylketene **(1e**) were used as starting materials.

The compound was obtained as a white solid, mp 76-77°; R_f: 0.44 (ethyl acetate:*n*-heptane 1:1 (v/v)); ir: 3192, 2980, 2880, 1660, 1632, 1480, 1448, 1288, 1248, 1136, 1088, 1036, 916, 872, 812, 744 cm^{-1}; ^{1}H nmr: δ 1.61 (d, 3H, Me, ^3J = 6.6 Hz), 2.08 (m, 2H, CCH_2C), 3.02 (m, 2H, $HNCH_2$), 3.57 (m, 2H, $CONCH_2$), 3.92 (br.s, 1H, NH), 5.34 (q, 1H, OCH, ^3J = 6.6 Hz), 6.82 and 7.12 (both d, 2H, CH(Ar), ^3J = 8.6 Hz), 7.36 (s, 1H, CH(Ar)); ^{13}C nmr: δ 17.63 (Me), 26.99 (CCH_2C), 44.42, 48.43 (CH_2), 73.68 (OCH) 115.97 (CH of Ar-group), 124.50, 126.29

(CCl), 127.43, 130.05 (CH of Ar-group), 152.54 (OC(Ar)), 170.71 (CO). ms: m/z 289 (M+).

Anal. Calcd for $C_{12}H_{14}Cl_2N_2O_2$ (289.16): C, 49.84; H, 4.88; Cl, 24.52; N, 9.69. Found: C, 50.02; H, 4.97; Cl, 24.86; N, 9.57.

1-[(4-Fluorophenyl)acetyl]pyrazolidine (**11f**).

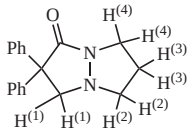
Yield 27%, 1,5-diazabicyclo[3.1.0]hexane **(8a**) and arylketene **(1f**) were used as starting materials.

The compound was obtained as a light yellow solid, mp 76-77°; R_f: 0.29 (ethyl acetate:*n*-heptane 1:1 (v/v)); ir: 3220, 2984, 2892, 1620, 1508, 1436, 1216, 1172, 1152, 1092, 1044, 980, 828, 720 cm^{-1}; ^{1}H nmr: δ 2.02 (m, 2H, CCH_2C), 2.95 (t, 2H, $HNCH_2$, ^3J = 7.5 Hz), 3.50 (t, 2H, $CONCH_2$, ^3J = 7.5 Hz), 3.83 (s, 2H, CH_2Ar), 3.89 (br.s, 1H, NH), 6.96 (t, 2H, CH(Ar) ^3J = 8.5 Hz), 7.29 (m, 2H, CH(Ar)); ^{13}C nmr: δ 27.53 (CCH_2C), 40.30, 44.21, 48.17 (CH_2), 115.02 and 115.30 (CH of Ar-group, $^2J_{C\text{-}F}$ = 20 Hz), 130.67 and 130.78 (CH of Ar-group, $^3J_{C\text{-}F}$ = 8.25 Hz), 131.70 (C of Ar-group), 160.01 and 163.25 (FC(Ar) $^1J_{C\text{-}F}$ = 240 Hz), 171.53 (CO). MS: m/z 208 (M+).

Anal. Calcd for $C_{11}H_{13}FN_2O$ (208.24): C, 63.45; H, 6.29; N, 13.45. Found: C, 63.73; H, 6.44; N, 13.23.

2,2-Diphenyltetrahydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazol-1-one-(3,3-diphenyl-1,5-diazabicyclo[3.3.0]octan-2-one) **(10a**).

The reaction was carried out in dry conditions under argon atmosphere. Solution of 2.31 g (10 mmol) of diphenylacetyl chloride in 10 ml of benzene was slowly added dropwise to a solution of 0.84 g (10 mmol) of 1,5-diazabicyclo[3.1.0]hexane (**8a)** and 1.31 g (13 mmol) of triethylamine (TEA) in 50 ml of dry benzene at room temperature with intense stirring. The resulting suspension was stirred for 5 hours at room temperature followed by addition of a few drops of water. The precipitated triethylammonium chloride was filtered off and washed twice with 10 ml of benzene. The combined filtrate was evaporated under reduced pressure. The resulting oil was purified by column chromatography eluted with hexanes/ethyl acetate 1:1 to 0:1 to yield 1-(diphenylacetyl)pyrazolidine (**11a**) (15%) and title compound **10a** (R_f: 0.46 (ethyl acetate:*n*-heptane 1:1(v/v))) which was recrystallized from ethyl acetate to give colourless crystals of **13a** (0.97 g, 35%), mp 172-174°; ir: 2820, 1660, 1444, 1136, 752, 708 cm^{-1}; ms: m/z 278 (M+).



10a

^{1}H nmr (-50°): δ 2.45 (m, 3H, $CH^{(3)}{}_2$ + $H^{(4)}$), 3.28 and 4.43 (both d, 2H, $CH^{(1)}{}_2$, ^2J = 9.56 Hz, Δν = 345 Hz), 3.46 (m, 2H, $H^{(2)}$ + $H^{(4)}$), 3.78 (bm , 1H, $H^{(2)}$), 4.39 (s, 2H, CH_2Ar), 7.27-8.55 (m, 10H, 2Ph); (60 °C) 2.33 (qv, 2H, $CH^{(3)}{}_2$, ^2J = 15.0 Hz, ^3J = 9.0 Hz), 3.78 (m, 2H, $CH^{(2)}{}_2$), 3.55 (t, 2H, $CH^{(4)}{}_2$, ^3J = 9.0 Hz), 3.84 (s, 2H, $CH^{(1)}{}_2$), 7.33-7.48 (m, 10H, 2Ph); ^{13}C nmr (-50°): δ 27.98 ($CH^{(3)}{}_2$), 39.24 ($CH^{(2)}{}_2$), 55.52 ($CH^{(4)}{}_2$), 64.06 (CPh_2), 67.04($CH^{(1)}{}_2$) 127.41, 127.88, 128.63, 129.03, (CH of Ph-group), 139.87, 141.58 (C of Ph-group), 165.07 (CO).

Anal. Calcd for $C_{18}H_{18}N_2O$ (278.35): C, 77.67; H, 6.52; N, 10.06. Found: C, 77.81; H, 6.67; N, 9.89.

X-ray quality crystals of the compound **10a** were grown by slow evaporation of a saturated ethyl acetate solution at room temperature.

2-(4-Chlorophenyl)tetrahydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazol-1-one(3-(4-chlorophenyl)-1,5-diazabicyclo[3.3.0]octan-2-one) **(10b**).

The reaction was carried out in dry conditions under argon atmosphere. To solution of 0.84 g (10 mmol) of 1,5-diazabicyclo[3.1.0]hexane (**8a**) and 1.31 g (13 mmol) of triethylamine (TEA) in 50 ml of dry toluene at 60° and intense stirring, the solution of 1.89 g (10 mmol) of 4-chlorophenylacetyl chloride in 10 ml of toluene was rapidly added (exothermic process was observed). The reaction mixture temperature grew up to 100-110°. The resulting suspension was stirred to allow the temperature fall down to 20° (approximately for 2 hours). The precipitated triethylammonium chloride was filtered off and washed two times with 10 ml of toluene. The combined filtrate was evaporated under reduced pressure. The resulting oil was purified by column chromatography eluted with ethyl acetate then chloroform/methanol 10:1(v/v) to yield an yellow oil which was crystallized from diethyl ether/hexanes 1:1 (v/v) to give 0.33 g of the title compound **10b** as a light yellow solid (14%).

mp 120-121°; ir: 2932, 1708, 1492, 1360, 1272, 1088, 1012, 7824, 792 cm^{-1}; ms: m/z 237 (M+).

^{1}H nmr: δ (60 °C) 2.38 (qv, 2H, CCH_2C, ^2J = 14.7 Hz, ^3J = 7.4 Hz), 2.81 (m, 2H, 2CH), 3.25, 3.42, 3.59 and 3.68 (all m, 1H, CH), 4.09 (t, 1H, CH_2Ar, ^3J = 9.5 Hz), 7.29 (m, 4H, Ar); ^{13}C nmr (-50°): δ 27.40 (CH_2), 39.91 (CH_2), 50.94 (*C*HAr), 54.32 (CH_2), 70.04 (CH_2) 128.99, 129.43, 132.76 (CH of Ar-group), 133.50, 129.03 (C of Ar-goup), 163.05 (CO).

Anal. Calcd for $C_{12}H_{13}ClN_2O$ (236.70): C, 60.89; H, 5.54; Cl, 14.98; N, 11.83. Found: C, 60.99; H, 5.67; Cl, 14.67; N, 11.76.

REFERENCES

[1] E. Schmitz, "Three-membered rings with two heteroatoms", *Advances in Heterocycl. Chem.*, **24**, 63 (1979).

[2] E. Schmitz, Three-membered rings with two heteroatoms and fused-ring derivatives, *Comprehensive Heterocycl. Chem.*, ed. W. Lwowski, Pergamon press, **1**, 195 (1984).

[3] H. W. Heine, "Diaziridines, 3H-Diazirines, Diaziridinones and Diaziridinimines", *Small ring Heterocycles*, part 2, ed. A. Hassner, Wiley-Interscience, chapter IV, pp. 547-629 (1983).

[4] R. Kostyanovsky, R. Murugan and M. Sutharchanadevi, "Diaziridines and diazirines", *Comprehensive Heterocycl. Chem. II*, ed. A. Padwa, Pergamon press, **1A**, pp. 348-364 (1996).

[5] A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov and R. R. Kostikov, *Synlett.*, 1779, (2000).

[6] M. Schulz, G. West, U. Muller and D. Henke, *J. Pract. Chem.*, **318**, 946 (1976).

[7] H. W Heine, R. H. Thomas, G. Paul and W. and R. Cowan Hoye, *J. Org. Chem*., **38**, 2984 (1973).

[8] B. Carbony, L. Toupet and R. Carric, *Tetrahedron*, **43**, 2293 (1987).

[9] E. V. Dehmlov and J. Schonefeld, *Z. Naturforsch*. **30B:** *Anorg. Chem., Org. Chem.*, 824 (1975).

[10] P. G. Kostyanovsky, K. S. Zakharov, M. Zaripova and V. F. Rudchenko, *Izv. Akad. Nauk SSSR, Ser. Khim.* (in Russian), 875 (1975); [*Bull. Acad. Sci. USSR, Div. Chem. Sci*. (Engl. Transl.) **24**, 791 (1975).]

[11] M. Komatsu, N. Nishikaze, M. Sakamoto, Y. Ohshiro and T. Agawa, *J. Org. Chem*., **22**, 3198 (1974).

[12a] A. V. Shevtsov, V. Yu. Petukhova, Yu. A. Strelenko, K. A. Lyssenko, I. V. Fedyanin and N. N. Makhova, *Mendeleev Commun.*, 221 (2003); [b] A. V. Shevtsov, V. Yu. Petukhova, Yu. A. Strelenko, K. A. Lyssenko, N. N. Makhova and Tartakovsky, *Izv. Akad. Nauk, Ser. Khim.*, (in Russian), 997 (2005) [*Rus. Chem. Bull., Int. Ed.*, 1021 (2005)]; [c] A. V. Shevtsov, V. Yu. Petukhova, Yu. A. Strelenko and N. N. Makhova, *Mendeleev Commun.*, 29 (2005).

[13] L. Fieser and M. Fieser, "*Reagents for Organic Synthesis*", M. Mir, **1**, p. 393 (1970) (in Russian).

[14] D. E. Davies and R. C. Storr, *Compehensive Heterocycl. Chem.*, ed. W. Lwowski, Pergamon press **1,** 237-284 (1984).

[15] G. V. Shustov, S. N. Denisenko, I. I. Chervin, N. L. Astandiarov and R. G. Kostyanovsky, *Tetrahedron*, **41**, 5719 (1985).

[16] A. Mannschreck and W. Seitz, *Angew. Chem.*, **81**, 224 (1969).

[17] H. Borme, E. Mundlos, and O. E. Herboth, *Chem. Ber*., **90**, 2003 (1957).

[18] J. E. Baldwin, *J. Chem. Soc., Chem. Commun*., 734 (1976).

[19] L. L. Rodina, A. B. Khalikova, O. A. Verzhba, and I. K. Korobizina, *Khim. Azometiniminov// Sovrem. Problemi organich. Khim.*, ed. K. A. Ogloblina, Izdatelstvo Leningradskogo univer., v.8, 135-171 (1986) (in Russian).

[20] A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov and R. R. Kostikov, *Zhurn. Org. Khim*., **37**, 888 ,(2001), *Synlett*, 1779 (2000).

[21] A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov and R. R. Kostikov, *Eur. J. Org. Chem.*, 453 (2002).

[22] L. N. Jungheim and S. K. Sigmund, *J. Org. Chem.*, **52,** 4007 (1987).

[23] L. N. Jungheim, *Tetrahedron Lett*, **30**, 1889 (1989).

[24] T. Toya, K. Yamaguchi, Y. Endo, *Bioorg. Med. Chem.*, 953 (2002).

[25] M. J. Laufersweiler, T. A. Brugel, M. P. Clark, A. Golebiowski, R. G. Bookland, S. K. Laughlin, M. P. Sabat, J. A. Townes, J. C. VanRens, B. De, L. C. Hsieh, S. A. Heitmeyer, K. Juergens, K. K. Brown, M. J. Mekel, R. L. Walter, and M. J. Janusz, *Bioorg. Med. Chem. Lett.*, **14**, 4267, (2004).

[26] M. P. Clark, S. K. Laughlin, M. J. Laufersweiler, R. G. Bookland, T. A. Brugel, A. Golobiowski, M. P. Sabat, J. A. Townes, J. C. VanRens, J. F. Djung, M. G. Natehus, B. De, L. C. Hsieh, S. C. Xu, R. L. Walter, M. J. Mekel, S. A. Heitmeyer, K. K. Brown, K. Juergens, Ye. O. Taiwo, and M. J. Janusz, *J. Med. Chem.*, **47**, 2724 (2004).

[27] SMART V5.051 and SAINT V5.00, Area detector control and integration software, Bruker AXS Inc., Madison,WI-53719, USA (1998).

[28] G.M. Sheldrick, SADABS, Bruker AXS Inc., Madison, WI-53719, USA (1997).

[29] G.M. Sheldrick, SHELXTL-97, Version 5.10, Bruker AXS Inc., Madison, WI-53719, USA.