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Synthesis and Spatial Structure of 3-Phenylacrylic Acid Octahydroquinolizin-1-Ylmethyl Ester and 2-(Octahydroquinolizin-1-Ylmethyl)Isoindole-1,3-Dione

Zh.S. Nurmaganbetov[1,2], O.A. Nurkenov[1], S.D. Fazylov[1]*, D.M. Turdybekov[3], Ye.V. Minayeva[4], G. Khabdolda[2], A.M. Ibraybekova[2], Zh.S. Tilla[2], K.M. Turdybekov[4]

[1]Institute of Organic Synthesis and Coal Chemistry of the Republic of Kazakhstan, Alikhanov str. 1, Karaganda, Kazakhstan
[2]Karaganda Medical University, Gogol str., 40, Karaganda, Kazakhstan
[3]Karaganda Technical University, Karaganda, N. Nazarbayev str., 56, Karaganda, Kazakhstan
[4]Karagandy Buketov University, Universitetskaya str., 28, Karaganda, Kazakhstan

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Abstract

The reactions of lupinine alkaloid and its chlorine derivative with cinnamoyl chloride and 2-K-isoindole-1,3-dione were investigated to obtain 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester and 2-(octahydroquinolizin-1-ylmethyl) isoindole-1,3-dione, respectively. The optimal conditions for carrying out the aforementioned reactions were determined, taking into account the nature of the solvent and medium. It was established that acylation of the molecule in a benzene medium, in the presence of trimethylamine, resulted in the formation of 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester, with an 82% yield. It was demonstrated that the interaction of chlorolupinine with 2-K-isoindole-1,3-dione under Gabriel reaction conditions resulted in the formation of 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione. The conformer with an axial orientation of the isoindole-1,3-dione substituent was observed to exhibit greater stability than the conformer with an equatorial orientation. The structure of the synthesized compounds was investigated by IR, ^{1}H, and ^{13}C NMR spectroscopy. The use of two-dimensional spectra in COSY (^{1}H-^{1}H) and HMQC (^{1}H-^{13}C) formats enabled the establishment of homo- and heteronuclear interactions, thereby confirming the structure of the compounds under investigation. The values of chemical shifts, multiplet and integrated intensity of ^{1}H and ^{13}C signals in one-dimensional NMR spectra of the novel compounds were determined. The crystal structures of 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester and 2-(octahydroquinolizin-1-ylmethyl) isoindole-1,3-dione were elucidated through X-ray analysis.

1. Introduction

The alkaloids of the lupinine series, which contain an octahydro-2H-quinolizine (quinolizidine) framework as their main structural fragment, are widely represented in plants of the *Lupinus* genus [1,2]. These alkaloids have been identified as promising pharmacophores [3,4]. Lupinine and its derivatives have been demonstrated to possess bactericidal [5], anti-inflammatory as well as hypotensive properties [6]. Lupinine esters represent the most extensively studied derivatives of this compound [1,2]. For instance, some lupinine esters have shown strong local anesthetic action and anticholinesterase activity [6,7]. The hydroxyl group of lupinine is readily converted to an amino group. As a result, a comprehensive series of substituted N-atom derivatives have been generated. They exhibit hypertensive, antiarrhythmic [8,9], antimalarial [10], and anticholinesterase [11] activities. A series of derivatives have been synthesized based on ω-chlorolupinane, ω-thiolupinane, and ω-cyanolupinane identified as promising ligands for sigma receptors of the central nervous system. They have been linked to the development of psychiatric and movement disorders [12,13].

*Corresponding author.
E-mail address: iosu8990@mail.ru

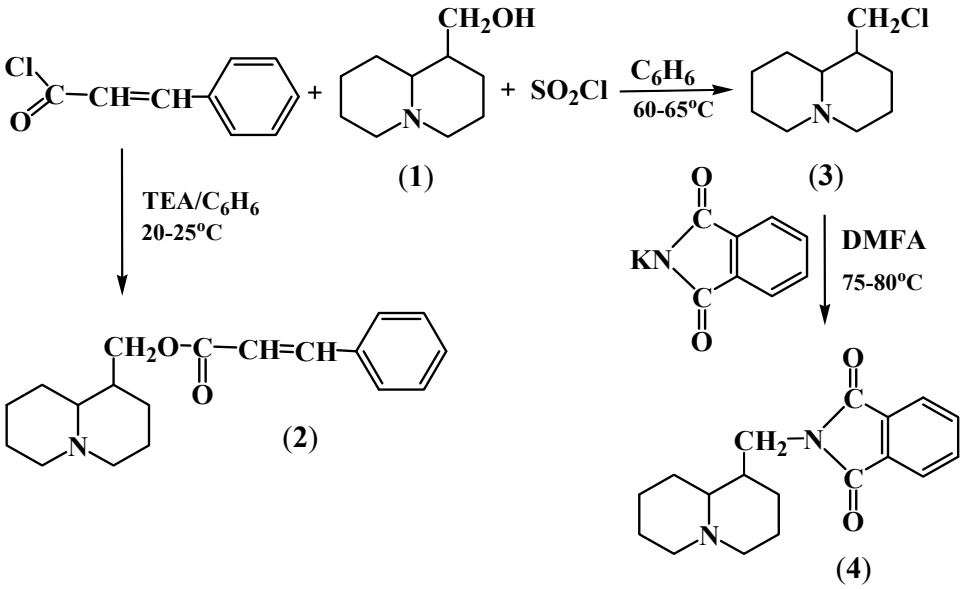
One of the defining characteristics of the trans-quinolizidine fragment of lupinine molecule with an axial oxymethyl group is its capacity to alter its configuration from a trans-member of the quinolizidine ring to a cis-member upon protonation of the nitrogen atom. Upon transition of the axial oxymethyl group to the equatorial position, there is a change in the sign of the rotation angle, indicating a change in the lability of the quinolizidine fragment of the lupinine molecule in solution [1–3]. Consequently, these properties should be manifested in their biological properties. The aforementioned characteristics of the lupinine molecule are of significant importance in the study of the structure-bioactivity relationship, thereby encouraging the synthesis and study of their novel derivatives.

2. Results and discussions

In continuation of our studies on the transformation of the lupinine molecule **(1)** [14–16], we have synthesized two new derivatives, namely 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester **(2)** and 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione **(4)**.

The acylation of lupinine with cinnamoyl chloride was carried out in an absolute benzene medium in the presence of triethylamine, resulting in the formation of the 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester **(2)**. The interaction of chlorolupinine **(3)** with 2-K-isoindole-1,3-dione under the conditions of Gabriel's method resulted in the formation of 2-(octahydroquinolizin-1-ylmethyl) isoindole-1,3-dione **(4)**. The synthesis of chlorolupinine **(3)** was carried out according to the method described in reference [17], whereby lupinine **(1)** was reacted with thionyl chloride in an absolute benzene solution, resulting in a 73% yield.

The structure of the synthesized compounds **(2,4)** was confirmed using physicochemical methods, including IR-, ^{1}H, and ^{13}C NMR spectroscopy and X-ray analysis.



The IR spectrum of compound **(2)** exhibits the presence of absorption bands corresponding to the methine (CH), diene (C=C), and keto (C=O) groups in the region of 525, 820, and 1725 cm^{-1}, respectively. Furthermore, the absorption bands of the quinolizidine skeleton framework manifest at 2738, 2755, and 2795 cm^{-1}, respectively.

The lupinine framework signals in the ^{1}H NMR spectrum of compound **(2)** showed multiplets in the following regions: 1.09-1.15 (H-8ax), 1.31-1.35 (H-3ax, 4ax, 7, 9ax), 1.43-1.46 (H-9eq), 1.52-1.55 (H-3eq), 1.61-1.64 (H-8eq), 1.74-1.89 (H-4eq, 5, 6, 2ax, 10ax) and 2.66-2.69 (H-2ax, 10ax) ppm. The oxymethylene protons of H-11 resonated as a two-proton multiplet at 4.22−4.35 ppm. The aliphatic unsaturated protons H-15 and H-16 showed single-proton doublets at 6.58 (^{3}J=16.0 Hz) and 7.60 (^{3}J=18.3 Hz) ppm, respectively. The aromatic ring protons produced a three-proton multiplet at 7.37−7.38 ppm (H-18, 20, 22) and a broadened two-proton singlet (H-19, 21) at 7.66 ppm.

The carbon atom signals of the lupinine cycle in compound **(2)** were detected in the ^{13}C NMR spectrum at the following chemical shifts: 21.12 (C-3), 25.14 (C-8), 25.74 (C-9), 27.23 (C-4), 29.81 (C-7), 37.81 (C-5), 57.42 (C-2, 10), and 64.34 (C-6) ppm.

The benzene ring carbon atoms resonated at 128.88 (C-19, 21), 129.43 (C-18, 22), 130.96 (C-20) and 134.54 (C-17) ppm. The signal at 63.57 ppm corresponded to the carbon atom of the bridging methylene group C-11. The carbon atoms C-15 and C-16, which are aliphatic and unsaturated, resonated at 118.67 and 144.92 ppm, respectively. The C-13 signal of the carbonyl carbon atom was observed at 166.80 ppm in the weak-field region.

The structure of compound **(2)** was confirmed using two-dimensional HMQC (^{1}H-^{13}C) NMR spectroscopy, which establishes heteronuclear spin-spin interactions (Fig. 1). The scheme displays the observed correlations in the molecule. Heteronuclear interactions between protons and carbon atoms through one bond were established for the following pairs in the compound using ^{1}H-^{13}C HMQC spectroscopy: H^{4ax}-C^{4} (1.30, 27.26), H^{4eq}-C^{4} (1.78, 27.20), H^{3ax}-C^{3} (1.20, 27.26), H^{3eq}-C^{3} (1.52, 27.26), H^{7}-C^{7} (1.40, 29.65), H^{5}-C^{5} (1.87, 37.78), $H^{2ax,10ax}$-$C^{2,10}$ (1.77, 57.13), $H^{2eq,10eq}$-$C^{2,10}$ (2.66, 57.17), H^{15}-C^{15} (6.60, 118.64), H^{20}-C^{20} (7.36, 130.98), $H^{18,20}$-$C^{18,20}$ (7.37, 129.42), $H^{19,21}$-$C^{19,21}$ (7.67, 128.92), H^{16}-C^{16} (7.62, 144.93).

In the IR spectrum of compound **(4)**, the valence vibrations of the CH and C=C groups of the phthalide fragment are observed in the region of 525 and 820 cm^{-1}, respectively. Additionally, absorption bands that are characteristic of the quinolizidine skeleton are present in the region of 2740, 2757, and 2798 cm^{-1}. Furthermore, vibrations of the CH_2-N bond are identified in the region of 2820 cm^{-1}.

The ^{1}H NMR spectrum of compound **(4)** displays a significant number of closely spaced protons, leading to overlapping spectra that complicate substance identification. In the 1.19−1.92 ppm region, there is a broad multiplet with an integral intensity of 10H, which includes protons of the lupinine cycle, namely $H^{8,3,4,7,9,8,2ax,5,10ax}$ of both axial and equatorial nature. The identification of some compounds was achieved through the use of two-dimensional HMQC (H^{1}-H^{1}) NMR spectroscopy. The multiplet signal in the 2.69−2.85 ppm region with 2H integral belongs to the remaining equatorial protons $H^{2eq,10eq}$ of the lupinine rings. The bridging protons of the methylene group H11 exhibited a multiplet in the 3.57−3.90 ppm region with a 2H integral. The four remaining aromatic protons $H^{15,16,17,18}$ resonated as a multiplet in the region of 7.79−7.91 ppm with an integral intensity of 4H.

The ^{13}C NMR spectrum of compound **(4)** showed signals of lupinine rings at 20.68 (C-3), 25.15 (C-8), 25.79 (C-9), 26.78 (C-4), 29.75 (C-7), 36.95 (C-5), 57.22 (C-2,10) and 64.58 (C-6) ppm. The carbon atoms of the benzene ring resonated at 123.51 (C-15,18), 132.08 (C-14,19) and 134.93 (C-16,17) ppm. The signal at 40.07 ppm corresponded to the carbon atom of the bridging methylene group C-11. The signals of carbonyl carbon atoms C-13 and C-20 were observed at 168.73 ppm in the weak-field region.

The structure of compound **(4)** was confirmed using two-dimensional ^{1}H-^{13}C HMQC NMR spectroscopy, which establishes heteronuclear spin-spin interactions. Heteronuclear interactions between protons and carbon atoms through a single bond were established by ^{1}H-^{13}C HMQC spectroscopy for the following pairs of compounds: $H^{2ax,10ax}$-$C^{2ax,10ax}$ (1.81, 57.56), $H^{2eq,10eq}$-$C^{2eq,10eq}$ (2.71, 57.73), H^{5}-C^{5} (1.95, 37.52), $H^{15,18}$-$C^{15,18}$ (7.80, 123.97), $H1^{6,17}$-$C^{16,17}$ (7.80, 135.25).

Table 1 presents the main crystallographic data for compounds **(2)** and **(4)**, obtained from the X-ray diffraction experiment. The coordinates of the atoms in fractions of the elementary crystallographic unit cell for compounds **(2)** and **(4)** are given in Table 2.

The X-ray diffraction method was used to determine the spatial structure of compounds **(2)** and **(4)**. Figures 1 and 2 provide a general view of molecules **(2)** and **(4)**, respectively. The configuration of the C5 chiral center is consistent with the absolute configuration in the crystal structure of lupinine chloride [18].

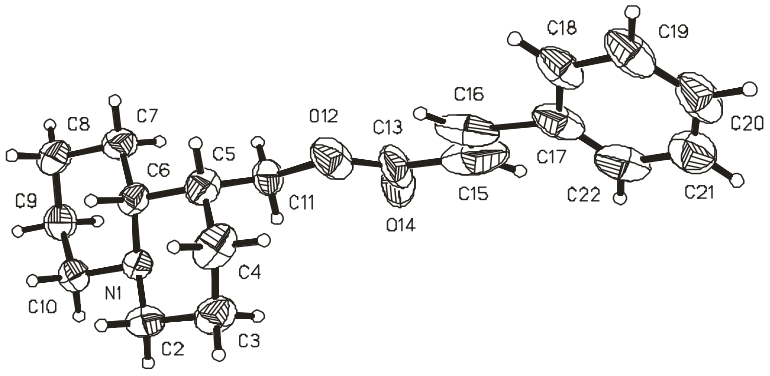


Fig. 1. Crystal structural of **(2)** (thermal vibration ellipsoids shown with a probability of 30%).

Table 1. Crystallographic data and characteristics of the X-ray diffraction experiment for structures **(2**) and **(4)**

Compound	**(2)**	**(4)**
Formula	$C_{18}H_{22}N_2O_2$	$C_{19}H_{25}NO_2$
M	298.37	299.40
Singonia	monoclinic	monoclinic
T, K	293	293
a, Å	5.435(1)	8.4783(5)
b, Å	14.124(1)	8.7702(6)
c, Å	10.280(2)	11.9319(7)
β, deg.	96.72(1)	106.471(6)
V, Å^3; Z	775.5(2); 2	850.80(9); 2
Space group	$P2_1$	$P2_1$
d_{calk}, g/cm^3	1.278	1.169
μ, mm^{-1}	0.667	0.589
Number of measured reflections	2863	3296
Number of independent reflections	2292 R(int) = 0.0392)	2509 (R(int) = 0.0309)
Number of reflections observed (I≥2σ(I))	2292	3088
Number of parameters to be specified	200	200
T_{min}, T_{max}(multiscan)	0.764, 0.994	0.807, 0.989
F(000)	320	324
θ area, deg.	4.330 ≤ θ ≤ 76.081	3.860 ≤ θ ≤ 76.020
R_1, WR_2 (I ≥ 2σ(I)	0.0531, 0.1166	0.0673, 0.1606
R_1, WR_2 (all reflexes)	0.0896, 0.1366	0.1100, 01955
GooF	0.986	1.049
$\Delta\rho_{max}$, $\Delta\rho_{min}$, *e*/Å^3	0.152-0.164	0.363-0.267

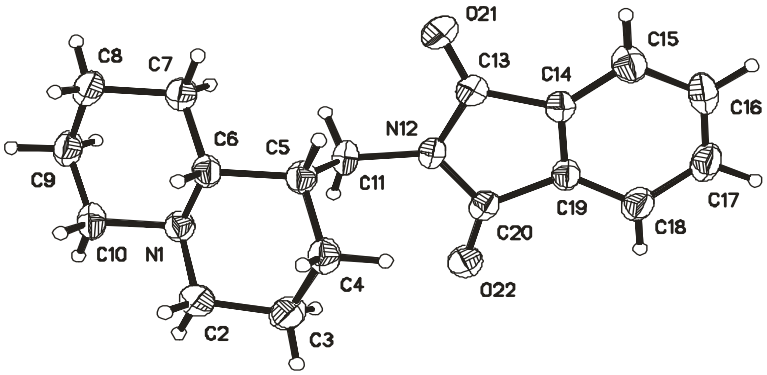


Fig. 2. Crystal structural of **(4)** (thermal vibration ellipsoids shown with a probability of 30%).

Analysis of the geometry of molecule **(2)** revealed that the bond lengths in the phenyl ring (Table 3) are slightly shorter than standard (1.384 Å) [19] due to significant thermal vibrations of the ring atoms. The constants of reduced isotropic thermal vibrations Ueq. range from 0.096−0.125 Å^2. High thermal vibrations at the O1, O2, C11-C13 atoms (Ueq. within 0.123−0.156 Å^2), connecting the lupinine framework and the phenyl ring, lead to a significant deviation of bond lengths from the standard ones (given in parentheses): O12-C13 1.361 (1.332), C13-C15 1.642 (1.340), C15-C16 1.063 (1.340) and C16-C17 1.759 (1.488) Å. It is important to note that the degree of disorder of these atoms is dynamic rather than static. The electron density values of the atoms mentioned above are somewhat spread out in space, but they are not separated into individual entities. In compound **(4)**, the bond lengths (refer to Table 3) and bond angles are similar to the usual values [19].

Table 2. The non-hydrogen atom coordinates in fractions of the cell (x10^4) for structures **(2)** and **(4)**

Atom	(2)			Atom	(4)		
	x	y	z		x	y	z
O12	4958(5)	4996(6)	6389(3)	O21	8629(6)	5256(2)	9294(4)
O14	5696(8)	2577(9)	6757(6)	O22	1390(6)	6247(3)	6923(3)
N1	3162(4)	5944(5)	9419(3)	N1	2248(6)	2794(2)	6215(3)
C2	4627(6)	6849(8)	9986(5)	C2	1402(9)	3206(3)	4938(5)
C3	5870(6)	6847(8)	9284(5)	C3	1768(8)	4269(3)	4902(5)
C4	5084(6)	7415(8)	8071(6)	C4	4485(8)	4526(3)	5354(4)
C5	3545(6)	6503(7)	7485(5)	C5	5353(8)	4075(3)	6670(4)
C6	2365(5)	6527(6)	8235(4)	C6	4911(7)	2999(3)	6584(4)
C7	2365(5)	5659(7)	7688(4)	C7	5904(9)	2496(3)	7856(5)
C8	-394(5)	5736(9)	8446(4)	C8	5465(8)	1421(3)	7770(5)
C9	459(6)	5163(8)	9640(4)	C9	2696(8)	1254(4)	7374(4)
C10	2056(6)	6016(8)	10149(4)	C10	1824(9)	1765(3)	6114(5)
C11	3961(6)	4902(7)	7202(4)	C11	4165(9)	4527(3)	7793(5)
C13	5815(10)	3715(15)	6291(8)	N12	4879(7)	5519(2)	8000(4)
C15	7168(14)	3740(12)	5542(9)	C14	7042(9)	6848(3)	8767(4)
C16	6956(12)	4741(9)	5018(5)	C15	8742(10)	7487(3)	9341(5)
C17	8465(9)	4768(8)	4266(4)	C16	8173(10)	8438(4)	9229(5)
C18	8026(8)	5721(7)	3341(4)	C17	5981(11)	8727(3)	8548(5)
C19	9076(10)	6011(9)	2673(5)	C18	4233(10)	8088(3)	7956(5)
C20	10607(10)	5340(11)	2955(6)	C19	4843(9)	7144(3)	8096(4)
C21	11036(9)	4372(10)	3890(6)	C20	3405(8)	6290(3)	7570(4)
C22	9968(11)	4108(10)	4546(5)				

Table 3. The bond lengths (d, Å) in structures **(2)** and **(4)**

(2)		(4)	
Bond	d	Bond	d
N1-C2	1.468(6)	N1-C2	1.459(5)
N1-C6	1.474(5)	N1-C6	1.466(5)
N1-C10	1.450(5)	N1-C10	1.473(5)
C2-C3	1.521(7)	C2-C3	1.515(6)
C3-C4	1.496(8)	C3-C4	1.524(6)
C4-C5	1.521(7)	C4-C5	1.518(6)
C5-C6	1.520(6)	C5-C11	1.523(6)
C5-C11	1.509(8)	C5-C6	1.540(5)
C6-C7	1.531(6)	C6-C7	1.529(6)
C7-C8	1.513(6)	C7-C8	1.537(6)
C8-C9	1.491(7)	C8-C9	1.516(5)
C9-C10	1.514(7)	C9-C10	1.508(6)
C11-O12	1.458(5)	C11-N12	1.462(5)
O12-C13	1.361(12)	N12-C13	1.381(5)
C13-O14	1.162(12)	N12-C20	1.388(5)
C13-C15	1.642(15)	C13-O21	1.219(5)
C15-C16	1.063(11)	C13-C14	1.492(5)
C16-C17	1.759(11)	C14-C19	1.363(6)
C17-C18	1.350(8)	C14-C15	1.369(6)
C17-C22	1.353(10)	C15-C16	1.379(6)
C18-C19	1.377(7)	C16-C17	1.362(6)
C19-C20	1.377(10)	C17-C18	1.391(7)
C20-C21	1.366(11)	C18-C19	1.376(6)
C21-C22	1.375(9)	C19-C20	1.500(6)
		C20-O22	1.205(4)

Table 3. The bond lengths (d, Å) in structures **(2)** and **(4)**

(2)		**(4)**	
Bond	d	Bond	d
N1-C2	1.468(6)	N1-C2	1.459(5)
N1-C6	1.474(5)	N1-C6	1.466(5)
N1-C10	1.450(5)	N1-C10	1.473(5)
C2-C3	1.521(7)	C2-C3	1.515(6)
C3-C4	1.496(8)	C3-C4	1.524(6)
C4-C5	1.521(7)	C4-C5	1.518(6)
C5-C6	1.520(6)	C5-C11	1.523(6)
C5-C11	1.509(8)	C5-C6	1.540(5)
C6-C7	1.531(6)	C6-C7	1.529(6)
C7-C8	1.513(6)	C7-C8	1.537(6)
C8-C9	1.491(7)	C8-C9	1.516(5)
C9-C10	1.514(7)	C9-C10	1.508(6)
C11-O12	1.458(5)	C11-N12	1.462(5)
O12-C13	1.361(12)	N12-C13	1.381(5)
C13-O14	1.162(12)	N12-C20	1.388(5)
C13-C15	1.642(15)	C13-O21	1.219(5)
C15-C16	1.063(11)	C13-C14	1.492(5)
C16-C17	1.759(11)	C14-C19	1.363(6)
C17-C18	1.350(8)	C14-C15	1.369(6)
C17-C22	1.353(10)	C15-C16	1.379(6)
C18-C19	1.377(7)	C16-C17	1.362(6)
C19-C20	1.377(10)	C17-C18	1.391(7)
C20-C21	1.366(11)	C18-C19	1.376(6)
C21-C22	1.375(9)	C19-C20	1.500(6)
		C20-O22	1.205(4)

The conformations of the six-membered rings A and B in structures **(2)** and **(4)** closely resemble those in the crystal structure of lupinine [20]. In structure **(2)**, cycles A and B take the form of an almost ideal chair (DC_S^1 = 0.3° and $DC_2^{1,6}$ = 1.5° for the first cycle, DC_S^1 = 0.9° and $DC_2^{1,6}$ = 0.2° for the second cycle). The corresponding cycles in structure **(4)** have the same conformation (DC_S^3 = 2.7° and $DC_2^{3,4}$ = 0.5° for cycle A, DC_S^1 = 0.8° and $DC_2^{6,7}$ = 1.8° DC_S^1 = 0.8° for cycle B. Torsion angles in cycles are given in Table 4.

In the cinnamoyl substituent of structure **(2)**, there is some violation of conjugation between the π-electrons of the C=O, C=C bond and the phenyl ring. The torsion angles O14-C13-C15-C16, C13-C15-C16-C17 and C15-C16-C17-C18 are 167.5(10), 178.0(5) and 162.0(7)°, respectively. The substituent attached through the axially oriented C11 atom of the lupinine framework rotates close to the ideal synclinal conformation. The torsion angle C4-C5-C11-O12 is -61.4(5)°.

In structure **(4)**, the atoms of the isoindole-1,3-dione substituent are almost coplanar (±0.02 Å) and the rotation of this substituent relative to the lupinine framework is in close proximity to the ideal synclinal conformation. The torsion angle C4-C5-C11-N12 is -64.0(5)°.

Table 4. Intracyclic torsion angles (τ, deg.) in the structures (**2**) and **(4)**

Angle	**(2)**	**(4)**
	τ	
Cycle A		
C6-N1-C2-C3	-58.1(6)	-58.7(5)
N1-C2-C3-C4	56.5(7)	54.3(6)
C2-C3-C4-C5	-54.6(7)	-52.3(5)
C3-C4-C5-C6	55.1(6)	54.8(5)
C4-C5-C6-N1	-56.6(6)	-59.1(5)
C2-N1-C6-C5	58.2(5)	60.5(4)
Cycle B		
C10-N1-C6-C7	-55.7(5)	-55.8(4)
N1-C6-C7-C8	56.1(6)	56.0(5)
C6-C7-C8-C9	-55.5(7)	-54.9(5)
C7-C8-C9-C10	54.3(7)	55.7(5)
C8-C9-C10-N1	-56.2(7)	-58.9(5)
C6-N1-C10-C9	56.7(6)	58.0(5)

3. Experimental part

^{1}H and ^{13}C NMR spectra were obtained using a JNN-ECA Jeol 400 Japan spectrometer operating at 399.78 and 100.53 MHz, respectively. Chemical shifts were measured relative to the signals of residual protons or DMSO-d_6 carbon atoms. IR spectra were registered on a Vector-22 Fourier transform spectrometer in KBr pellets. The reaction progress and purity of the compounds were monitored by thin layer chromatography on Silufol UV-254 plates in an ethanol-trichloromethane system (1:4). The plates were developed using iodine vapour. The reaction products underwent separation through silicagel column chromatography and recrystallisation. The melting point was determined using a Mettler Toledo Melting Point System MP55 "USA" heating table. All solvents used in this work were purified and made absolute according to standard methods [21].

X-ray diffraction study of compounds **(2)** and **(4)** was carried out on an Xcalibur Ruby diffractometer with a CCD detector (Agilent. Technologies, United Kingdom). CuKα radiation was applied with a graphite monochromator (λ 1.54184 Å) using the ω-scanning method. The initial array of diffracted reflections was processed and absorption was taken into account using the CrysAlisPro (multi-scan) program [22]. The structures were deciphered using the direct method. The coordinates of non-hydrogen atoms were refined in the anisotropic approximation using the full-matrix least squares method. The coordinates of hydrogen atoms were calculated geometrically and their positions were refined in an isotropic approximation with fixed positional and thermal parameters (the "rider" model). The structures were deciphered using the SHELXS-97 program. The atomic coordinates were refined using the SHELXL-97 software package. The X-ray analysis data of compounds **(2)** and **(4)** were deposited at the Cambridge Crystallographic Data Centre (CCDC) in the form of CIF files. The CCDC accession numbers for compounds **(2)** and **(4)** are 1869785 and 1919742, respectively.

Synthesis of 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester (2). Under stirring, a solution of 5.9 g (35.5 mmol) of cinnamoyl chloride in 40 mL of benzene and 4.94 mL (35.5 mmol) of triethylamine were added to a solution of 6 g (35.5 mmol) of lupinine **(1)** dissolved in 100 mL of benzene. The reaction mixture was stirred at room temperature for 3 h until a precipitate formed. The triethylamine hydrochloride precipitate was filtered off, and the mother liquor was evaporated. The residue underwent chromatography on silica gel using a petroleum ether-benzene eluent. A total of 4.94 g (82%) of yellow crystals of 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester **(2)** was obtained with a melting point of 75−78 °C. The elemental analysis data were in agreement with the calculated data. The compound has the molecular formula $C_{19}H_{25}NO_2$.

IR spectrum, ν, cm^{-1}: 525 (CH), 820 (C=C), 1725 (C=O), 2738, 2755, 2795 (quinolizine).

Elemental analysis: Found, %: C 76.00; H 8.22; N 4.56. $C_{19}H_{25}NO_2$. Calculated, %: C 76.44; H 8.62; N 4.8.

^{1}HNMR spectrum, δ, ppm (J, Hz): 1.09-1.15 (1H, H-8), 1.31-1.35 (4H, H-3, 4, 7, 9), 1.43-1.46 (1H, H-9), 1.52-1.55 (1H, H-3), 1.61-1.64 (1H, H-8), 1.74-1.89 (5H, H-4, 5, 6, 2, 10), 2.66-2.69 (2H, H-2, 10), 4.22-4.35 (1 H, m., H-11), 6.58 (1H, d., J=16.0, H-15), 7.60 (1H, d., J=18.3, H-16), 7.37-7.38 (3H, m., H-18, 20, 22), 7.66 (2H, s., H-19, 21).

^{13}C NMR spectrum, δ, ppm (J, Hz): 21.12 (C-3), 25.14 (C-8), 25.74 (C-9), 27.23 (C-4), 29.81 (C-7), 37.81 (C-5), 57.42 (C-2, 10), 64.34 (C-6), 128.88 (C-19, 21), 129.43 (C-18, 22), 130.96 (C-20), 134.54 (C-17), 63.57 (C-11), 118.67 (C-15), 144.92 (C-16) 166.80 (C-13).

Synthesis of 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione (4). To a 40 mL of suspension solution containing 9.214 g (49.74 mmol) of 2-K-isoindole-1,3-dione in DMF, 8.48 g (45.22 mmol) of chlorolupinine was added. The reaction mixture

was stirred at a temperature of 75–80 °C for 8 h and subsequently cooled. After being left to settle for 15 h, the reaction mixture was dissolved in 300 mL of ice-cold water and then extracted with trichloromethane (4x150 mL). The combined extracts underwent four washes with 100 mL of water each and were subsequently dried using $MgSO_4$.The solvent was evaporated under vacuum, and the residue was chromatographed on silica gel using hexane-benzene as the eluent. Clear crystals of 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione **(4)** were obtained, yielding 7.96 g (86%) with a melting point of 161–164 °C.

IR spectrum, ν, cm^{-1}: 522 (CH), 1715 (C=O), 2740, 2757, 2798 (quinolizine), 2820 (CH_2-N).

Elemental analysis: Found, %: C 72.32; H 7.34; N 9.26. $C_{18}H_{22}N_2O_2$. Calculated, %: C 72.60; H 7.52; N 9.52.

^{1}H NMR spectrum, δ, ppm (J, Hz): 1.19-1.92 (12H, m., H-2_{ax}, H-$_{3a,b}$, H-$4_{a,b}$, H-5, H-6, H-$7_{a,b}$, H-$8_{a,b}$, H-$9_{a,b}$, H-10_{ax}), 2.69-2.85 (2-H, m., H-2_{eq}, H-10_{eq}), 3.57-3.90 (2-H, m., H-$11_{a,b}$), 7.79-7.91 (4-H, m., H-15, H-18).

^{13}C NMR spectrum, δ, ppm (J, Hz): 20.68 (C-3), 25.15 (C-8), 25.79 (C-9), 26.78 (C-4), 29.75 (C-7), 36.95 (C-5), 40.07 (C-11), 57.22 (C-2, C-10), 64.58 (C-6), 123.51 (C-15, C-18), 132.08 (C-14, C-19), 134.93 (C-16, C-17), 168.73 (C-13, C-20).

4. Conclusions

The reactions of lupinine alkaloid and its halogen derivative with cinnamoyl chloride and 2-K-isoindole-1,3-dione were studied to obtain 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester and 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione. The optimal conditions for conducting the studied reactions depending on the nature of the solvent and the nature of the medium were considered. It was found that acylation of the studied alkaloid proceeded successfully smoothly in benzene in the presence of triethylamine and resulted in the formation of the corresponding derivative 3-phenylacrylic acid octahydroquinolizin-1-ylmethyl ester in good yield. As a result of studying the interaction of chlorolupinine with 2-K-isoindole-1,3-dione, the optimal conditions for the synthesis of 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione under the conditions of the Gabriel method were found. The spatial structure of 2-(octahydroquinolizin-1-ylmethyl)isoindole-1,3-dione was established and it was shown that the conformer with chair cycle conformations with axial orientation of isoindole-1,3-dione substituent is more stable than with equatorial one.

The conformations of the six-membered cycles A and B in structures **(2)** and **(4)** are close to the ideal chair conformation. In the cinnamoyl substituent of structure **(2)**, some disruption of the conjugation between the π-electrons of the C=O, C=C bond and the phenyl cycle is observed. The isoindole-1,3-dione atoms of the substituent in structure **(4)** are practically in the same plane.

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