Pergamon

Tetrahedron 58 (2002) 6103–6110

TETRAHEDRON

Synthesis of novel tricyclic derivatives of 7-azabenzonorbornene system

V. P. Samoylenko,[a] Z. V. Voitenko,[a,*] B. Donnadieu[b] and J.-J. Bonnet[b]

[a]*Department of Chemistry, Kiev Taras Shevchenko University, 60 Volodymyrska St., 01033 Kiev, Ukraine*
[b]*Laboratoire de Chimie de Coordination, CNRS, 205 route de Narbonne, 31077 Toulouse Cedex 4, France*

Received 7 March 2002; revised 27 May 2002; accepted 30 May 2002

Abstract—The reaction of 6-methyl-5,6-dihydroisoindolo[2,1-*a*]quinazolin-5-one with maleinimides in the ratio 1:2 was investigated. The products of the reaction were tricyclic derivatives of 7-azabenzonorbornene system 2-methyl-20-*R*-11-(1-*R*-2,5-dioxotetrahydro-1*H*-3-pyrrolyl)-2,10,20-triazahexacyclo[9.6.5.$0^{1,10}$.$0^{4,9}$.$0^{12,17}$.$0^{18,22}$]docosa-4(9),5,7,12,14,16-hexaene-3,19,21-trione. Their structure was established by the X-ray analysis, and a probable mechanism of the reaction is considered.

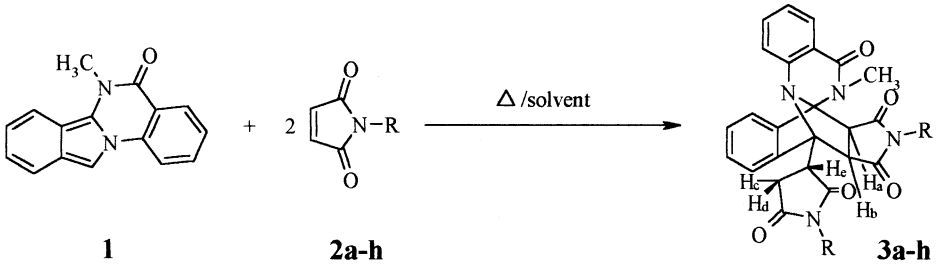
1. Introduction

Easy cycloaddition reaction is a characteristic feature of isoindoles.[1,2] Such reactions have been widely studied for the simplest isoindoles, but only few papers concerning annelated isoindoles[3–7] have been reported. 6-Methyl-5,6-dihydroisoindolo[2,1-*a*]quinazolin-5-one **1** is a 1,2-disubstituted isoindole, and exhibits similar properties to the parental isoindole.[8] Moreover **1** is synthetically one of the most available heterocyclic compounds in this series of isoindoles.[9] Data obtained from the PPP and CNDO/2 calculations show that the cycloaddition to **1** would proceed at positions 6a, 11.[10] Both 1:2 ratio adducts[11–13] and rearrangement adducts[14,15] are allowed to form from 1,2-disubstituted isoindoles and maleinimides. Our interest to cycloaddition products of annelated isoindoles came from the possibility of creating unusual three-dimensional structures that can hardly be obtained by other ways. Moreover these substances are potentially biological active molecules as they combine two active fragments: the isoindoloquinazolone one[16] and the 7-azabenzonorbornene one.[17]

2. Results and discussion

Recently we reported that 6-methyl-5,6-dihydroisoindolo-[2,1-*a*]quinazolin-5-one reacts with maleinimides as standard dienophiles in 1:1 ratio to give unusual rearrangement adducts 1-*R*-3-(*E*)-1-[2-(3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl)phenyl]methylidene-2,5-pyrrolidinedione.[6]

In the present paper we describe a reaction between isoindole **1** and maleinimides **2a**–**h** in the 1:2 ratio. Under heat or reflux of reagents in different solvents (C_2H_5OH, *i*-C_3H_7OH, dioxane, acetone, benzene), 2-methyl-20-*R*-11-(1-*R*-2,5-dioxotetrahydro-1*H*-3-pyrrolyl)-2,10,20-triazahexacyclo[9.6.5.$0^{1,10}$.$0^{4,9}$.$0^{12,17}$.$0^{18,22}$]docosa-4(9),5,7,12,14,



1 **2a-h** **3a-h**

Scheme 1. 2, **3**, **a**: R=H; **b**: R=CH_2Ph; **c**: R=CH_3; **d**: R=Ph; **e**: R=2-Nph; **f**: R=$C_6H_4CH_3$-*p*; **g**: R=2,5-dimethylphenyl; **h**: R=$C_6H_4NO_2$-*p*.

Keywords: 7-azabenzonorbornenes; cycloaddition; annelated isoindoles; maleinimides.
* Corresponding author. Tel.: +38-44-2351273; fax: +38-561556568; e-mail: z_voitenko@mail.univ.kiev.ua; zoia@chimie.ups-tlse.fr

0040–4020/02/$ - see front matter
PII: S0040-4020(02)00567-7

Table 1. Some physical and spectral data for **3a–h**

Compound	Molecular formula	Analysis, % found (calcd)			Mp (°C)	R_f	IR ν (cm^{-1}) C=O	UV, λ_{max} (log ϵ) (nm)	Yield (%)
		C	H	N					
3a	$C_{24}H_{18}N_4O_5$ (R=H)	65.53 (65.15)	4.19 (4.10)	12.86 (12.66)	205–207	0.20	1775; 1705; 1640	–	59
3b	$C_{38}H_{30}N_4O_5$ (R=CH_2Ph)	73.03 (73.30)	4.74 (4.86)	9.21 (9.00)	170–172	0.75	1775; 1700; 1650	312.0 (3.24)	66
3c	$C_{26}H_{22}N_4O_5$ (R=CH_3)	66.11 (66.38)	4.79 (4.71)	12.06 (11.91)	190–192	0.69	1765; 1685; 1655	–	71
3d	$C_{36}H_{26}N_4O_5$ (R=Ph)	73.12 (72.72)	4.47 (4.41)	9.22 (9.42)	160–162	0.72	1780; 1710; 1650	–	60
3e[a]	$C_{44}H_{30}N_4O_5$ (R=2-Nph)	75.96 (76.07)	4.40 (4.35)	8.21 (8.06)	168–169	0.73	1775; 1705; 1650	222.6 (4.42); 271.1 (3.45); 281.2 (3.48); 292.0 (3.38)	78
3f	$C_{38}H_{30}N_4O_5$ (R=$C_6H_4CH_3$-*p*)	73.21 (73.30)	4.94 (4.86)	9.07 (9.00)	164–166	0.76	1775; 1700; 1650	–	74
3g	$C_{40}H_{34}N_4O_5$ (R=2,5-dimethylphenyl)	73.37 (73.83)	5.13 (5.27)	8.88 (8.61)	214–216	0.75	1775; 1700; 1640	–	69
3h	$C_{36}H_{24}N_6O_9$ (R=$C_6H_4NO_2$-*p*)	63.45 (63.16)	3.62 (3.53)	12.58 (12.28)	204–206	0.70	1780; 1715; 1655	309.7 (3.34)	61

[a] UV spectrum measured in ethanol.

Table 2. ^{1}H NMR data for **3a–h**

Molecular Formula (R)	δ (ppm)										J (Hz)				
	N–CH_3, 3H, s	H_a 1H, d	H_b 1H, d	H_c 1H, dd	H_d 1H, dd	H_e 1H, dd	$H_{aromatic}$			The other protons	^3J, H_a, H_b	^3J H_c, H_e; ^3J H_d, H_e	^2J H_c, H_d	^3J 15-H, 16-H	^3J 5-H, 6-H
							5-H, 1H, d	16-H, 1H, d	6-, 7-, 8-, 13-, 14-, 15-H, R						
$C_{24}H_{18}N_4O_5$ (R=H)	3.61	3.77	3.16	3.06	2.58	4.72	7.75	7.64	6.93 (1H, t, ^3J=7.5 Hz); 7.00 (1H, d, ^3J=8.5 Hz); 7.10–7.50 (4H, m)	11.52 (1H, s, NH); 11.84 (1H, s, NH)	7.5	6.9; 10.1	18.1	7.3	7.3
$C_{38}H_{30}N_4O_5$ (R=CH_2Ph)	3.67	3.94	3.28	3.06	2.31	4.86	7.77	7.66	6.94 (1H, t, ^3J=7.5 Hz); 6.97 (1H, d, ^3J=8.3 Hz); 7.10–7.50 (14H, m)	4.59 (1H, d, ^2J=15.2 Hz, CH_2^aPh); 4.66 (1H, d, CH_2^aPh); 4.74 (1H, d, ^2J=15.1 Hz, CH_2^bPh); 4.81 (1H, d, CH_2^bPh)	7.6	6.6; 9.7	17.9	7.2	7.6
$C_{26}H_{22}N_4O_5$ (R=CH_3)	3.65	3.83	3.16	3.11	2.58	4.74	7.75	7.68	6.93 (1H, t, ^3J=7.2 Hz); 6.97 (1H, d, ^3J=6.6 Hz); 7.15–7.47 (4H, m)	2.86 (3H, s, NCH_3); 3.03 (3H, s, NCH_3)	7.6	5.9; 9.2	16.4	7.0	6.2
$C_{36}H_{26}N_4O_5$ (R=Ph)[a]	4.17	4.44	4.12	3.89	3.55	5.36	8.38	8.15	6.97 (1H, t, ^3J=7.5 Hz); 7.13 (1H, t, ^3J=8.3 Hz); 7.20–7.65 (12H, m); 7.88 (2H, d, ^3J=7.1 Hz)	–	7.7	6.7; 10.0	18.7	7.4	7.6
$C_{44}H_{30}N_4O_5$ (R=2-Nph)	3.69	4.18	3.63	3.47	2.80	5.43	7.94	7.86	7.00–7.80 (16H, m); 8.00–8.20 (4H, m)	–	7.5	7.0; 10.6	17.6	7.6	7.7
$C_{38}H_{30}N_4O_5$ (R=$C_6H_4CH_3$-*p*)	3.66	4.03	3.37	3.39	2.77	5.00	7.79	7.72	6.97 (1H, t, ^3J=8.5 Hz); 7.08 (1H, d, ^3J=8.9 Hz); 7.11 (2H, d, ^3J=8.3 Hz); 7.19–7.47 (10H, m)	2.34 (3H, s, $CH_3C_{arom.}$); 2.37 (3H, s, $CH_3C_{arom.}$)	7.7	7.5; 10.5	17.5	7.3	7.8
$C_{40}H_{34}N_4O_5$ (R=2,5-dimethylphenyl)	3.66	4.00	3.47	3.38	2.72	5.13	7.79	7.70	6.81–7.46 (12H, m)	2.23 (3H, s, $CH_3C_{arom.}$); 2.25 (3H, s, $CH_3C_{arom.}$); 2.27 (3H, s, $CH_3C_{arom.}$); 2.31 (3H, s, $CH_3C_{arom.}$)	7.6	7.1; 9.4	16.8	7.3	7.9
$C_{36}H_{24}N_6O_9$ (R=$C_6H_4NO_2$-*p*)	3.69	4.16	3.46	3.51	2.91	5.10	7.80	7.75	6.99 (1H, t, ^3J=7.4 Hz); 7.03 (1H, d, ^3J=7.5 Hz); 7.20–7.74 (10H, m); 8.37 (2H, d, ^3J=9.0 Hz); 8.46 (2H, d, ^3J=8.9 Hz)	–	7.8	7.0; 10.0	18.3	8.0	7.9

[a] Spectrum was recorded in pyridine-D_5.

16-hexaene-3,19,21-trione **3** was obtained in *exo*-configuration (Scheme 1).

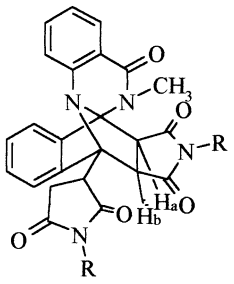
Isomeric purity of the products was controlled by TLC. Their structures have been established by elemental analysis data, spectral data and single crystal X-ray structure determination for **3b**. Nitrogen elemental analysis data confirmed that the obtained products were 1:2 ratio adducts (Table 1). For adducts **3a** and **3c** mass spectra corresponding to 1:2 ratio adducts were also obtained.

The IR spectra of these products revealed intensive bands characteristic of the C=O groups and skeleton C=C aromatic bonds (Table 1). The UV spectral data of the compounds **3b**, **e**, **h** (Table 1) were similar and not contradictory to structures proposed **3a**–**h**, indeed a band characteristic of the conjugated chromophores λ_{max}=280–300 nm was present and the isoindole longwave absorption was absent. Proposed structures **3a**–**h** was confirmed by ^{1}H and ^{13}C NMR spectra (see Tables 2 and 3), all spectra exhibit quite similar characteristics. All of the aliphatic and some aromatic protons have been identified. The signal of 5-H aromatic proton was observed in the 7.75–8.38 ppm region, it was shifted by 0.2–0.5 ppm to lower field in comparison with the other protons. This fact can be explained by the deshield influence of the quinazoline moiety carbonyl group. As predictable Michael fragment (1-*R*-2,5-dioxotetrahydro-1*H*-3-pyrrolyl) gave three doublets of doublets in structures **3a**–**h**. For this fragment geminal spin coupling constants have been found in the range: 17–18 Hz, which are similar to typical values.[7] Two bridged protons were shown as two doublets with spin coupling constant 7.5–7.8 Hz such values are characteristic of bridged protons of the 7-azabenzonorbornene system and coincide with the average calculated by Karplus formula. Additional evidence for the structure of the compounds **3a**–**h** comes from COSY {H–H} spectrum for the **3b**: an interaction between the bridged protons H_a and H_b and between Michael fragment protons H_c, H_d, H_e has been observed.

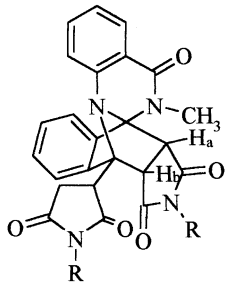
However ^{1}H NMR data do not exclude the possibility of formation of Diels–Alder *endo*-adducts **4** and an unusual rearrangement adducts **5**. Indeed we reported[7] the formation of the adducts similar to **5**. A reaction between pyrido[2,1-*a*]-isoindole (14π-electron system) and maleinimides in 1:2 ratio resulted in nontraditional rearrangement adducts 1-*R*-3-(*E*)-1-(1-*R*-2,5-dioxotetrahydro-1*H*-3-pyrrolyl)-1-[2-(2-pyridyl)phenyl]methylidene-2,5-pyrrolidinediones.

Three signals of the aliphatic CH-groups, and signals of the CH_3-group and the aliphatic CH_2-group were observed in ^{13}C NMR spectra of the synthesized compounds (Table 3). This clearly indicates that the structure discussed would have either structure **3** or **4** but not the structure **5**. As the presence of two quaternary aliphatic carbon signals contradicts this structure **5**.

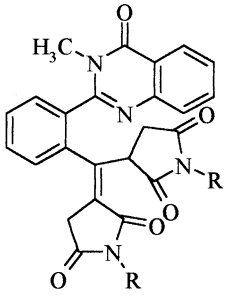
Finally the formation of Diels–Alder *exo*-adducts **3** but not *endo*-adducts **4** has been confirmed by single crystal X-ray structure determination for adduct **3b**, which exists as 1:1 chloroform solvate (Fig. 1). Without going into a complete description of the whole structure some unusual structural



3



4



5

characteristics for the 7-azabenzonorbornene fragment seemed us interesting to point out (Table 4). The pyrimidinone fragment shows a configuration of a distorted half-chair, bridged nitrogen N(2) atom is located in top of a flat distorted pyramid and significantly deviated from benzene ring plane (torsion angle N(2)–C(13)–C(21)–H(21) 8.3°). It is thus supposed that this nitrogen atom possesses basic properties. Pyrimidinone carbonyl group also significantly deviates from benzene ring plane (torsion angle O(3)–C(15)–C(17)–C(18) 15.7°). Amide fragment $C(O)NCH_3$ is not plane (torsion angle O(3)–C(15)–N(3)–C(16) 13.8°). Interestingly, single bond C(3)–C(14) is unusually elongated to 1.582(3) Å in comparison with usual single C–C bond: this elongation could be related to the presence of relatively strong steric constraints for the tricyclic azabenzonorbornene system.

We suggest the reaction mechanism to be as follows (Scheme 2): a maleinimide molecule attacks the isoindole **1** in α position with formation of Michael adduct **6**, and the intermediate formed reacts with the second maleinimide molecule for give the Diels–Alder *exo*-adduct **3**. Consequently the mechanism is based on the fact that formation of a Michael adduct cannot occur after a Diels–Alder reaction.

It is still unclear, whether the *endo*-adduct **4** is formed as an intermediate in the second reaction step or the product **3** is formed immediately from the Michael intermediate **6**. We bring up such a question because a transformation of an *endo*-adduct into a thermodynamically stable *exo*-adduct is a typical phenomenon of Diels–Alder reaction.

The formation of products **3** in the reaction of 6-methyl-5,6-dihydroisoindolo[2,1-*a*]quinazolin-5-one with maleinimides was a surprise, indeed Diels–Alder adducts are strained tricyclic systems, and one could thus assume that

Table 3. ^{13}C NMR data for **3a–c**, **h**

Molecular formula (R)	δ (ppm)								
	$N–CH_3$	$CH_2^{pyrrol.}$	$CH^{pyrrol.}$	$CH^{bridged}$	$C^{aliphatic}$	$CH^{aromatic}$	$C^{aromatic}$	C=O	The other carbon atoms
$C_{24}H_{18}N_4O_5$ (R=H)	32.34	34.97	43.75	49.56; 50.02	73.13; 85.63	115.94; 120.65; 121.70; 122.32; 127.56; 128.02; 128.49; 133.48	119.14; 143.25; 143.99; 145.33	160.98; 174.40; 176.34; 176.55; 177.73	–
$C_{38}H_{30}N_4O_5$ (R=CH_2Ph)	32.43	33.35	42.35	48.43; 48.87	73.19; 85.95	115.87; 120.87; 121.85; 122.28; 127.32; 127.44; 127.53; 127.60; 127.79; 128.10; 128.24; 128.34; 128.53; 133.43;	119.11; 135.24; 135.98; 143.09; 143.69; 145.11	161.00; 172.88; 174.80; 174.88; 176.30	41.75 (NCH_2); 41.93 (NCH_2)
$C_{26}H_{22}N_4O_5$ (R=CH_3)	32.37	33.54	42.38	48.46; 48.84	73.12; 85.73	115.86; 120.86; 121.78; 122.24; 127.71; 128.14; 128.50; 133.46	119.20; 143.19; 143.89; 145.18	160.98; 173.11; 175.00; 175.31; 176.51	24.84 (NCH_3); 24.98 (NCH_3)
$C_{36}H_{24}N_6O_9$ (R=$C_6H_4NO_2$-*p*)	32.54	33.93	42.81	48.73; 49.42	73.47; 86.34	115.87; 121.29; 122.12; 122.25; 124.35; 124.48; 127.78; 127.97; 128.13; 128.39; 128.70; 133.62	119.41; 136.89; 137.86; 143.07; 143.85; 144.90; 146.79; 147.12	161.10; 171.82; 173.53; 174.32; 175.02	–

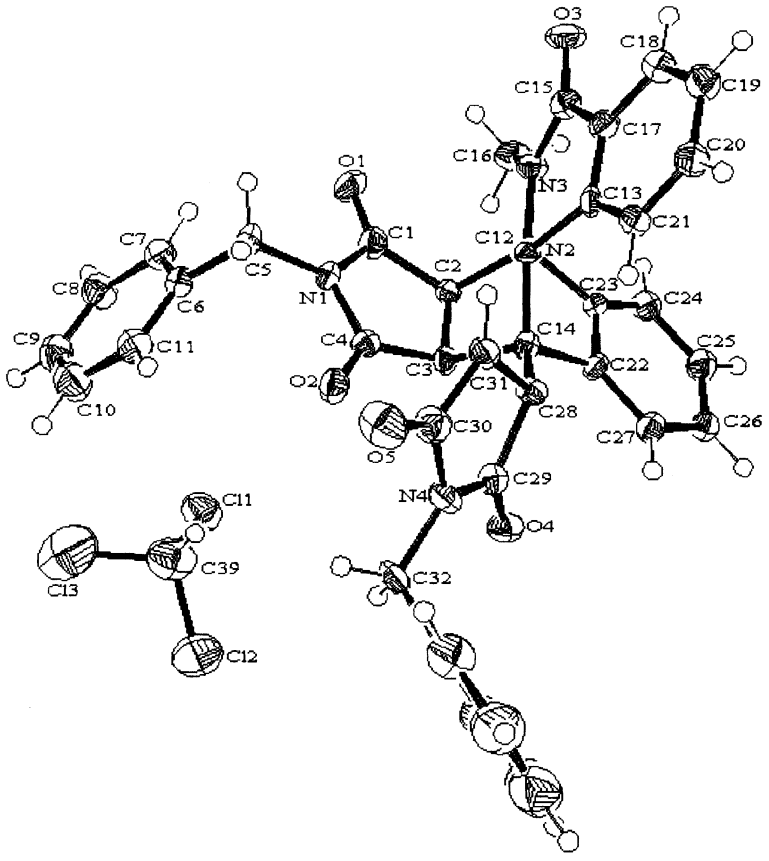
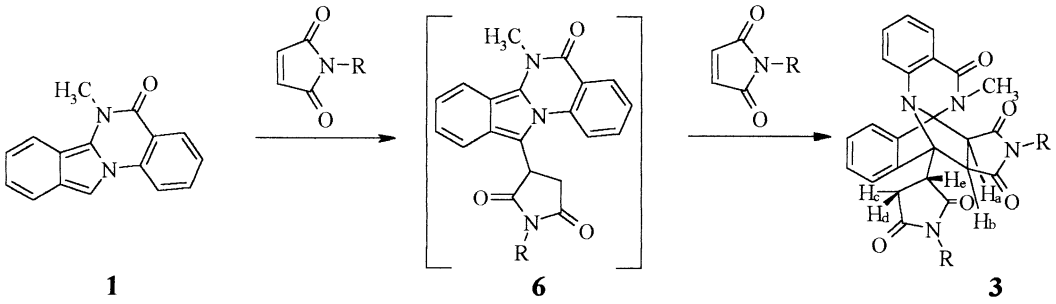


Figure 1. Molecular structure of the **3b** (R=CH_2Ph).

Table 4. Selected bond distances and angles for the **3b**

Bond	*d* (Å)	Angle	ϑ (deg)	Angle	ϑ (deg)
C(1)–C(2)	1.513 (4)	N(1)–C(1)–C(2)	109.1 (2)	C(3)–C(14)–C(22)	105.4 (2)
C(2)–C(3)	1.556 (4)	N(1)–C(1)–O(1)	122.8 (3)	C(3)–C(14)–C(28)	115.0 (2)
C(1)–O(1)	1.215 (3)	C(2)–C(1)–O(1)	128.1 (3)	N(2)–C(14)–C(22)	101.6 (2)
C(2)–C(12)	1.549 (4)	C(1)–C(2)–C(3)	104.7 (2)	N(2)–C(14)–C(28)	119.0 (2)
C(3)–C(4)	1.520 (4)	C(1)–C(2)–C(12)	114.1 (2)	C(22)–C(14)–C(28)	115.2 (2)
C(3)–C(14)	1.582 (3)	C(3)–C(2)–C(12)	101.6 (2)	N(3)–C(15)–C(17)	115.4 (3)
C(4)–N(1)	1.378 (3)	C(2)–C(3)–C(4)	103.7 (2)	N(3)–C(15)–O(3)	121.4 (3)
C(4)–O(2)	1.218 (3)	C(2)–C(3)–C(14)	103.1 (2)	C(17)–C(15)–O(3)	123.2 (3)
N(1)–C(1)	1.380 (3)	C(4)–C(3)–C(14)	114.8 (2)	C(13)–C(17)–C(15)	122.3 (2)
N(2)–C(12)	1.489 (3)	C(3)–C(4)–N(1)	109.5 (2)	C(13)–C(17)–C(18)	120.2 (3)
C(12)–N(3)	1.449 (3)	C(3)–C(4)–O(2)	126.9 (2)	C(15)–C(17)–C(18)	117.4 (3)
N(3)–C(15)	1.365 (3)	N(1)–C(4)–O(2)	123.5 (2)	C(17)–C(18)–C(19)	120.6 (3)
N(3)–C(16)	1.479 (3)	C(4)–N(1)–C(1)	113.0 (2)	C(18)–C(19)–C(20)	119.5 (3)
C(15)–C(17)	1.482 (4)	C(4)–N(1)–C(5)	123.6 (2)	C(19)–C(20)–C(21)	120.5 (3)
C(15)–O(3)	1.219 (3)	C(1)–N(1)–C(5)	123.4 (2)	C(20)–C(21)–C(13)	120.6 (3)
N(2)–C(13)	1.434 (3)	C(2)–C(12)–N(2)	101.2 (2)	C(14)–C(22)–C(27)	132.6 (3)
C(13)–C(17)	1.404 (4)	C(2)–C(12)–N(3)	114.7 (2)	C(14)–C(22)–C(23)	106.1 (2)
C(17)–C(18)	1.387 (4)	C(2)–C(12)–C(23)	106.7 (2)	C(27)–C(22)–C(23)	121.2 (3)
C(18)–C(19)	1.393 (4)	N(2)–C(12)–N(3)	112.9 (2)	C(12)–C(23)–C(22)	105.7 (2)
C(19)–C(20)	1.365 (4)	N(2)–C(12)–C(23)	102.1 (2)	C(12)–C(23)–C(24)	132.0 (2)
C(20)–C(21)	1.404 (4)	N(3)–C(12)–C(23)	117.4 (2)	C(22)–C(23)–C(24)	122.2 (3)
C(21)–C(13)	1.385 (4)	C(12)–N(2)–C(13)	113.7 (2)	C(23)–C(24)–C(25)	116.8 (3)
N(2)–C(14)	1.519 (3)	C(12)–N(2)–C(14)	95.52 (17)	C(24)–C(25)–C(26)	121.1 (3)
C(12)–C(23)	1.530 (3)	C(13)–N(2)–C(14)	123.3 (2)	C(25)–C(26)–C(27)	120.6 (3)
C(14)–C(22)	1.528 (4)	C(12)–N(3)–C(15)	122.9 (2)	C(26)–C(27)–C(22)	117.9 (3)
C(22)–C(23)	1.390 (4)	C(12)–N(3)–C(16)	117.3 (2)		
C(23)–C(24)	1.390 (4)	C(15)–N(3)–C(16)	119.0 (2)		
C(24)–C(25)	1.390 (4)	N(2)–C(13)–C(21)	125.3 (3)		
C(25)–C(26)	1.406 (4)	N(2)–C(13)–C(17)	116.0 (2)		
C(26)–C(27)	1.404 (4)	C(21)–C(13)–C(17)	118.5 (2)		
C(27)–C(22)	1.367 (4)	C(3)–C(14)–N(2)	98.29 (19)		



Scheme 2.

such Diels–Alder adducts would undergo a readily transformation into peculiar substances similar to adducts described earlier for pyrido[2,1-*a*]isoindole.[7] However, the three-dimensional structures discussed occur to be enough stable for 6-methyl-5,6-dihydroisoindolo[2,1-*a*]quinazolin-5-one system.

3. Conclusion

In conclusion, we described synthesis of the complex derivatives of 7-azabenzonorbornene system by the reaction of 6-methyl-5,6-dihydroisoindolo[2,1-*a*]quinazolin-5-one with maleinimides in the ratio 1:2. It should be mentioned that synthesis of such novel heterocyclic system is the first example of isolation of stable tricyclic 7-azabenzonorbornenes.

4. Experimental

4.1. General methods

NMR spectra were recorded in DMSO-d_6 on a multinuclear Bruker AC 250 spectrometer operating at 250.133 and 62.896 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts are expressed in ppm (downfield from an internal TMS standard). IR spectra were measured on a Pye Unicam SP3-300 spectrometer (KBr tablets). UV spectra were recorded in 1,4-dioxane solutions on a Perkin–Elmer Lambda-19 spectrometer. Mass spectra were measured on a Nermag R10. Melting points were determined on a Boetius apparatus and were uncorrected. Isomeric purity of the products obtained was controlled by TLC on Silufol UV-254 plates in chloroform–methanol 10:1 system. Properties of the compounds obtained are depicted in Tables 1–3.

4.2. X-Ray crystallographic analysis data for adduct 3b

$C_{38}H_{26}N_4O_5]\cdot CHCl_3$, M=738.00, monoclinic, space group $C2/c$ (no. 15), a=25.088(2), b=13.048(2), c=20.538(2) Å, β=91.32(2)°, V=6721(1) Å^3, Z=8, $F(000)$=3040, d_{calc}=1.459 g cm^{-3}, Mo Kα radiation (λ=0.71073 Å), μ=0.326 mm^{-1}, colorless plate, 0.40×0.25×0.10 mm^3. X-Ray data were collected on a IPDS-Stoe diffractometer at low temperature (T=160 K) from 32,756 measures, 6616 reflections, were unique (R(int)=0.0781), 3030 with $I>2\sigma(I)$ have been used for the refinement. Data/parameters ratio was 3040/460; $R1$=0.0529, $WR1$=0.0964, S=0.736. Data reduction and cell refinement were carried out by using STOE-IPDS softwares.[18] The structure was solved by direct methods and refined by full-matrix least-squares procedures using the SHELXS-97 program package.[19,20] All of the non-hydrogen atoms were refined anisotropically and hydrogen atoms were introduced in idealized positions, with an isotropic thermal parameter fixed at 20% higher than those carbon atoms with which there are connected. Drawing was performed by using the program ORTEP32.[21]

4.3. General procedure of synthesis of the 2-methyl-20-*R*-11-(1-*R*-2,5-dioxotetrahydro-1*H*-3-pyrrolyl)-2,10,20-triazahexacyclo[9.6.5.0^{1,10}.0^{4,9}.0^{12,17}.0^{18,22}]docosa-4(9),5,7,12,14,16-hexaene-3,19,21-trione 3a–h

The mixture of the corresponding maleinimide **2** (6 mmol) and 6-methyl-5,6-dihydroisoindolo[2,1-*a*]quinazolin-5-one **1** (3 mmol) was refluxed in 15–30 ml ethanol during 1–2 h. The solution was cooled and the corresponding Compound **3** was precipitated, the solid was filtered and recrystallized from 1,4-dioxane to give a colorless product.

Mass spectrum of the Compound **3a** (electrospray, 5 μl min^{-1}, CH_3CN) (*m/z* (*I*, %)): [2MH]$^+$ 885 (8), [MH]$^+$ 443 (72), [MH− ]$^+$ 346 (100), [M−2 ]$^+$ 248 (19).

Mass spectrum of the compound **3c** (electrospray, 5 μl min^{-1}, DMSO/CH_3CN) (*m/z* (*I*, %)): [MH]$^+$ 471 (100), [MH− ]$^+$ 360 (26).

4.4. Supplementary material

Crystallographic data (excluding structure factors) for the structure in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 180403. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, [fax: +44-0-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgements

The authors thank the 'Service commun de spectrométrie de Masse de l'Université Paul Sabatier' for mass spectra measurements.

References

1. Babitchev, F. S.; Kovtunenko, V. A. *Khimiya izoindola*; Naukova dumka: Kiev, 1983; pp 68–85.
2. Kovtunenko, V. A.; Voitenko, Z. V. *Russ. Chem. Rev.* **1994**, *63* (12), 997–1018.
3. Hennige, H.; Kreher, R. P. *Synthesis* **1982**, *10*, 842–844.
4. Kajigaeshi, S.; Mori, S.; Fujisaki, S.; Kanemasa, S. *Bull. Chem. Soc. Jpn* **1985**, *58*, 3547–3551.
5. Matsumoto, K.; Uchida, T.; Aoyama, K.; Nishikawa, M.; Kuroda, T.; Okamoto, T. *J. Heterocycl. Chem.* **1988**, *25*, 1793–1801.
6. Voitenko, Z. V.; Samoylenko, V. P.; Kovtunenko, V. A.; Gurkevich, V. Yu.; Tyltin, A. K.; Scherbakov, M. V.; Shishkin, O. V. *Khim. Geterosickl. Soedin.* **1999**, *5*, 669–677.
7. Voitenko, Z. V.; Pocholenko, O. A.; Chkarov, O. O.; Shishkin, O. V.; Shishkina, S. V.; Dall'ava, A.; Vedrenne, M.; Sanchez, M.; Wolf, J. *Eur. J. Org. Chem.* **2001**, 1401–1405.
8. Kovtunenko, V. A.; Voitenko, Z. V.; Sheptun, V. L.; Savransky, L. I.; Tyltin, A. K.; Babitchev, F. S. *Ukr. Khim. Zh.* **1985**, *51*, 976–987.
9. Babitchev, F. S.; Tyltin, A. K. *Ukr. Khim. Zh.* **1970**, *36*, 175–178.
10. Kovtunenko, V. A.; Voitenko, Z. V.; Savransky, L. I.; Tyltin, A. K.; Babitchev, F. S. *Khim. Geterosickl. Soedin.* **1988**, *2*, 216–222.
11. Kreher, R. P.; Konrad, M. R. *Chem. -Ztg.* **1988**, *112*, 335–342.
12. Kreher, R. P.; Hennige, H.; Jellito, F.; Preut, J. *Z. Naturforsch., B: Chem. Sci.* **1989**, *44*, 1132–1148.
13. Kovtunenko, V. A.; Kutcherenko, T. T.; Turov, A. V.; Voitenko, Z. V.; Tyltin, A. K.; Babitchev, F. S. *Ukr. Khim. Zh.* **1992**, *58*, 588–590.
14. Kovtunenko, V. A.; Turov, A. V.; Kutcherenko, T. T.; Tyltin, A. K.; Voitenko, Z. V.; Kornilov, M. Yu.; Babitchev, F. S. *Ukr. Khim. Zh.* **1991**, *57*, 71–77.
15. Kovtunenko, V. A.; Voitenko, Z. V.; Kutcherenko, T. T.; Turov, A. V.; Tyltin, A. K.; Babitchev, F. S. *Khim. Geterosickl. Soedin.* **1990**, *2*, 190–202.
16. Ischenko, V. V. PhD Thesis, Kiev Taras Shevchenko University, 1988.
17. Shen, T. Y.; Harman, W. D.; Huang, D. F.; Gonzalez, J. PCT Int. Appl., WO 9606093, 29th February, 1996.
18. Stoe; Cie IPDS Manual. Version 2.93, Darmstadt: Germany, 1997.
19. Sheldrick, G. M. *SHELXS-97: Program for Crystal Structure Solution*, University of Göttingen: Göttingen, Germany, 1990.
20. Sheldrick, G. M. *SHELXL-97: Program for the Refinement of Crystal Structures from Diffraction Data*, University of Göttingen: Göttingen, Germany, 1997.
21. Farrugia, L. J. ORTEP32 for Windows. *J. Appl. Crystallogr.* **1997**, *30*, 565.