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Synthesis of Novel 13a-(ω-Aminoalkyl)-8-oxoberbines by Means of Reaction of Homophthalic Anhydride with 1-Substituted 3,4-Dihydroisoquinolines. An Unexpected Formation of a Pyrrolo[3,4-*i*]berbindione

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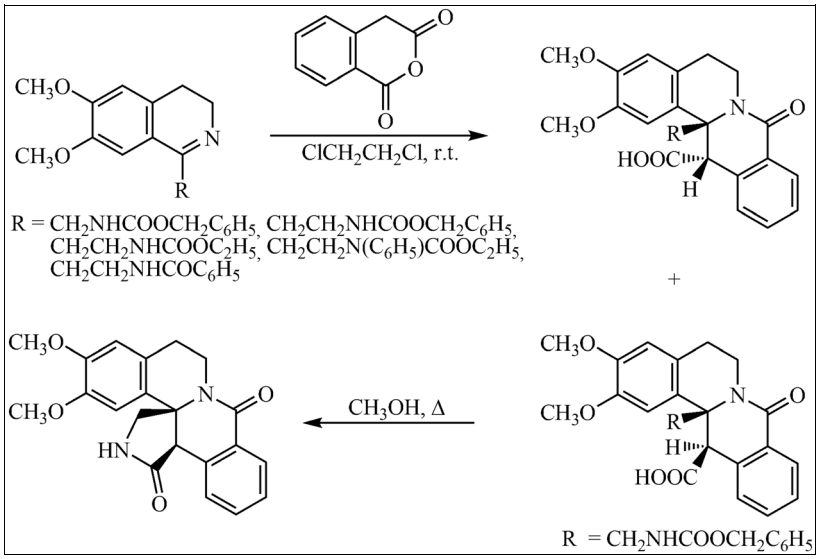


The reaction of 1-[ω-(*N*-acylated amino)alkyl]-3,4-dihydroisoquinolines (**7a–e**) with homophthalic anhydride (**1**) leads to the formation of 8-oxo-13a-[(*N*-acylated amino)alkyl]-8*H*-dibenzo[*a*,*g*]quinolizine-13-carboxylic acids (**8a–e**) with predomination of *cis* diastereomers, together with small amount of *trans*-**8a**. *cis*-13a-[(*N*-Cbzaminomethyl)]-8-oxo-dibenzoquinolizine-13-carboxylic acid (**8a**) cyclized to the unknown dibenzo[*a*,*g*]pyrrolo[3,4-*i*]quinolizinedione (**10**) upon moderate heating in methanol.

INTRODUCTION

The protoberberine (berbine-; dibenzo[*a*,*g*]quinolizine-) alkaloids constitute a big group of alkaloids incorporating a fused isoquinoline moiety [1–3]. Some 13-substituted tetrahydroprotoberberines possess different biological activities [3]. Berbines play a crucial role in the metabolism of isoquinoline alkaloids [4–6]. The reaction of homophthalic anhydride (**1**) with 3,4-dihydroisoquinolines provides a ready entry for one-pot construction of the protoberberine skeleton, leading to 8-oxo-13-carboxytetrahydroprotoberberines (8-oxo dibenzo[*a*,*g*]quinolizidine-13-carboxylic acids) [7–17]. Total syntheses of the protoberberine alkaloids thalictricavine, thalictrifoline, berlambine, canadine, cavidine, and corydaline have been performed from suitably substituted homophthalic anhydrides and 3,4-dihydroisoquinolines [9,11,12]. When 1-substituted 3,4-dihydroisoquinolines are used, the reaction products possess a substituent at C-13a position of the protoberberine skeleton [9,10,16]. There are few examples of 13a-substituted tetrahydroprotoberberines in the literature, including the naturally occurring (±)-solidaline (**2**) [18] and zijinlongine (**3**) [18,19] as well as the synthetically obtained 8,13a-propanoberbines [20] and 8-oxo-5,6,13,13a-tetrahydro-8*H*-dibenzo[*a*,*g*]quinolizin-13a-carboxylic acids [21] (Fig. 1). Recently, we showed that the reaction of homophthalic anhydride (**1**) with 1-(chloromethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline gives rise to *cis*-13a-(chloromethyl)-8-oxo-5,6,13,13a-tetrahydro-8*H*-dibenzo[*a*,*g*]quinolizin-13-carboxylic acid (**4**) [16] (Fig. 1). The molecular structure of the ester (**5**) was investigated by means of X-ray analysis, which showed *cis* configuration, with pseudoequatorial 13-$COOCH_3$ and pseudoaxial 13a-CH_2Cl groups with respect to the C-ring of the protoberberine skeleton [16]. The acid **4** was converted into the furodibenzoquinolizidinedione (**6**) by reaction of C-13a-CH_2Cl—substituent with the *cis*-oriented C-13-carboxyl group, in the presence of a base [16] (Fig. 1).

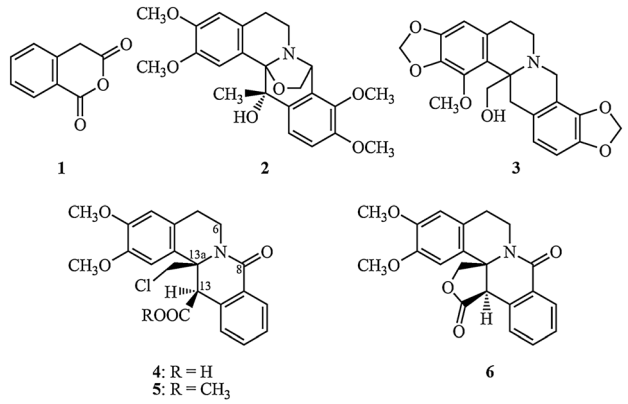


Figure 1. Homophthalic anhydride (**1**) and tetrahydroprotoberberine derivatives (**2–6**).

The aim of this paper is to further specify the scope of the reaction of homophthalic anhydride (**1**) with 1-substituted 3,4-dihydroisoquinolines of type **7** [22–25], which bear at C-1 position [ω-(*N*-acylated amino)]alkyl group, thus varying the structure of the 1-substituent in the cyclic imine. The targeted dibenzo[*a*,*g*]quinolizidinones—the acids **8**, and their methyl esters **9** will bear amino group in the C-13a-alkyl chain. Compounds **8** and **9** can be regarded as β,β′-, respectively, β,γ′—diamino acid derivatives, and as such, they are expected to possess biological activity [26–30] or they could serve as starting materials for further functional groups transformations of the protoberberines. From the other hand, the versatility of 1-substituted 3,4-dihydroisoquinolines as synthons for the preparation of fused polyheterocyclics containing bridgehead nitrogen atom [23,31–34] is demonstrated by this research once more.

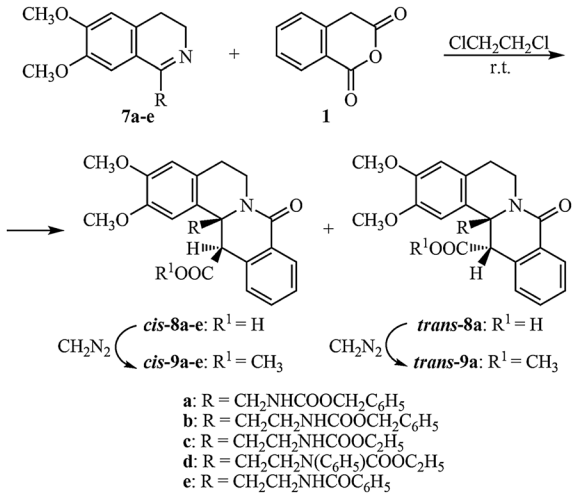
RESULTS AND DISCUSSION

Starting imines **7a** [22,25], **7b** [23,25], **7c** [25], and **7e** [24] have been described previously. The imine **7d** [35] was prepared in analogy to the preparation of imines **7a–c** and **e**.

The reaction of homophthalic anhydride (**1**) with the imines **7a–e** was carried out in dichloroethane at RT overnight, in analogy to the preparation of the previously described 13a-chloromethyl-8-oxoberbine-13-carboxylic acid (**4**) [16] (Scheme 1):

The anhydride (**1**) was taken in slight molar excess to increase the degree of the conversion of the cyclic imine (**7**). The reaction products, 13a-[(ω-*N*-acylamino)alkyl]-8-oxo-5,6,13,13a-tetrahydro-8*H*-dibenzo[*a*,*g*]quinolizin-13-carboxylic acids (**8a–e**), precipitated from the reaction mixture in 62–87% yield. TLC and ^{1}H-NMR spectra of the crystallized crude acidic reaction products **8a–e** showed that they consist of one product mainly. In analogy with our previous paper [16] and the comparison of the ^{1}H-NMR spectra of *cis*-**4** [16] with the spectra of major isomers of **8a–e**, we ascribed to them also a configuration with *cis* positioned 13-COOH and 13a-alkyl chain, which will be

Scheme 1. Synthesis of carboxylic acids (**8a–e**) and their methyl esters (**9a–e**) (the compounds are racemic; only one enantiomer is shown).



designated further in the text for shortness as *cis*. However, from the mother liquors of the acid **8a**, small amount of another isomer was isolated in 7% yield. Thus, we accepted that the structure of the minor diastereomer (**8a**) includes *trans*-oriented substituents at the C-13 and C-13a stereocentres and called shortly this product as *trans* isomer.

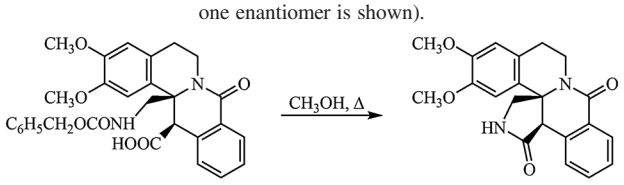
Similar formation of *cis*- and *trans*-8-oxotetrahydrodibenzo[*a*,*g*]quinolizin-13-carboxylic acids by reaction of homophthalic anhydrides with 3,4-dihydroisoquinolines was already observed. It was shown that *cis* isomers are products of thermodynamic, and *trans* isomers—of kinetic control [7–9,11,12,17,36]. Thermal treatment of *trans*-8-oxoberbin-13-carboxylic acids with acetic acid caused *trans* to *cis* epimerization [8,9]. Our attempts for epimerization of *trans*-**8a** upon reflux in acetic acid in analogy to the literature [8,9] proved to be unsuccessful. We observed a decomposition of the starting acid *trans*-**8a** and a formation of complex reaction mixture, from which we could not isolate the expected *cis* isomer. The failure of the epimerization is probably due to the steric hindrance of the substituent at C-13a.

The acidic compounds **8a–e** were converted into the corresponding methyl esters **9a–e** by reaction with diazomethane [7,8,16] (Scheme 1). Having in mind that the reaction of the acids *cis*-**8a-e** and *trans*-**8a** with diazomethane do not affect the chiral centers, we accepted *cis* relative configuration for the methyl esters **9a–e** obtained from *cis*-**8a-e**, and *trans* relative configuration for the ester **9a** obtained from *trans*-**8a**. This conclusion was supported by the comparison of ^{1}H-NMR spectra of the acids **8** and esters **9**: spectra of *cis*–**8a-e** are similar to the spectra of *cis*–**9a-e**, whereas the spectrum of *trans*-**8a** is similar to the spectrum of *trans*-**9a**. Thus, in the spectra of *cis*-**8a** and *cis*-**9a**, the signals for PhCH_2O appear as two doublets, each with $^2J = 12.2$ Hz. The signal of the same grouping in the spectra of *trans*-**8a** and *trans*-**9a** is a singlet,

that is, carbobenzoxy-CH_2 protons are isochronous. In ^{1}H-NMR spectrum of *cis*-**9a**, the singlet for $COOCH_3$ is shifted upfield, at δ 3.21, in comparison with the spectrum of *trans*-**9a**. Similar difference of chemical shifts of $COOCH_3$ singlets in ^{1}H-NMR spectra of *trans*- and *cis*-13-methoxycarbonyl-8-oxotetrahydroprotoberberines has been reported earlier [8]. In the spectra of *cis*-**9b-e**, however, the singlets for $COOCH_3$ appear in much lower field, relative to that of *cis*-**9a**. The ^{1}H-NMR spectra of the whole series of compounds **8** and **9**, regardless of their configuration, typically exhibit a strong deshielding of the signal for the equatorial 6-*H* (H_{eq}) proton, in comparison with the signal for axial 6-*H* (H_{ax}) proton, probably because of the anisotropic influence of 8-C═O group [7,8,16]. Similarly, deshielding is observed for the signal of the aromatic 9-*H* proton, influenced by the same 8-C═O group [7,8,16,37].

The relative configuration of *cis*-**8a** was further supported by its reactivity at reflux. A sample of *cis*-**8a** was dissolved in boiling methanol, then cooled, and treated with ethereal diazomethane. Immediate crystallization of a product occurred, which did not exhibit signals for COO*Me* as well as for C*H*$_2$Ph in its ^{1}H-NMR spectrum. The spectral data, coupled with the elemental analysis data of this product, are in agreement with the structure of 2,3-dimethoxy-5,6,14,15-tetrahydro-8*H*-dibenzo[*a*,*g*]pyrrolo[3,4-*i*]quinolizine-8,13(12b*H*)-dione (**10**) (pyrrolo[3,4-*i*]berbindione) (Scheme 2). The easy closure to the pyrrolidinone ring by reaction of C-13a-$PhCH_2OC(O)NHCH_2$ substituent with 13-COOH group, from one side, is in agreement with *cis* relationship of both substituents—the spatial orientation of the reacting groups is suitable for the cycle formation. From the other hand, such a behavior shows the thermal instability of the carbobenzyloxy-group in *cis*-**8a**, which is readily cleaved by moderate heating. This cyclization is probably auto catalytically assisted by the COOH group of the starting *cis*-**8a** (Scheme 2). Up to our knowledge, such dibenzo[*a*,*g*]pyrrolo[3,4-*i*]quinolizidine heterocyclic system as **10** has not been described previously. The formation of annelated lactam ring was not observed neither from *cis*-**8b**, which contains CbzNH—substituent, nor from *cis*-**8c-e**, under the conditions leading to **10**. However, in the case of acids *cis*-**8b-e**, the cyclization would lead to a six-membered, that is, piperidinone ring, which seems to influence the reactivity of the compounds in such a ring closure. This problem needs additional investigations. All compounds of types **8**, **9**, and **10** are new. They are obtained as racemic forms. For shortness, only one enantiomer is shown on the schemes.

Scheme 2. Synthesis of compound **10** (the compounds are racemic; only one enantiomer is shown).



cis-**8a** **10**

EXPERIMENTAL

Melting points (mps, °C) were determined on a Boetius PHMK 05 micro hot-stage apparatus (Germany) and are uncorrected. IR spectra were recorded on a Carl Zeiss-Jena Specord IR-75 spectrometer (Germany) using Nujol mulls, unless otherwise stated. NMR spectra were taken on Bruker DRX spectrometer (Germany) at 250 MHz for ^{1}H-NMR and at 62.5 MHz for ^{13}C-NMR spectra or on JEOL JNM-EX (Japan) at 270 and 300 MHz for ^{1}H-NMR and at 67.5, respectively, 75.0 MHz for ^{13}C-NMR spectra. For unambiguous signal assignment, standard DEPT and 2D homonuclear and heteronuclear spectra were recorded. $CDCl_3$ and DMSO-d_6 were used as solvents. The chemical shifts are given in parts per million (δ scale) from TMS as internal standard, and coupling constants (*J*) are given in hertz. Mass spectra (ms) of positive ions obtained by electron impact (EI, 70 eV) were measured on a Hewlett-Packard 5973 GC–MS Instrument (Germany). Analytical TLC was carried out on Merck (Germany) 1.05554 silica gel 60 F254 aluminum plates, layer thickness 0.2 mm. Spots were detected with UV light. Elemental analyses were carried out at the Faculty of Chemistry and Pharmacy, University of Sofia. Solvents and reagents were purchased and used without purification.

General procedure for preparation of (±)-*cis*- and (±)-*trans*-2,3-dimethoxy-13a-[(benzyloxycarbonylamino)methyl-], respectively, [2-(*N*-acylamino)ethyl]-8-oxo-5,6,13,13a-tetrahydro-8*H*-dibenzo[*a*,*g*]quinolizin-13-carboxylic acids (*cis*-8a-e and *trans*-8a). To a stirred solution of 3,4-dihydroisoquinoline (**7a–e**) (2 mmol) in dry dichloroethane (4 mL), homophthalic anhydride (**1**, 0.340 g, 2.1 mmol) was added portionwise. The reaction mixture was stirred overnight at RT, and the precipitated product was filtered and recrystallized. In this way, the following compounds were obtained:

(±)-cis-13a-[(Benzyloxycarbonylamino)methyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid (cis-8a). Yield 83% of white crystals, mp 190–192°C (ethyl acetate). IR: 1615 (C═O and C—C, aromatic), 1680 and 1715 (C═O), 2400–3200 (OH), 3350 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.75 (dd, 1H, *J* = 3.7, 12.9 Hz, 5-H_{eq}), 2.80 (m, 1H, 6-H_{ax}), 2.95 (bd, 1H, *J* = 12.9 Hz, 5-H_{ax}), 3.74 (m, 1H, N*H*CO), 3.85 (s, 3H, CH_3O), 3.91 (s, 3H, CH_3O), 4.08 (t, 2H, *J* = 6.1 Hz, NHC*H*$_2$), 4.37 (s, 1H, 13-H), 4.71 (d, 1H, *J* = 12.2 Hz, PhC*H*O), 4.90 (d, 1H, *J* = 12.2 Hz, PhC*H*O), 4.96 (m, 1H, 6-H_{eq}), 6.83 (s, 1H, 4-H), 7.02 (s, 1H, 1-H), 7.20–7.40 (m, 6H, ArH), 7.43 (t, 1H, *J* = 7.4 Hz, ArH), 7.49 (t, 1H, *J* = 7.4 Hz, ArH), 8.13 (dd, 1H, *J* = 1.0 Hz, 7.7 Hz, 9-H), 13.38 (bs, 1H, COOH). ^{13}C-NMR (62.5 MHz): δ 29.8 (5-CH_2), 38.8 (6-CH_2), 44.7 (NCH_2), 55.1 (CH_3O), 55.3 (CH_3O), 57.6 (13-C), 63.6 (13a-C), 65.1 (CH_2O), 106.6, 110.8, 112.0, 125.1, 125.6, 126.8, 127.4, 127.7, 127.8, 128.0, 128.2, 129.0, 129.7, 132.2, 134.5, 137.2, 146.6, 147.6 (aromatic C), 156.4 (NCO), 161.7 (NCO), 173.0 (COOH). MS: *m/z* (%) = no M$^+$, 354 (64), 246 (100), 219 (34), 205 (96), 190 (24), 162 (6), 118 (46), 91 (57). *Anal.* Calcd for $C_{29}H_{28}N_2O_7$ (516.5): C, 67.43; H, 5.46. Found: C, 67.37; H, 5.65.

(±)-trans-13a-[(Benzyloxycarbonylamino)methyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid (trans-8a). Mother liquors from two batches of the reaction between **1** and **7a** obtained after the filtration of crude

cis-**8a**, were united, and concentrated under vacuum to give *trans*-**8a**. Yield 7% of white crystals, mp 165–167°C (ethyl acetate). IR: 1640, 1700, and 1720 (C═O), 2800–3600 (OH), 3350 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$/DMSO-d_6 3:1): δ 2.76 (m, 3H, 5-CH_2, 6-H_{ax}), 3.55 (dd, 1H, *J* = 6.5, 14.5 Hz, C*H*NH), 3.73 (s, 3H, CH_3O), 3.77 (s, 3H, CH_3O), 4.13 (s, 1H, 13-H), 4.30 (dd, 1H, *J* = 6.5, 14.5 Hz, C*H*NH), 4.88 (s, 2H, PhCH_2O), 4.95 (m, 1H, 6-H_{eq}), 6.83 (s, 1H, 4-H), 7.02 (s, 1H, 1-H), 7.10–7.30 (m, 7H, ArH, NH), 7.34 (t, 1H, *J* = 7.7 Hz, ArH), 7.55 (t, 1H, *J* = 7.7 Hz, ArH), 7.95 (d, 1H, *J* = 7.7 Hz, 9-H), 13.15 (bs, 1H, COOH). ^{13}C-NMR (62.5 MHz): δ 29.9 (5-CH_2), 37.9 (6-CH_2), 45.3 (13a-CH_2), 55.7 (CH_3O), 55.9 (CH_3O), 56.9 (13-C), 63.8 (13a-C), 66.3 (CH_2O), 109.8, 111.7, 125.1, 127.3 (2 × C), 127.7 (2 × C), 128.1 (2 × C), 128.3, 129.0, 129.2, 132.4, 131.9, 133.8, 136.1, 147.2, 147.9 (aromatic C), 155.8 (NCO), 162.8 (NCO), 173.8 (COOH). *Anal*. Calcd for $C_{29}H_{28}N_2O_7$ (516.5): C, 67.43; H, 5.46. Found: C, 67.28; H 5.70.

(±)-cis-13a-[2-(Benzyloxycarbonylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid (cis-8b). Yield 62% of white crystals, mp 180–183°C (ethyl acetate). IR: 1615 (C═O and C—C aromatic), 1665 and 1705 (C═O), 2400–3200 (OH), 3420 (NH) cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$/DMSO-d_6 1:1): δ 2.10–2.26 (m, 1H, 13a-C*H*), 2.82–2.88 (m, 3H, 5-CH_2, 6-H_{ax}), 2.89–3.10 (m, 3H, 13a-CH, NHC*H*, PhC*H*O); 3.30–3.40 (m, 1H, NHC*H*), 3.91 (d, 1H, *J* = 11.4 Hz, PhC*H*O), 3.94 (s, 3H, CH_3O), 3.96 (s, 3H, CH_3O), 4.18 (s, 1H, 13-H), 5.24 (bd, 1H, *J* = 9.5 Hz, 6-H_{eq}), 6.44 (s, 1H, 4-H), 6.68 (bs, 1H, NH); 6.92 (s, 1H, 1-H), 7.18–7.41 (m, 8H, ArH), 8.16 (dd, 1H, *J* = 1.9, 7.6 Hz, 9-H), 13.08 (bs, 1H, COOH). ^{13}C-NMR (67.5 MHz): δ 30.2 (5-CH_2), 45.2 (6-CH_2), 33.9 (13a-CH_2), 35.7 (NCH_2), 55.2 (CH_3O), 55.6 (CH_3O), 58.9 (13-C), 59.7 (13a-C), 62.6 (CH_2O), 102.2, 109.5, 111.2, 112.5, 125.6, 126.4, 127.0, 127.4, 127.6, 128.0, 128.3, 130.3, 131.6, 133.9, 134.3, 140.5, 147.0, 147.3 (aromatic C), 162.4 (NCO), 166.3 (NCO), 172.4 (COOH). *Anal*. Calcd for $C_{30}H_{30}N_2O_7$ (530.6): C 67.90; H 5.70. Found: C 67.57; H 5.90%.

(±)-cis-13a-[2-(Ethoxycarbonylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid (cis-8c). Yield 64% of white crystals, mp 192–194°C (dichloroethane). IR: 1620, 1660, and 1700 (C═O), 2400–3200 (OH), 3420 (NH) cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.18 (t, 3H, *J* = 7.2 Hz, CH_3), 2.17 (m, 1H, 13a-CH), 2.66–2.73 (m, 3H, 13a-CH, 5-CH_2), 2.81–2.94 (m, 2H, NHC*H*, 6-H_{ax}), 3.28 (s, 3H, CH_3O), 3.36 (m, 1H, NHC*H*), 3.82 (s, 3H, CH_3O), 3.96 (q, 2H, *J* = 4.1, 7.2 Hz, CH_2O), 4.18 (s, 1H, 13-H), 5.16 (bd, 1H, *J* = 10.0 Hz, 6-H_{eq}), 6.67 (s, 1H, 4-H), 6.90 (s, 1H, 1-H), 7.10 (d, 1H, *J* = 8.0 Hz, ArH), 7.34 (bd, 1H, *J* = 6.4 Hz, NH), 7.41–7.51 (m, 2H, ArH), 8.14 (bd, 1H, *J* = 8.0 Hz, 9-H), 12.30 (bs, 1H, COOH). ^{13}C-NMR (75 MHz): δ 14.6 (CH_3), 30.8 (5-CH_2), 39.4 (6-CH_2), 35.9 (13a-CH_2), 37.3 (NCH_2), 55.0 (CH_3O), 55.8 (CH_3O), 58.2 (13-C), 62.2 (13a-C), 62.9 (CH_2O), 107.5, 111.8, 126.3, 126.7, 128.0, 128.3, 129.1, 147.8, 147.9 (aromatic C), 158.8 (NCO), 163.0 (NCO), 176.4 (COOH). MS: *m/z* (%) = no M^+, 354 (64), 246 (100), 219 (34), 205 (96), 190 (24), 162 (6), 118 (46), 91 (57). *Anal*. Calcd for $C_{25}H_{28}N_2O_7$ (468.5): C, 64.09, H, 6.02. Found: C 63.78; H 6.32.

(±)-cis-13a-[2-(Ethoxycarbonylanilino)-ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid (cis-8d). Yield 87% of white crystals, mp 171–173°C (methanol). IR: 1615, 1700, and 1730 (C═O), 2400–3200 and 3560 (OH) cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$): δ 1.09 (t, 3H, *J* = 7.1 Hz, CH_3), 2.33 (t, 1H, *J* = 12.6 Hz, 13a-CH), 2.63–3.05 (m, 4H, 5-CH_2, 6-H_{ax}, 13a-C*H*), 3.23–3.44 (m, 1H, NC*H*), 3.54 (s, 3H, CH_3O), 3.57–3.72 (m, 1H, NC*H*), 3.88 (s, 3H, CH_3O), 4.00 (q, 2H, *J* = 7.0 Hz, CH_2O), 4.18 (s, 1H, 13-H), 5.15 (bd, 1H, *J* = 11.3, 6-H_{eq}), 6.68 (s, 1H, 4-H), 6.83 (s, 1H, 1-H), 6.92–7.10 (m, 3H, ArH), 7.10–7.28 (m, 3H, ArH), 7.39–7.55 (m, 2H, ArH), 8.09 (dd, 1H, *J* = 1.4, 7.4 Hz, 9-H), 12.05 (bs, 1H, COOH). ^{13}C-NMR (67.5 MHz): 14.4 (CH_3), 26.3 (5-CH_2), 47.0 (6-CH_2), 30.7 (13a-CH_2), 40.1 (NCH_2), 55.6 (CH_3O), 55.7 (CH_3O), 58.9 (13-C), 61.7 (13a-C), 63.0 (CH_2O), 102.6, 109.1, 111.7, 125.9, 126.3, 126.5, 126.8, 128.0, 128.2, 128.3, 128.4, 128.8, 129.0, 132.5, 134.2, 141.6, 147.5, 147.9 (aromatic C), 155.2 (NCO), 163.4 (NCO), 173.1 (COOH). *Anal*. Calcd for $C_{31}H_{32}N_2O_7$ (544.6): C, 68.37; H 5.92. Found: C, 68.02; H, 6.29.

(±)-cis-13a-[2-(Benzoylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid (cis-8e). Yield 86% of white crystals, mp 181–182°C (ethyl acetate). IR: 1610 (C═O, C—C aromatic), 1660, and 1705 (C═O), 2400–3200 (OH) and 3420 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$/DMSO-d_6 1:1): δ 2.04–2.24 (m, 1H, 13a-CH), 2.73–3.06 (m, 4H, 5-CH_2, 6-H_{ax}, 13a-CH), 3.10–3.25 (m, 1H, NHC*H*), 3.35–3.50 (m, 1H, NHC*H*), 3.90 (s, 3H, CH_3O), 3.93 (s, 3H, CH_3O), 4.17 (s, 1H, 13-H), 5.13 (bd, 1H, *J* = 8.6 Hz, 6-H_{eq}), 6.71 (s, 1H, 4-H), 6.86 (bs, 1H, NH), 7.18 (s, 1H, 1-H), 7.20–7.40 (m, 6H, ArH), 7.60 (m, 2H, Ar H), 8.13 (dd, 1H, *J* = 1.6, 7.4 Hz, 9-H), 12.5 (bs, 1H, COOH). ^{13}C-NMR (62.5 MHz): δ 30.2 (5-CH_2), 39.2 (6-CH_2), 33.9 (13a-CH_2), 35.7 (NCH_2), 55.2 (CH_3O), 55.7 (CH_3O), 58.9 (13-C), 62.7 (13a-C), 109.7, 111.4, 118.7, 125.7, 126.5, 126.5, 127.2, 127.6, 127.8, 128.2, 128.5, 130.5, 132.5, 131.8, 134.0, 134.5, 147.2, 147.6 (aromatic C), 162.7 (NCO), 166.6 (NCO), 172.7 (COOH). *Anal*. Calcd for $C_{29}H_{28}N_2O_6$ (500.5): C, 69.58; H, 5.64. Found: C, 69.90; H, 6.00.

General procedure for preparation of methyl esters of (±)-*cis*- and (±)-*trans*-13a-[*N*-(benzyloxycarbonylamino)methyl]- and [2-*N*-(acylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8*H*-dibenzo[*a*,*g*]quinolizine-13-carboxylic acids (*cis*-9a-e and *trans*-9a) and (±)-5,6,14,15-tetrahydro-2,3-dimethoxy-8*H*-dibenzo[*a*,*g*]pyrrolo[3,4-*i*]quinolizine-8,13(12b*H*)-dione (10). The corresponding acid **8b–e** (0.5 mmol) was dissolved in solution of CH_2Cl_2/methanol (1:1, 4 mL) and treated with a solution of diazomethane in ether [38], prepared from *N*-nitroso-*N*-methyl-*p*-toluenesulfonamide. After evaporation of the solvents, the residue was recrystallized to give the methyl esters **8b–e**. The acid *cis*-**8a** was dissolved in methanol at heating. Upon cooling, the solution was treated with ethereal solution of diazomethane. Immediate deposition of crystals occurred. These crystals were filtered off to give **10**, and the mother liquor was concentrated to give *cis*-**9a**. The following compounds were obtained:

(±)-cis-13a-[(Benzyloxycarbonylamino)methyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid methyl ester (cis-9a). Yield 50% of white solid, mp 273–274°C (ethyl acetate). IR: 1640, 1690, and 1730 (C═O), 3350 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.67 (bd, 1H, *J* = 14.9 Hz, 5-H_{ax}), 2.90–3.10 (m, 2H, 5-H_{eq}, 6-H_{ax}), 3.21 (s, 3H, $COOCH_3$), 3.54 (dd, 1H, *J* = 4.9, 14.1 Hz, 13a-C*H*NH), 3.86 (s, 4H, CH_3O, 13a-C*H*NH), 3.88 (s, 3H, CH_3O), 4.47 (s, 1H, 13-H), 4.71 (d, 1H, *J* = 12.2 Hz, PhC*H*O), 4.90 (d, 1H, *J* = 12.2 Hz, PhC*H*O), 4.96 (bs, 1H, NH), 5.09 (bd, 1H, *J* = 12.0 Hz, 6-H_{eq}), 6.63 (s, 1H, 4-H), 6.86 (s, 1H, 1-H), 7.21 (s, 1H, ArH), 7.20–7.30 (m, 5H, ArH), 7.44 (m, 2H, ArH), 8.10 (d, 1H, *J* = 7.4 Hz, 9-H). ^{13}C-NMR (62.5 MHz): δ 28.5 (5-CH_2), 37.1 (6-CH_2), 49.8

(13a-CH_2), 51.8 (COO*C*H_3), 53.5 (CH_3O), 55.8 (CH_3O), 56.3 (13-C), 62.5 (13a-C), 66.9 (CH_2O), 109.1, 109.2, 111.7, 112.1, 125.0, 126.4, 127.3, 127.4, 127.7, 127.9, 128.0, 128.4, 129.5, 131.8, 133.4, 136.2, 146.8, 147.7 (aromatic C), 156.1 (NCO), 162.3 (NCO), 171.7 (COOH). *Anal*. Calcd for $C_{30}H_{30}N_2O_7$ (530.6): C, 67.90; H, 5.70. Found: C, 68.20; H, 5.56.

(±)-5,6,14,15-Tetrahydro-2,3-dimethoxy-8H-dibenzo[a,g]pyrrolo[3,4-i]quinolizine-8,13(12bH)-dione (10). Yield 50% of white solid, mp 131–132°C (methanol/ether). IR (KBr): 1637 and 1700 (C═O), 3341 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.73 (dt, 1H, *J* = 3.9, 16.2 Hz, 5-H_{ax}), 3.00–3.20 (m, 1H, 5-H_{eq}), 3.40 (dq, 1H, *J* = 2.5, 4.3, 6.3, 13.0 Hz, 6-H_{ax}), 3.70 (dd, 1H, *J* = 1.1, 10.2 Hz, 13a-C*H*NH), 3.82 (d, 1H, *J* = 10.2 Hz, 13a-C*H*NH), 3.86 (s, 3H, CH_3O), 3.88 (s, 3H, CH_3O), 4.17 (s, 1H, 13-H), 4.84 (dq, 1H, *J* = 3.5, 5.6, 13.0 Hz, 6-H_{eq}), 6.06 (bs, 1H, NH), 6.63 (s, 1H, 4-H), 6.91 (s, 1H, 1-H), 7.40 (t, 1H, *J* = 7.6 Hz, ArH), 7.52 (td, 1H, *J* = 1.5, 7.6 Hz, aromatic H), 7.73 (d, 1H, *J* = 7.7, ArH), 8.18 (dd, 1H, *J* = 1.2, 7.8 Hz, 9-H). MS: *m/z* = 364 (M^+, 13), 354 (33), 308 (21), 307 (51), 292 (28.5), 247 (25), 246 (100), 231 (29), 205 (76), 203 (32), 202 (21), 191 (8), 160 (14), 118 (60), 108 (33). *Anal*. Calcd for $C_{21}H_{20}N_2O_4$ (364.4): C, 69.22; H, 5.53. Found: C, 69.02; H, 5.56.

(±)-trans-13a-[(Benzyloxycarbonylamino)methyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid methyl ester (trans-9a). Yield 85% of white crystals, mp 203–206°C (ethyl acetate). IR: 1645, 1725, and 1730 (C═O), 3270 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.74 (bd, 1H, *J* = 10.5 Hz, 5-H_{ax}), 2.86–2.99 (m, 2H, 5-H_{eq}, 6-H_{ax}), 3.78 (s, 3H, $COOCH_3$), 3.84 (s, 3H, CH_3O), 3.86 (q, 1H, *J* = 6.8, 14.9 Hz, 13a-C*H*NH), 3.90 (s, 3H, CH_3O), 4.26 (s, 1H, 13-H), 4.30 (q, 1H, *J* = 7.0, 14.9 Hz, 13a-C*H*NH), 4.64 (t, 1H, *J* = 6.7 Hz, NH), 4.95 (s, 2H, CH_2O), 5.19 (bd, 1H, *J* = 9.7 Hz, 6-H_{eq}), 6.71 (s, 1H, 4-H), 6.82 (s, 1H, 1-H), 6.91 (d, 1H, *J* = 7.3 Hz, aromatic H), 7.30–7.50 (m, 7H, ArH), 8.14 (d, 1H, *J* = 7.1 Hz, 9-H). ^{13}C-NMR (62.5 MHz): δ 26.0 (5-CH_2), 37.1 (6-CH_2), 43.6 (13a-CH_2), 48.0 (CH_2O), 53.5 (COO*C*H_3), 54.3 (13-C), 54.7 (CH_3O), 54.3 (CH_3O), 64.3 (13a-C), 107.2, 110.5, 112.2, 125.0, 126.1, 126.2, 126.4 (2 × C), 127.2, 127.3 (2 × C), 128.0, 130.6, 130.7, 136.2, 146.0, 146.8, 147.0 (aromatic C), 160.0 (NCO), 161.4 (NCO), 172.2 (COOH). *Anal*. Calcd for $C_{30}H_{30}N_2O_7$ (530.6): C, 67.90; H, 5.70. Found: C, 67.65; H, 6.06.

(±)-cis-13a-[2-(Benzyloxycarbonylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid methyl ester (cis-9b). Yield 81% of white crystals, mp 228–231°C (ethyl acetate–hexane). IR: 1650, 1710, and 1730 (C═O), 3380 (NH) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.15–2.30 (m, 1H, 13a-C*H*), 2.78–3.10 (m, 5H, 5-CH_2, 6-H_{ax}, 13a-CH, PhC*H*O), 3.10–3.26 (m, 1H, NHC*H*), 3.40–3.65 (m, 1H, NHC*H*), 3.71 (s, 3H, $COOCH_3$), 3.91 (s, 4H, CH_3O, PhC*H*O), 3.92 (s, 3H, CH_3O), 4.23 (s, 1H, H-13), 5.23 (ddd, 1H, *J* = 2.5, 5.4, 10.8 Hz, 6-H_{eq}), 5.98 (t, 1H, *J* = 5.0 Hz, NH), 6.72 (s, 1H, 4-H), 6.92 (s, 1H, 1-H), 6.98 (m, 1H, ArH), 7.30–7.40 (m, 6H, ArH), 7.56 (m, 1H, ArH), 8.16 (d, 1H, *J* = 9.1 Hz, 9-H). ^{13}C-NMR (75 MHz): δ 30.8 (5-CH_2), 43.0 (6-CH_2), 37.5 (13a-CH_2), 40.0 (NCH_2), 51.9 (COO*C*H_3), 59.2 (13-C), 55.8 (CH_3O), 56.2 (CH_3O), 63.2 (13a-C), 69.0 (CH_2O), 109.1, 112.1, 118.0, 125.9, 126.7, 127.2, 128.2, 128.4, 128.5, 128.7, 129.2, 131.3, 132.5, 134.2, 134.5, 135.5, 148.0, 148.4 (aromatic C), 163.4 (NCO), 167.2 (NCO), 172.0 (COOH); MS *m/z* (%) = no M^+, 366 (100), 307 (18), 292 (21), 217 (37), 205 (8), 176 (5), 105 (14), 77 (9). *Anal*. Calcd for $C_{31}H_{32}N_2O_7$ (544.6): C, 68.37; H, 5.99. Found: C, 67.67; H 5.65.

(±)-cis-13a-[2-(Ethoxycarbonylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-$32#13-carboxylic acid methyl ester (cis-9c). Yield 82% of white crystals, mp 236–238°C (ethyl acetate). IR: 1640, 1710, and 1730 (C═O), 3400 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.15 (t, 3H, *J* = 7.1 Hz, CH_3), 2.07–2.17 (m, 1H, 13a-C*H*), 2.75–2.98 (m, 5H, 5-CH_2, 13a-CH, 6-H_{ax}, NHC*H*), 3.10–3.20 (m, 1H, NHC*H*), 3.69 (s, 3H, $COOCH_3$), 3.89 (s, 3H, CH_3O), 3.91 (s, 3H, CH_3O), 3.99 (q, 2H, *J* = 4.1, 7.1 Hz, CH_2O), 4.19 (s, 1H, 13-H), 4.43 (bs, 1H, NH), 5.21 (ddd, 1H, *J* = 2.3, 3.9, 10.1 Hz, 6-H_{eq}), 6.71 (s, 1H, 4-H), 6.88 (s, 1H, H-1), 6.97 (m, 1H, ArH), 7.44–7.50 (m, 2H, ArH), 8.14 (dd, 1H, *J* = 2.4, 7.5 Hz, 9-H). ^{13}C-NMR (125 MHz): δ 14.5 (CH_3), 30.8 (5-CH_2), 39.9 (6-CH_2), 34.8 (13a-CH_2), 37.0 (NCH_2), 52.0 (COO*C*H_3), 55.8 (CH_3O), 56.1 (CH_3O), 59.1 (13-C), 62.9 (13a-C), 60.5 (CH_2O), 102.2, 108.9, 111.9, 125.9, 127.0, 128.1, 128.7, 128.8, 129.1, 132.5, 134.3, 147.8, 148.2 (aromatic C), 156.2 (NCO), 163.2 (NCO), 172.0 (COOH). *Anal*. Calcd for $C_{26}H_{30}N_2O_7$ (482.5): C, 64.71; H, 6.27. Found: C, 64.41; H, 6.58.

(±)-cis-13a-[2-(Ethoxycarbonylanilino)-ethyl]-2,3-dimethoxy-8-oxo- 5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid methyl ester (cis-9d). Yield 78% of white crystals, mp 195–197°C (ethyl acetate). IR: 1635, 1705, and 1730 (C═O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.10 (t, 3H, *J* = 7.1 Hz, CH_3), 2.27–2.45 (m, 1H, 13a-CH), 2.72–3.00 (m, 4H, 5-CH_2, 6-H_{ax},13a-CH), 3.28–3.3 (m, 1H, NCH), 3.60 (s, 3H, $COOCH_3$), 3.63 (s, 3H, CH_3O), 3.59–3.70 (m, 1H, NCH), 3.87 (s, 3H, CH_3O), 4.01 (q, 2H, *J* = 7.1 Hz, CH_2O), 4.15 (s, 1H, 13-H), 5.18 (dd, 1H, *J* = 2.2, 9.9 Hz, 6-H_{eq}), 6.62 (s, 1H, 4-H), 6.67 (s, 1H, 1-H), 6.93–7.24 (m, 6H, ArH), 7.39–7.50 (m, 2H, ArH), 8.09 (dd, 1H, *J* = 1.5, 7.2 Hz, 9-H). ^{13}C-NMR (75 MHz): δ 14.4 (CH_3), 30.8 (5-CH_2), 39.8 (6-CH_2), 32.8 (13a-CH_2), 37.0 (NCH_2), 51.8 (COO*C*H_3), 55.6 (CH_3O), 55.7 (CH_3O), 59.1 (13-C), 61.4 (13a-C), 62.8 (CH_2O), 100.4, 108.5, 111.8, 125.7, 126.3, 126.7, 127.0, 128.1, 128.5, 128.7, 128.8, 129.2, 130.5, 132.3, 134.1, 141.9, 147.6, 147.9 (aromatic C), 155.0 (NCO), 163.0 (NCO), 171.9 (COOH). *Anal*. Calcd for $C_{32}H_{34}N_2O_7$ (558.6): C, 68.80; H, 6.14. Found: C, 69.01; H, 6.00.

(±)-cis-13a-[2-(Benzoylamino)ethyl]-2,3-dimethoxy-8-oxo-5,8,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine-13-carboxylic acid methyl ester (cis-9e). Yield 78% of white crystals, mp 229–230°C (ethyl acetate–hexane). IR: 1620, 1660, and 1700 (C═O), 3410 (NH) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.15–2.25 (m, 1H, 13a-C*H*), 2.78–3.06 (m, 4H, 5-CH_2, 13a-C*H*, 6-H_{ax}), 3.06–3.25 (m, 1H, NHC*H*), 3.45–3.60 (m, 1H, NHC*H*), 3.71 (s, 3H, $COOCH_3$), 3.90 (s, 3H, CH_3O), 3.91 (s, 3H, CH_3O), 4.23 (s, 1H, 13-H), 5.24 (dd, 1H, *J* = 2.2, 8.2 Hz, 6-H_{eq}), 5.97 (m, 1H, NH), 6.73 (s, 1H, 4-H), 6.94 (s, 1H, 1-H), 7.0 (m, 1H, ArH), 7.20–7.40 (m, 5H, ArH), 7.56 (m, 2H, ArH), 8.16 (d, 1H, *J* = 1.5, 7.2 Hz, 9-H). ^{13}C-NMR (62.5 MHz): δ 30.9 (5-CH_2), 40.0 (6-CH_2), 34.2 (13a-CH_2), 36.2 (NCH_2), 52.1 (COO*C*H_3), 55.8 (CH_3O), 56.2 (CH_3O), 59.2 (13-C), 63.1 (13a-C), 105.8, 108.9, 112.0, 126.0, 126.7, 127.2, 127.0, 128.1, 128.5, 128.6, 128.8, 129.2, 131.4, 132.5, 134.3, 134.5, 148.0, 148.4 (aromatic C), 163.3 (NCO), 167.2 (NCO), 172.1 (COOH). *Anal*. Calcd for $C_{30}H_{30}N_2O_6$ (514.6): C, 70.02; H, 5.88. Found: C, 70.32; H, 5.88.

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REFERENCES AND NOTES

[1] Shamma, M. In Chemistry of the Alkaloids; Pelletier, S. W., Ed.; Van Nostrand Reinhold Co.: New York, 1970; pp 56–64.

[2] Shamma, M.; Moniot, J. Isoquinoline Alkaloid Research: 1972–1977; Plenum Press: New York and London, 1978; pp 209–259.

[3] Reimann, E. Curr Org Chem 2009, 13, 353.

[4] Simeon, S.; Rios, J. L. J.; Villar, A. Plant Med Phytother 1989, 23, 202.

[5] Iwasa, K. In The Alkaloids; Brossi, A.; Cordell, G. A., Ed.; Academic Press: New York, 1995; Vol. 46, pp 273–346.

[6] Valpuesta, M.; Diaz, A.; Torres, G.; Suau, R. Tetrahedron 2002, 58, 5053.

[7] Haimova, M.; Mollov, N.; Ivanova, S.; Dimitrova, A.; Ognyanov, V. Tetrahedron 1977, 33, 331.

[8] Cushman, M.; Gentry, J.; Dekow, F. J Org Chem 1977, 42, 1111.

[9] Cushman, M.; Dekow, F. Tetrahedron 1978, 34, 1435.

[10] Haimova, M.; Mihovska, S.; Stanoeva, E.; Veleva, K.; Dimitrova, A. Commun Dept Chem Bulg Acad Sci 1979, 12, 325; Chem Abstr 1980, 92, 163824 m.

[11] Cushman, M.; Dekow, F. J Org Chem 1979, 44, 407.

[12] Iwasa, K.; Gupta, Y. P.; Cushman M. J Org Chem 1981, 46, 4744.

[13] Cushman, M.; Dekow, F.; Jacobsen L. J Med Chem 1979, 22, 331.

[14] Haimova, M.; Ognyanov, V.; Mollov N. Synthesis 1980, 845–847.

[15] Stanoeva, E.; Haimova, M.; Ognyanov, V. Liebigs Ann Chem. 1984, 389–394.

[16] Georgieva, A.; Stanoeva, E.; Spassov, S.; Macicek, J.; Angelova, O.; Haimova, M.; De Kimpe, N. Tetrahedron 1991, 47, 3375.

[17] Gonzales-Lopez, M.; Shaw, J. Chem Rev 2009, 109, 164.

[18] Suau, R.; Najera, F.; Rico, R. Tetrahedron 1999, 55, 4019.

[19] Zhang, G. L.; Pan, W. E.; Peng, S. L.; Chen, L.; Chen, W. X.; Yaoxue Xuebao 1990, 25, 604; Chem Abstr 1991, 114, 160667y.

[20] Naruto, S.; Nishimura, H.; Kaneko, H. Chem Pharm Bull 1975, 23, 1271.

[21] Reimann, E.; Grasberger, F.; Polborn, K. Monatsh Chem 2003, 134, 991.

[22] Hetényi, A.; Martinek, T.; Lázár, L.; Zalán, Z.; Fülöp, F. J Org Chem 2003, 68, 5705.

[23] Zalán, Z.; Martinek, T.; Lázár, L.; Fülöp F. Tetrahedron 2003, 59, 9117.

[24] Kametani, T.; Shinzo, K. Yakugaku Zasshi 1963, 83, 1043.

[25] Mihályi, A.; Gáspár, R.; Zalán, Z.; Lázár, L.; Fülöp, F.; De Witte, P. A. M. Anticancer Res 2004, 24, 1631.

[26] Weimar, C.; von Angerer, S.; Wiegrebe, W. Arch Pharm (Weinheim) 1991, 324, 509.

[27] Weimar, C.; von Angerer, S.; Wiegrebe, W. Arch Pharm (Weinheim) 1991, 324, 907.

[28] von Angerer, S.; Brandl, G.; Mannschreck, A.; Weimar, C.; Wiegrebe, W. Anti-Cancer Drug Design 1992, 7, 351.

[29] Park, J.-S.; Yeom, C.-E.; Choi, S. H.; Ahn, Y. S.; Ro, S.; Jeon, Y. H.; Shin, D.-K.; Kim B. M., Tetrahedron Lett 2003, 44, 1611.

[30] Trabocchi, A.; Guarna, F.; Guarna, A. Curr Org Chem 2005, 9, 1127.

[31] Szawkalo, J.; Czarnocki, Z. Monatsh Chem 2005, 136, 1619.

[32] Vincze, Z.; Nemes, P. Tetrahedron 2011, 67, 3380.

[33] Worayuthakarn, R.; Nealmongkol, P.; Ruchiwarat, S.; Thasana, N. Tetrahedron 2012, 68, 2864.

[34] Korotaev, V. Y.; Sosnovskikh, V. Y.; Barkov, A. Y.; Slepukhin, P. A.; Shklyaev, Y. V. J Heterocycl Chem 2012, 49, 856.

[35] Lázár, L. To be published.

[36] Cushman, M.; Madaj, E. J Org Chem 1987, 52, 907.

[37] Collado, M. I.; Manteca, I.; Sotomayor, N.; Villa, M.-J.; Lete, E. J Org Chem 1997, 62, 2080.

[38] A. H. Blatt, Ed.; Organic Syntheses; Wiley: New York, 1965; Coll. Vol. II, p 165.