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REGIOSELECTIVE SYNTHESIS OF 1,5-DIARYL-2-(HYDROXYALKYL)-8-METHYLGLYCOLURILS

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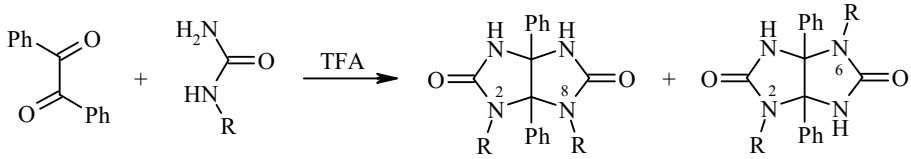
The cyclocondensation of N-methylurea with derivatives of tetrahydroimidazooxazolone, tetrahydroimidazooxazinone, dihydroimidazooxazinone, and tetrahydroimidazooxazepinone was studied for the first time. It was shown that the reactions take place with high regioselectivity, are regular in character, and lead to the formation of previously inaccessible 1,5-diaryl-2-(hydroxyalkyl)-8-methylglycolurils with high yields.

Keywords: 1,5-diaryl-2-(hydroxyalkyl)-8-methylglycolurils, imidazooxazepinones, imidazooxazinones, imidazooxazolones, *N*-methylurea, regioselectivity.

Glycolurils have a broad spectrum of practically useful properties: they are used in medicine [1-3], agriculture [4], and organic and supramolecular chemistry [5-16]. In recent years, great attention has been paid to 2,8-substituted glycolurils, which are used as an efficient molecular template for intramolecular Claisen-type condensation [10, 11] and in combinatorial [12] and supramolecular chemistry [13-17]. For example, during study of supramolecular organization in the crystals of 2,8-di(hydroxyalkyl)-1,5-diphenylglycolurils we established that chirality is generated in these compounds (the chirality appears as a result of stabilization of the conformers of the achiral compounds) [17]. A similar effect was described in [18]. However, the synthesis of 2,8-disubstituted 1,5-diphenylglycolurils **1** has not been sufficiently well developed – only particular representatives have been obtained: 2,8-dimethyl(dibenzyl, dibenzoxycarbonylmethyl)-1,5-diphenylglycolurils, together with which minor 2,6-disubstituted glycolurils were obtained [12, 19, 20]. They were synthesized by



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R = Me, Bn, CH_2COOBn, CH_2COOH, $(CH_2)_2COOH$, $(CH_2)_3COOH$

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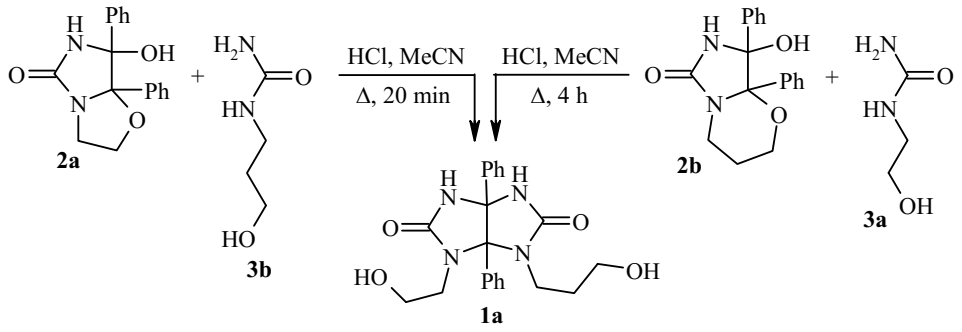
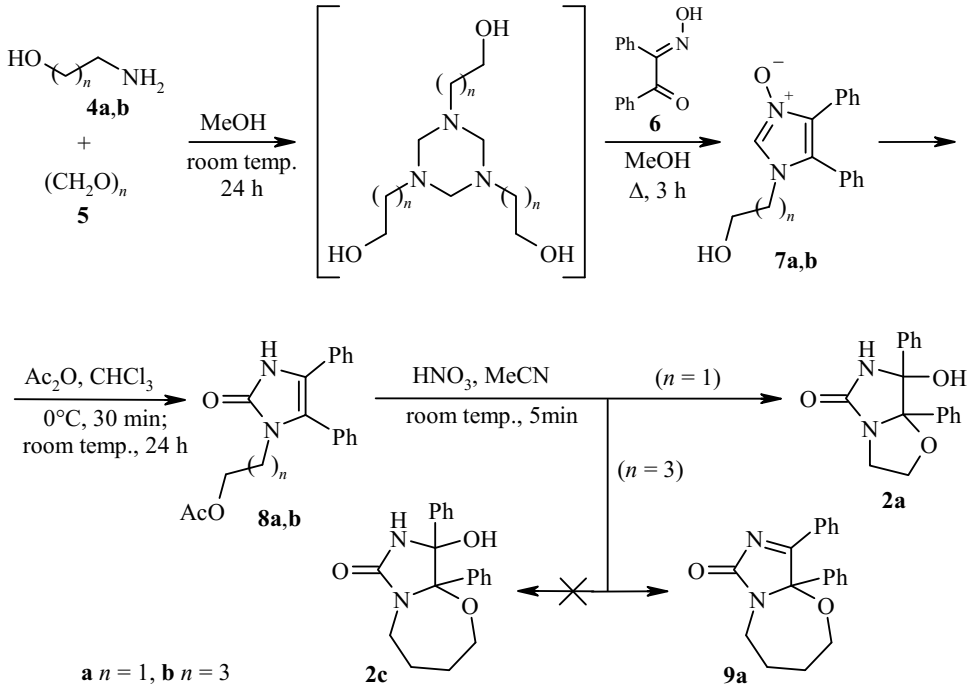
condensation of 1,2-dioxo-1,2-diphenylethane (benzil) with 1-substituted ureas. In order to find analogous reactions, we recently investigated the reaction of benzil with *N*-carbamoylamino acids (ureido acids) and ureido alcohols [17, 21]. It was shown that the fraction of the 2,6-disubstituted glycolurils in the reactions of ureido acids with benzil increases with increase in the length of the alkyl chain [21].

During investigation of the condensation of ureido alcohols with benzil new precursors of 2,8-di-(hydroxyalkyl)-1,5-diphenylglycolurils were found, namely, tetrahydroimidazooxazolone **2a** and tetrahydro-imidazooxazinone **2b**. On the basis of their reaction with 1-(hydroxyalkyl)ureas **3a**,**b**, a new method was proposed for the regiospecific synthesis of 2,8-disubstituted 1,5-diphenylglycolurils [17]. In the course of these investigations the first representative of 2,8-disubstituted 1,5-diphenylglycolurils **1a** with different substituents at the nitrogen atoms was obtained [17]. Compounds of such a type were previously inaccessible.



It seemed of interest to find out whether the applicability limits of this reaction could be extended for possible synthesis of other representatives of 2,8-disubstituted 1,5-diphenylglycolurils with different substituents at the nitrogen atoms. For this purpose, we proposed to investigate the condensation of compounds **2a**,**b** and their analogs with *N*-methylurea (**3c**).

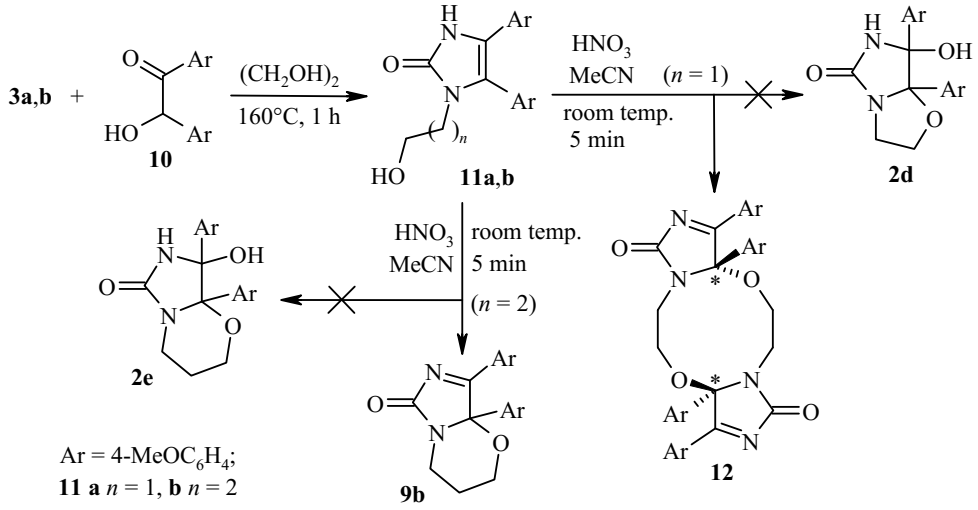
The bicyclic compounds were synthesized by the procedure that we developed earlier [17]. A method based on the condensation of 4-aminobutanol (**4b**), paraform (**5**), and 2-hydroxyimino-1,2-diphenylethanone (**6**) was tried for the production of 9-hydroxy-9,9a-diphenylhexahydroimidazo[5,1-*b*][1,3]oxazepin-7(8*H*)-one (**2c**).



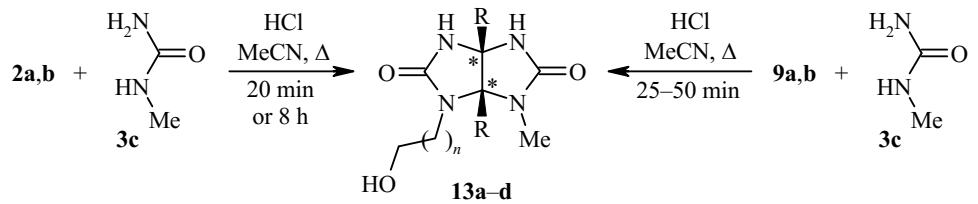
The synthesis of 2-(2-oxo-4,5-diphenyl-2,3-dihydro-1*H*-imidazol-1-yl)ethyl acetate (**8a**) from 2-aminoethanol (**4a**), paraform (**5**), and hydroxyaminoethanone **6** through the formation of the *N*-oxide **7a** had been described in the literature [22]. Using our previously developed method for the preparation of 5-hydroxy-1-(2-hydroxyethyl)-4,5-diphenyl-1*H*-imidazol-2(5*H*)-one from 1-(2-hydroxyethyl)-4,5-diphenyl-1*H*-imidazol-2(3*H*)-one by the action of concentrated HNO_3 [17] as model we realized the synthesis of tetrahydroimidazooxazolone **2a** in the reaction of the acetate **8a** with concentrated HNO_3 in MeCN. We also realized analogous transformations with 4-aminobutanol (**4b**); having synthesized the intermediate acetate **8b**, during treatment with HNO_3 instead of the expected hexahydroimidazooxazepinone **2c** we obtained its dehydration product 9,9a-diphenyl-2,3,4,5-tetrahydroimidazo[5,1-*b*][1,3]oxazepin-7(9a*H*)-one (**9a**).

A different approach, based on condensation of the ureas **3a**,**b** and anisoin **10** by analogy with the preparation of compound **2a** [17], was used for the synthesis of the previously undescribed compounds **2d**,**e**. Here it was found that the synthesized 1-(hydroxyalkyl)-4,5-di(*p*-methoxyphenyl)-1*H*-imidazol-2(5*H*)-ones **11a**,**b** formed different products during the action of concentrated HNO_3 under the same conditions. From the dihydroimidazoline **11a**, 3,3a,10,10a-tetrakis(4-methoxyphenyl)-5,6,12,13-tetrahydroimidazo[5,1-*b*:5',1'-*g*]-[1,6,3,8]dioxadiazecine-1,8(3a*H*,10a*H*)-dione (**12**), the product from cyclocondensation of two molecules of compound **11a**, was formed instead of the expected compound **2d**. According to data from the ^{1}H NMR spectra it is seen that compound **12** is one of the diastereomeric racemates with the 3a*R**,10a*S** configuration at the chiral carbon atoms, established by the data from X-ray structural analysis. Signals of the other racemate were not detected, showing that the formation of compound **12** is highly diastereoselective.

In the reaction of dihydroimidazoline **11b** with concentrated HNO_3 only the dihydroimidazooxazinone **9b** was formed instead of compound **2e**.



The preparation of compounds **9a**,**b** instead of compounds **2c**,**e** is of no lesser interest since the mechanism we proposed earlier for the formation of 2,8-di(hydroxyalkyl)-1,5-diphenylglycolurils [17] makes it possible to suppose that both compounds **2** and compounds **9**, which we were previously unable to isolate in the individual state, can be used for the regioselective synthesis of glycolurils.



13 a *n* = 1, **b**,**d** *n* = 2, **c** *n* = 3; **a**–**c** R = Ph, **d** R = 4-$MeOC_6H_4$

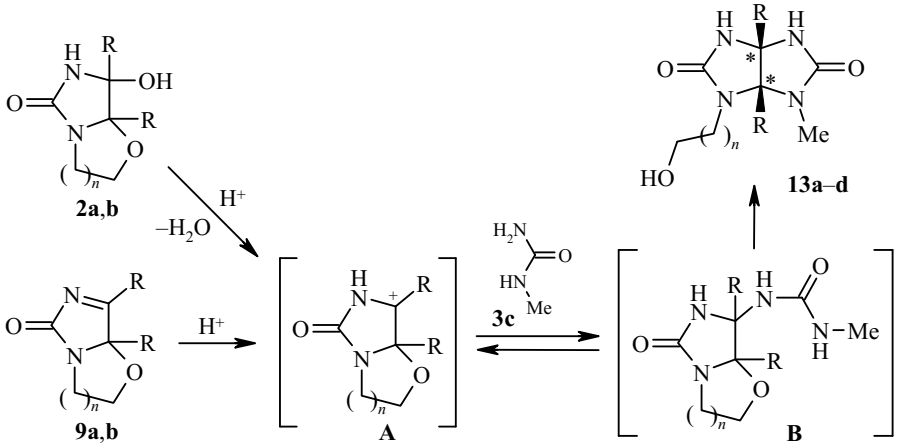
The condensation of compounds **2a**,**b** and **9a**,**b** with *N*-methylurea (**3c**) was conducted under conditions similar to those used for the synthesis of 2,8-di(hydroxyalkyl)glycoluril **1a** [17].

The reactions were monitored by means of the ^{1}H NMR spectra of the precipitated glycolurils **13a-d** (filtered and dried) in experiments carried out at specific time intervals. The optimum reaction time was determined from the maximum constant weight of the glycoluril precipitates from two consecutive experiments. Such monitoring was possible since no impurities of other products were found in the ^{1}H NMR spectra of the precipitates. In the case of the glycoluril **13b** the reaction took place in a suspension, and the formation of the glycoluril was determined from the appearance of signals for the protons of the NCH_3 group at 2.74 ppm (3H, s), the OH group at 4.39-4.80 ppm (1H, m), and the two singlets of the protons of the NH groups at 8.00 and 8.11 ppm and total disappearance of the signals of the initial compound **2b**: the protons of the CH_2 group at 1.20-1.33 (1H, m) and 1.72-1.92 ppm (1H, m) and the protons of the OH group at 5.89-5.97 ppm (1H, m) [17]. It was established that the glycoluril **13a** is formed after 20 min with a yield of 88% and the glycoluril **13b** after 8 h with a yield of 79%. The glycolurils **13c**,**d** were obtained with yields of 82 and 80%, respectively.

After extraction of the targeted compounds **13a-d**, signals for the protons of benzil and ammonium chloride, i.e., the products from decomposition of the reagents **2a** and **3c**, were detected in the residues of the reaction mixtures that had been evaporated to dryness. Signals of the protons of the isomeric 2,6-disubstituted 1,5-diphenylglycolurils were not found. It can therefore be stated that the reaction takes place with high regioselectivity.

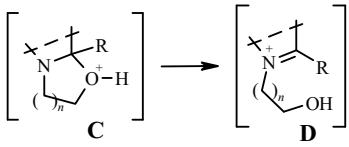
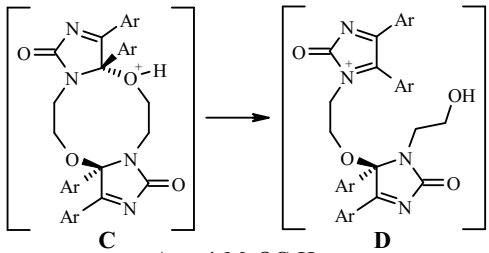
Unfortunately, compound **12** does not react with *N*-methylthiourea (**3c**).

The regioselectivity of the formation of 2,8-disubstituted 1,5-diphenylglycolurils **13a-d** when derivatives of imidazooxazolone **2a**, imidazooxazinones **2b** and **9b**, or imidazooxazepinone **9a** are used is evidently due to the fact that compounds **2** and **9** are capable in an acidic medium of generating a carbenium ion (the intermediate **A**), which then reacts with the *N*-methylurea (**3c**), forming the intermediate **B**, which undergoes cyclization to the 2,8-disubstituted glycolurils **13**.



In order to explain and confirm the obtained results we did quantum-chemical calculations on the opening of the oxazole, oxazine, oxazepine, and dioxadiazecine rings in the intermediates **C** and **D** by the Hartree–Fock method in the STO-3G basis set. This enabled us to obtain a relationship between the length of the reactions and the activation energies of the rate-controlling stages of the process (Table 1). The energy difference between the cyclic and open-chain protonated forms **C** and **D** was used as the activation energy of this process. It can be seen from the Table 1 that the energy of ring opening correlates with the experimental data (the length of the reactions), but in the case of compound **12** the calculations give reason to suppose that the opening of the dioxadiazecine ring will not.

TABLE 1. Correlations between the Reaction Time and Activation Energy (ΔE) of Compounds **2a**,**b**, **9a**,**b**, **12**

Compound	Reaction activation scheme	$\Delta E = E_C - E_D$, kcal/mol	Reaction time
13a	 **C** **D**	7.94	20 min
	n = 1, R = Ph		
13b	n = 2, R = Ph	14.82	8 h
13c	n = 3, R = Ph	10.34	50 min
13d	n = 2, R = 4-$MeOC_6H_4$	8.74	25 min
12	 **C** **D** Ar = 4-$MeOC_6H_4$	45.25	–

The structure of compounds **7b**, **8b**, **9**a,**b**, **11a**,**b**, **12**, and **13a-d** synthesized for the first time was confirmed by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. The structure of compounds **8b**, **9a**, and **12** was proved by X-ray structural analysis (Fig. 1).

In addition to the unambiguous confirmation of the structure of the synthesized compounds it was interesting to study these objects from the standpoint of supramolecular chemistry. Among the investigated compounds **8b**, **9a**, and **12**, only in compound **8** do the molecules form a clearly defined supramolecular associate – a hydrogen bonded centrosymmetric dimer (N(3)···O(l) 2.7716(19) Å, NHO angle 171(1)°). In the crystal of compound **12** a fairly short O···Cl contact (3.250(2) Å) links the molecules of the product with the chloroform solvate molecules, which are present in the crystal in a ratio of 1:4. According to X-ray structural analysis, compound **12** is a racemate with a configuration of chiral carbon atoms C(4)-(*S*), C(4A)-(*R*) and C(4)-(*R*), C(4A)-(*S*) (the atom numeration agrees with X-ray structural analysis). Compound **8b** crystallizes as a racemate.

The geometric parameters in the three crystals lie in the range of values characteristic of the given classes of compounds with the expected elongation of the N(3)–C(4) and C(4)–C(5) bonds and with shortening of the C(5)–N(1) bond in the transition from compound **8b** to compounds **9a** and **12**. The imidazole ring in compounds **8b** and **12** is planar with the atoms deviating from the mean-square plane by not more than 0.01(1) Å. In the case of compound **9a**, it has a flattened "envelope" conformation with the C(4) atom deviating by 0.09(1) Å. In compounds **9a** and **12,** the oxazine seven-membered and central ten-membered heterocycles have "chair" and "boat–boat" conformations, respectively. The sum of the valence angles at the nitrogen atoms is close to 360° within the limits from 359.9(1)° in compound **8b** to 358.9(2) and 357.8(2)° for the N(3) atom in compounds **9a** and **12**. The mutual arrangement of the aromatic substituents at the C(4) and C(5) atoms in compounds **8b** and **9a** is expectedly different: the torsional angle C(6)–C(4)–C(5)–C(12) amounts to 4.4(1) and 70.4(2)°. For comparison, the analogous angle in the case of the *p*-methoxyphenyl fragments in compound **12** amounts to 65.6(2)°. The bond lengths in the imidazole rings of compounds **8b**, **9a**, **12** are: N(1)–C(2) 1.3725(19), 1.441(2), and 1.434(3) Å; C(2)–N(3) 1.3608(19), 1.361(2), and 1.366(3) Å; N(3)–C(4) 1.3998(18), 1.452(2), and 1.463(2) Å; C(4)–C(5) 1.362(2), 1.544(2), and 1.547(3) Å; C(5)–N(1) 1.4014(18), 1.287(2), and 1.295(3) Å.

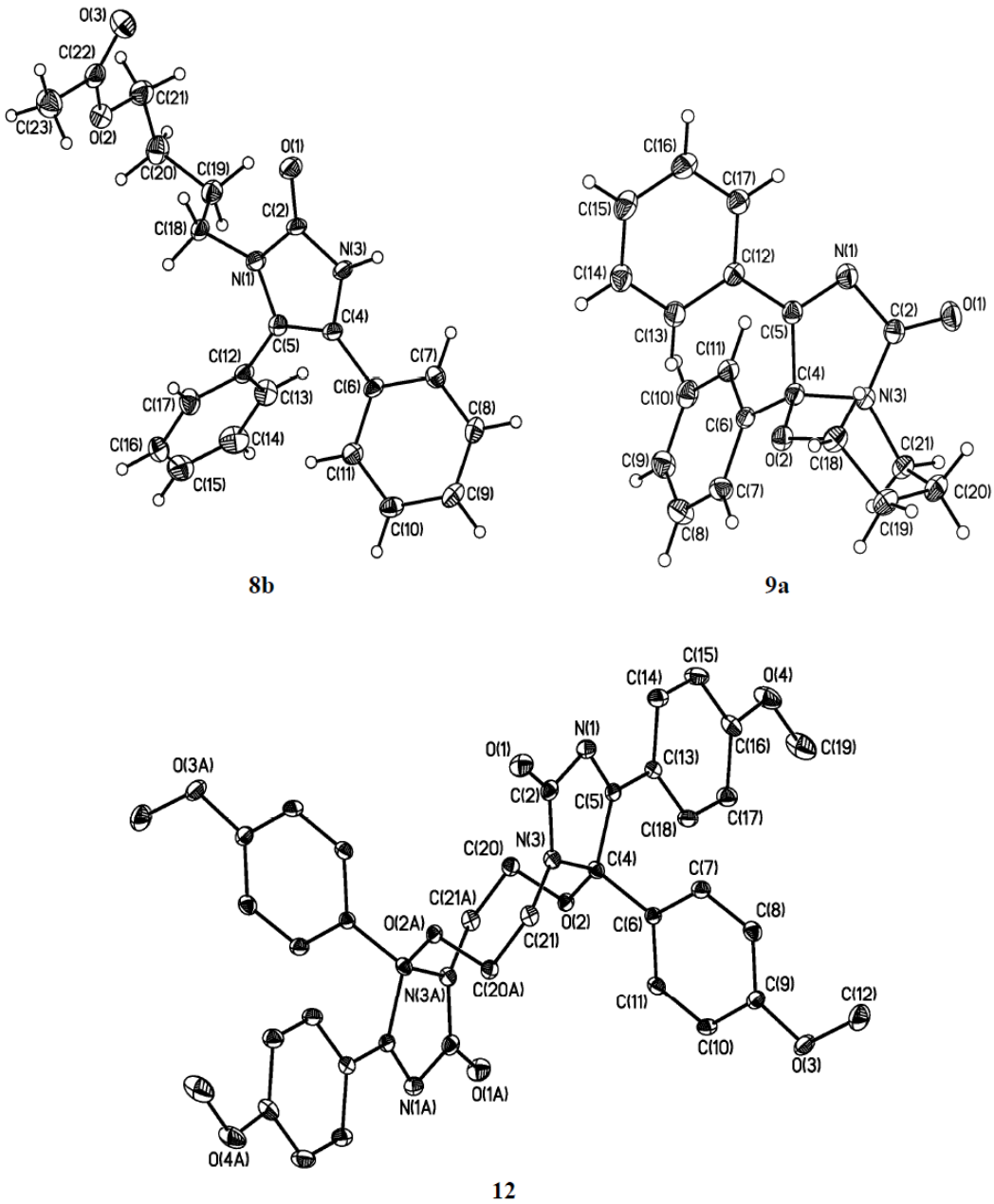


Fig. 1. General view of the molecules of compounds **8b**, **9a**, and **12** with the non-hydrogen atoms represented by thermal vibration ellipsoids with 50% probability. The chloroform solvate molecules in the crystal of compound **12** are not shown.

Thus, as a result of the investigations previously inaccessible 2,8-disubstituted 1,5-diarylglycolurils with different substituents at the nitrogen atoms were synthesized with high yields. It was possible to obtain these compounds as a result of the condensation of a representative of the monosubstituted ureas (*N*-methylurea) with derivatives of tetrahydroimidazooxazolone and tetrahydroimidazooxazinone. Moreover, it was shown for the first time that derivatives of dihydroimidazooxazinones (oxazepinones) can also be used for the regioselective synthesis of glycolurils. The developed methods are general in nature and may prove useful for the regioselective synthesis of other representatives of 2,8-disubstituted 1,5-diarylglycolurils.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75 MHz, respectively) in DMSO-d_6 with TMS as internal standard. Mass spectra were recorded on a Kratos MS30 instrument (EI, 70 eV). The high-resolution mass spectra were recorded on a Bruker micrOTOF II instrument with electrospray ionization. The measurements were made with positive (capillary potential 4500 V) or negative (capillary potential 3200 V) ions. The mass scanning rate was 50-3000 Da with external or internal calibration (Electrospray Calibrant Solution, Fluka). Injection of the substance in solutions in MeCN, MeOH, or H_2O, flow rate 3 μl/min. Spray gas N_2 (4 l/min), interface temperature 180°C. Elemental analysis was performed on Perkin Elmer 2400 CHN Analyzer and Euro EA Elemental Analyzer instruments. Melting points were determined on a Sanyo Gallenkamp instrument.

7-Hydroxy-7,7a-diphenyltetrahydroimidazo[5,1-*b*]oxazol-5(5*H*)-one (**2a**) was obtained from 1-(2-hydroxyethyl)urea (**3a**) and 2-hydroxy-1,2-diphenylethanone (benzoin) by the method in [17]. 8-Hydroxy-8,8a-diphenyltetrahydro-2*H*-imidazo[5,1-*b*][1,3]oxazin-6(7*H*)-one (**2b**) was synthesized by reaction of 1,2-dioxo-1,2-diphenylethane (benzil) with 1-(3-hydroxypropyl)urea (**3b**) [17]. 1-(2-Hydroxyethyl)urea (**3a**) and 1-(3-hydroxypropyl)urea (**3b**) were synthesized by N-carbamoylation of 2-aminoethanol (**4a**) and 3-aminopropanol, respectively, by treatment with KOCN according to the method in [23]. 2-Hydroxyimino-1,2-diphenylethanone (**6**) was synthesized from benzil and hydroxylamine hydrochloride by the method in [24]. 1-(2-Hydroxyethyl)-4,5-diphenyl-1*H*-imidazole 3-oxide (**7a**) was obtained by the method in [21]. 2-(2-Oxo-4,5-diphenyl-2,3-dihydro-1*H*-imidazol-1-yl)ethyl acetate (**8a**) was synthesized by the method in [22]. 2-Hydroxy-1,2-bis(4-methoxyphenyl)ethanone was the commercial product (Acros).

1-(4-Hydroxybutyl)-4,5-diphenyl-1*H*-imidazole 3-Oxide (7b). To a mixture of 4-aminobutan-1-ol (**4b**) (2.5 ml, 30 mmol) and paraform (**5**) (1.28 g, 40 mmol), MeOH (50 ml) was added. The reaction mixture was stirred at room temperature for 24 h and was then evaporated to dryness. The obtained resinous mixture was dissolved in MeOH (50 ml), and 2-(hydroxyimino)-1,2-diphenylethanone (**6**) (6.36 g, 30 mmol) was added. The reaction mixture was refluxed for 3 h. After that, it was evaporated to half and left to crystallize. The next day the product was filtered off. Yield 7.30 g (79%), white powder, mp 149-151°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15-1.35 (2H, m, CH_2); 1.47-1.70 (2H, m, CH_2); 3.20-3.30 (2H, m, CH_2); 3.82 (2H, t, *J* = 7.5, CH_2); 4.50-4.62 (1H, m, OH); 7.15-7.30 (2H, m, H Ph); 7.31-7.54 (8H, m, H Ph); 8.58 (1H, s, H-2). ^{13}C NMR spectrum, δ, ppm: 26.5, 29.1, 45.3, 59.9 ($4CH_2$); 125.9; 126.3; 127.6; 127.7; 127.8; 127.9; 128.3; 128.5; 129.0; 129.1; 129.2; 129.4; 130.0; 130.7; 132.9. Mass spectrum, *m*/*z* (I_{rel}, %): 308 $[M]^+$ (20), 292 (100), 262 (58), 233 (13), 219 (26), 176 (15), 165 (32), 135 (63), 119 (38), 104 (86). Found, %: C 74.02; H 6.53; N 9.05. $C_{19}H_{20}N_2O_2$. Calculated, %: C 74.00; H 6.54; N 9.08.

4-(2-Oxo-4,5-diphenyl-2,3-dihydro-1*H*-imidazol-1-yl)butyl Acetate (8b). To a suspension of compound **7b** (7.30 g, 25.0 mmol) in $CHCl_3$ (20 ml), a solution of Ac_2O (6.4 ml, 62.5 mmol) in $CHCl_3$ (10 ml) was added dropwise over 30 min with cooling on an ice bath. The reaction mixture was stirred at room temperature for 24 h, after which EtOH (30 ml) was added. The mixture was stirred for 30 min, evaporated to half, and left to crystallize. The crystals of the product were filtered off and washed with EtOH. Yield 4.73 g (54%), colorless crystals, mp 160-162°C. ^{1} H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (3H, s, CH_3); 1.80-2.10 (4H, m, $2CH_2$); 3.32-3.51 (2H, m, CH_2); 3.70-3.95 (2H, m, CH_2); 7.03-7.27 (4H, m, H Ph); 7.28-7.58 (6H, m, H Ph); 10.79 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 20.7 (CH_3); 25.2, 25.3, 63.2, 66.4 ($4CH_2$); 117.3, 120.4 (C-4,5); 125.4, 126.5, 128.4, 128.8, 129.0, 129.1, 129.7, 129.8, 130.4, 130.7 (C Ph); 153.2 (C=O); 170.3 (COO). Found, %: C 71.96; H 6.34; N 7.95. $C_{21}H_{22}N_2O_3$. Calculated, %: C 71.98; H 6.33; N 7.99.

9,9a-Diphenyl-2,3,4,5-tetrahydroimidazo[5,1-*b*][1,3]oxazepin-7(9*H*)-one (9a). 63% HNO_3 (5 ml) was added dropwise to a suspension of compound **8b** (4.73 g, 0.014 mol) in MeCN (35 ml). The reaction was monitored by the change in color and by the dissolution of the precipitated compound **8b**. The reaction mixture was extracted with a 1:1 $CHCl_3$–H_2O mixture, the chloroform layer was evaporated, and the product was rubbed with Et_2O. Yield 1.50 g (35%), white powder, mp 226-228°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.50-1.81

(4H, m, $2CH_2$); 2.54-2.70 (1H, m) and 3.07 (1H, t, J = 11.4, CH_2); 3.66 (1H, d, J = 14.6) and 3.98 (1H, d, J = 13.3, CH_2); 7.28-7.48 (7H, m, H Ph); 7.57 (1H, t, J = 7.4, H Ph,); 7.98 (2H, d, J = 7.6, H Ph). ^{13}C NMR spectrum, δ, ppm: 25.3, 29.5, 38.9, 65.0 ($4CH_2$); 96.8 (C-9a); 125.3, 128.3, 128.9, 129.0, 129.1, 129.5, 133.8, 136.7 (C Ph); 163.9 (C=O); 185.2 (C=N). Mass spectrum, m/z (I_{rel}, %): 306 $[M]^+$ (11), 203 (100), 175 (21), 147 (28), 117 (30), 105 (63). Found, %: C 74.46; H 5.95; N 9.16. $C_{19}H_{18}N_2O_2$. Calculated, %: C 74.49; H 5.92; N 9.14.

8,8a-Bis(4-methoxyphenyl)-3,4-2*H*-imidazo[5,1-*b*][1,3]oxazin-6(8a*H*)-one (9b). 63% HNO_3 (10 ml) was added dropwise to a suspension of 1-(3-hydroxypropyl)-4,5-bis(4-methoxyphenyl)-1*H*-imidazol-2(3*H*)-one (**11b**) (3.54 g, 0.01 mol) in MeCN (35 ml). The reaction was monitored by the change in color and by the dissolution of the precipitate. The reaction mixture was extracted with a 1:1 $CHCl_3$–H_2O mixture, the chloroform layer was evaporated, and the residue was rubbed with Et_2O. Yield 2.18 g (70%), white powder, mp 188-190°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.50-1.60 (1H, m) and 1.61-1.80 (1H, m, CH_2); 2.80-3.00 (1H, m) and 3.50-3.67 (1H, m, CH_2); 3.69-3.76 (2H, m, CH_2); 3.73 (3H, s, OCH_3); 3.79 (3H, s, OCH_3); 6.93-7.05 (4H, m, H Ar); 7.39 (2H, t, J = 8.6, H Ar); 8.03 (2H, d, J = 8.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 24.4, 36.0 ($2CH_2$); 55.1, 55.5 ($2OCH_3$); 62.8 (CH_2); 93.5 (C-9a); 112.1, 113.1, 114.3, 114.8, 120.9, 125.1, 126.4, 128.4, 129.3, 130.8, 131.9, 159.7 (C Ar); 163.4 (C=O); 184.6 (C=N). Found, m/z: 375.1305 $[M+Na]^+$. $C_{20}H_{20}N_2NaO_4$. Calculated, m/z: 375.1315 $[M+Na]^+$.

1-(2-Hydroxyethyl)-4,5-bis(4-methoxyphenyl)-1*H*-imidazol-2(3*H*)-one (11a). Ethylene glycol (10 ml) was added to a mixture of 2-hydroxy-1,2-bis(4-methoxyphenyl)ethanone (**10**) (2.72 g, 0.01 mol) and the urea **3a** (5.20 g, 0.05 mol). The mixture was stirred at 160°C for 1 h. It was then extracted with a 1:1 $CHCl_3$–H_2O mixture, the chloroform layer was evaporated, and the residue was rubbed with Et_2O. Yield 2.38 g (70%), white powder, mp 214-216°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.30-3.50 (4H, m, $2CH_2$); 3.68 (3H, s, OCH_3); 3.80 (3H, s, OCH_3); 4.48 (1H, s, OH); 6.78 (2H, d, J = 8.4, H Ar); 6.98-7.12 (4H, m, H Ar); 7.28 (2H, d, J = 8.4, H Ar); 10.67 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 42.9 (CH_2); 55.1 ($2OCH_3$); 58.9 (CH_2); 113.9; 114.1; 114.5; 117.0; 119.2; 121.8; 122.5; 126.7; 128.3; 132.4; 153.3 (C=O); 157.8, 159.4 (2C–OMe). Found, %: C 67.07; H 5.94; N 8.21. $C_{19}H_{20}N_2O_4$. Calculated, %: C 67.05; H 5.92; N 8.23.

1-(3-Hydroxypropyl)-4,5-bis(4-methoxyphenyl)-1*H*-imidazol-2(3*H*)-one (11b). This compound was obtained similarly from compound **10** (5.44 g, 0.02 mol) and the urea **3b** (11.80 g, 0.10 mol). Yield 0.86 g (12%), white powder, mp 218-220°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.40-1.60 (2H, m, CH_2); 3.20-3.31 (2H, m, CH_2); 3.40-3.52 (2H, m, CH_2); 3.68 (3H, s, OCH_3); 3.80 (3H, s, OCH_3); 4.47 (1H, t, J = 4.9, OH); 6.78 (2H, d, J = 8.5, H Ar); 6.98-7.12 (4H, m, H Ar); 7.28 (2H, d, J = 8.5, H Ar); 10.66 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 32.3, 37.7 ($2CH_2$); 55.0, 55.1 ($2OCH_3$); 58.1 (CH_2); 113.4; 114.5; 117.1; 118.9; 121.8; 122.4; 126.6; 132.2; 153.2 (C=O); 157.8, 159.4 (2C–OMe). Found, %: C 67.75; H 6.27; N 7.92. $C_{20}H_{22}N_2O_4$. Calculated, %: C 67.78; H 6.26; N 7.90.

(3a*R,10a*S**)-3,3a,10,10a-Tetrakis(4-methoxyphenyl)-5,6,12,13-tetrahydrodiimidazo[5,1-*b*:5',1'-*g*]-[1,6,3,8]dioxadiazecine-1,8(3a*H*,10a*H*)-dione (12)**. 63% HNO_3 (20 ml) was added dropwise to a suspension of compound **11a** (8.50 g, 0.025 mol) in MeCN (30 ml). The reaction was monitored by the change in color and by the dissolution of the precipitate. The reaction mixture was extracted with a 1:1 $CHCl_3$–H_2O mixture, the chloroform layer was evaporated, and the residue was rubbed with Et_2O. Yield 1.85 g (22%), white powder, mp >355°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.43-2.60 (2H, m, CH_2); 2.98-3.07 (2H, m, CH_2); 3.62-3.70 (2H, m, CH_2); 3.79 (6H, s, $2OCH_3$); 3.88 (6H, s, $2OCH_3$); 4.00-4.25 (2H, m, CH_2); 7.02 (8H, d, J = 8.6, H Ar); 7.19-7.35 (4H, m, H Ar); 7.95 (4H, d, J = 8.7, H Ar). ^{13}C NMR spectrum, δ, ppm: 55.2, 55.7 ($4OCH_3$); 55.9, 58.4 ($4CH_2$); 96.7 (O–C–Ar); 114.9, 120.5, 126.3, 126.4 131.5, 132.0 (C Ar); 159.7 (C–OMe); 164.0 (C=O); 183.5 (C=N). Found, m/z: 677.2593 $[M+H]^+$. $C_{38}H_{37}N_4O_8$. Calculated, m/z: 677.2606 $[M+H]^+$.

1-(2-Hydroxyethyl)-6-methyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (13a). Conc. HCl (0.1 ml) was added to a solution of compound **2a** (0.296 g, 1 mmol) and *N*-methylurea (**3c**) (0.074 g, 1 mmol) in MeCN (10 ml). The mixture was refluxed for 20 min. When the reaction mixture had

cooled the precipitate was filtered off, washed with a 1:1 $CHCl_3$–H_2O mixture (4 ml), and dried. Yield 0.310 g (88%), white powder, mp 337-339°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.75 (3H, s, CH_3); 2.83-2.90 (1H, m) and 3.33-3.43 (1H, m, CH_2); 3.49-3.59 (1H, m) and 3.63-3.73 (1H, m, CH_2); 4.79 (1H, t, *J* = 5.5, OH); 6.60-6.90 (2H, m, H Ph); 6.92-7.20 (8H, m, H Ph); 8.11 (2H, s, 2NH). ^{13}C NMR spectrum, δ, ppm: 27.5 (CH_3); 45.2, 59.5 ($2CH_2$); 79.1, 89.1 (C-3a,6a); 127.2, 127.4, 127.9, 128.0, 128.2, 128.3, 133.2, 133.6 (C Ph); 160.0, 160.1 (2C=O). Found, *m*/*z*: 353.1603 $[M+H]^+$. $C_{19}H_{21}N_4O_3$. Calculated, *m*/*z*: 353.1617 $[M+H]^+$.

1-(3-Hydroxypropyl)-6-methyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (13b). Conc. HCl (0.2 ml) was added to a suspension of compound **2b** (0.310 g, 1 mmol) and urea **3c** (0.074 g, 1 mmol) in MeCN (20 ml). The mixture was refluxed for 8 h. When the reaction mixture had cooled the precipitate was filtered off, washed with a 1:1 $CHCl_3$–H_2O mixture (4 ml), and dried. Yield 0.29 g (79%), white powder, mp 300-302°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.59-1.73 (2H, m, CH_2); 1.80-1.96 (2H, m, CH_2); 2.74 (3H, s, CH_3); 2.78-2.91 (1H, m) and 3.35-3.53 (1H, m, CH_2); 4.39-4.80 (1H, m, OH); 6.68-6.80 (2H, m, H Ph); 6.94-7.18 (8H, m, H Ph); 8.00 (1H, s, NH); 8.11 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 27.6 (CH_3); 32.6, 40.2, 58.5 ($3CH_2$); 79.0, 89.1 (C-3a,6a); 127.2, 127.3, 127.9, 128.0, 128.2, 128.3, 133.4, 137.7 (C Ph); 159.6, 159.8 (2C=O). Found, *m*/*z*: 389.1581 $[M+Na]^+$. $C_{20}H_{22}N_4NaO_3$. Calculated, *m*/*z*: 389.1584 $[M+Na]^+$.

1-(4-Hydroxybutyl)-6-methyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (13c). Conc. HCl (0.1 ml) was added dropwise to a solution of compound **9a** (0.310 g, 1 mmol) and urea **3c** (0.074 g, 1 mmol) in MeCN (10 ml). The mixture was refluxed for 50 min. When the reaction mixture had cooled the precipitate was filtered off, washed with a 1:1 $CHCl_3$–H_2O mixture (4 ml), and dried. Yield 0.31 g (82%), white powder, mp 235-237°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.38-1.45 (2H, m, CH_2); 1.49-1.65 (1H, m) and 1.70-1.87 (1H, m, CH_2); 2.65-2.71 (1H, m) and 3.29-3.33 (1H, m, CH_2); 2.73 (3H, s, CH_3); 3.37 (2H, t, *J* = 6.2, CH_2); 6.69-6.85 (2H, m, H Ph); 6.95-7.12 (8H, m, H Ph); 7.97 (1H, s, NH); 8.10 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 26.2 (CH_2); 27.5 (CH_3); 29.9, 42.6, 60.4 ($3CH_2$); 79.0, 89.1 (C-3a,6a); 127.2, 127.3, 127.9, 128.0, 128.2, 128.3, 133.9, 137.8 (C Ph); 159.6 (2C=O). Found, *m*/*z*: 381.1915 $[M+H]^+$. $C_{21}H_{25}N_4O_3$. Calculated, *m*/*z*: 381.1921 $[M+H]^+$.

1-(3-Hydroxypropyl)-3a,6a-bis(4-methoxyphenyl)-6-methyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (13d). Conc. HCl (0.1 ml) was added to dropwise a solution of compound **9b** (0.352 g, 1 mmol) and urea **3c** (0.074 g, 1 mmol) in MeCN (10 ml). The mixture was refluxed for 25 min. When the reaction mixture had cooled the precipitate was filtered off, washed with a 1:1 $CHCl_3$–H_2O mixture (4 ml), and dried. Yield 0.341 g (80%), mp 263-265°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.55-1.73 (1H, m) and 1.80-1.95 (1H, m, CH_2); 2.70 (3H, s, CH_3); 2.74-2.90 (1H, m) and 3.37-3.46 (3H, m, $2CH_2$); 3.62 (3H, s, OCH_3); 3.64 (3H, s, OCH_3); 4.45 (1H, t, *J* = 5.1, OH); 6.59-6.74 (6H, m, H Ar); 6.89 (2H, d, *J* = 8.5, H Ar); 7.89 (1H, s, NH); 8.01 (1H, s, NH). ^{13}C NMR spectrum , δ, ppm: 27.6 (CH_3); 32.8 (CH_2); 40.2 (CH_2); 55.2, 55.3 (2OMe); 58.6 (CH_2); 79.0, 89.1 (C-3a,6a); 112.9, 113.7, 125.3, 128.6, 129.3, 129.9 (C Ar); 159.1, 159.2 (2C–OMe); 159.7, 159.9 (2C=O). Found, *m*/*z*: 427.1970 $[M+H]^+$. $C_{22}H_{27}N_4O_5$. Calculated, *m*/*z*: 427.1984 $[M+H]^+$.

X-ray Structural Investigations of Compounds 8b, 9a, 12. The investigations were carried out on Smart 1000 CCD (compounds **8b**, **9a**) and Apex2 Duo CCD (compound **12**) diffractometers (MoKα radiation, graphite monochromator, ω-scan). The structures were solved by the direct method and refined by least-squares treatment in anisotropic full-matrix approximation in F^2_{hkl}. The hydrogen atom of the NH group in compound **8b** was located from difference Fourier electron density syntheses. The positions of the hydrogen atoms of the methyl and methylene groups were calculated geometrically. The remaining nitrogen atoms were refined in isotropic approximation by the "rider" method. All the calculations were carried out by the Shelxtl Plus software [25]. Basic crystallographic data and refinement parameters are shown in Table 2. The atomic coordinates and the full structural data have been deposited at the Cambridge Crystallographic Data Center (deposits CCDC 984562, CCDC 984563, and CCDC 984564, respectively).

TABLE 2. Basic Crystallographic Data and Refinement Parameters of Compounds **8b**, **9a**, and **12**

Compound	**12**	**8b**	**9a**
Empirical formula	$C_{42}H_{40}Cl_{12}N_4O$	$C_{21}H_{22}N_2O_3$	$C_{19}H_{18}N_2O_2$
Molecular mass	1154.18	350.41	306.35
T, K	120	100	298
Crystal system	Triclinic	Triclinic	Monoclinic
Space group	*P*1	*P*1	$P2_1/c$
Z	1	2	4
a, Å	10.2280(11)	9.2954(7)	10.1326(5)
b, Å	11.1377(12)	9.3535(7)	9.2941(4)
c, Å	11.4784(13)	11.9198(9)	16.6039(6)
α, deg	98.922(2)	76.053(2)	90.00
β, deg	101.361(2)	85.791(2)	99.144(4)
γ, deg	92.763(2)	62.0690(10)	90.00
V, Å^3	1262.3(2)	887.70(12)	1543.77(12)
D_{calc}, g·cm^{-3}	1.518	1.311	1.318
μ, cm^{-1}	7.12	0.88	0.87
F(000)	588	372	648
$2\theta_{max}$, °	56	57	58
Number of measured reflections	10918	9884	11044
Number of independent reflections	6067	4694	4092
Number of reflections with $I > 2\sigma(I)$	5038	3471	2305
Number of refined parameters	301	236	208
R_1	0.0473	0.0539	0.0565
wR_2	0.1363	0.1318	0.1308
GOOF	1.004	1.003	1.007
Residual electron density, e·Å^{-3} (d_{min}/d_{max})	1.162 / -1.106	0.342 / -0.279	0.248 / -0.224

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