Influence of *N*-substituents of carbamoyl-stabilized azomethine ylides in 1,3-dipolar cycloadditions

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Dedicated to Professor Fritz Sauter on the occasion of his birthday anniversary
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Abstract
Upon treatment with base N-substituted carbamoylmethylphenanthridinium salts were converted into azomethine ylides. These intermediates were intercepted with symmetrically substituted dipolarophiles, and the stereochemistry of the cycloadducts has been found to be dependent on the substitution at the amide nitrogen atom.

Keywords: 1,3-Dipolar cycloaddition, azomethine ylides, *N*-substituted 2-bromoacetamides, phenanthridinium salts, pyrrolidino[1,2-*f*]phenanthridines

Introduction

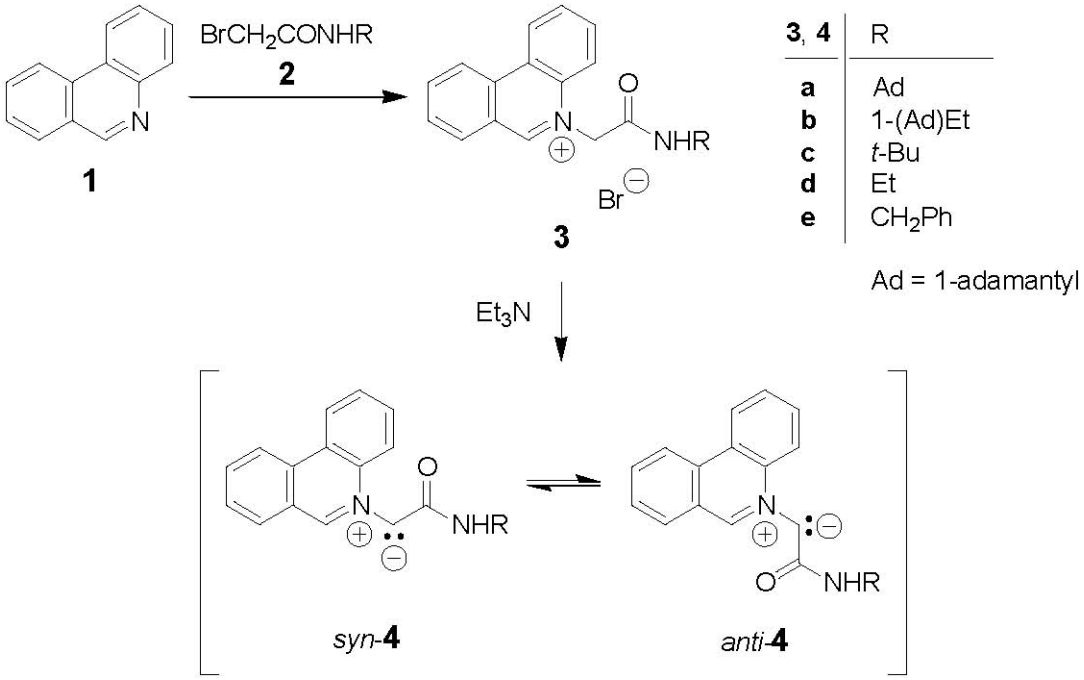
Carbonyl-stabilized azomethine ylides (1,3-dipoles) derived from phenanthridinium salts are known to undergo versatile 1,3-dipolar cycloaddition reactions with a series of dipolarophiles (fumaronitrile, dimethyl fumarate, and dimethyl maleate). In this way five-membered rings can be fused to the phenanthridine scaffold to form pyrrolidino[1,2-*f*] phenanthridines.[1–7] Such 1,3-dipolar cycloaddition reactions have been observed to proceed stereoselectively.[1–5] We are investigating the stereochemistry of pyrrolidino[1,2-*f*]phenanthridines resulting from these reactions. In addition, we have revealed that the reactivity of these azomethine ylides and hence the stereoselectivity of the cycloadducts strongly depend on the group attached to the carbonyl group stabilising the ylide. In the case of alkoxycarbonyl derivatives (esters) a high reactivity and a relatively low selectivity have been observed.[1–5] Moreover, the cycloadducts obtained from these reactions are often accompanied by dehydrogenated products derived from them. On the other hand, a rather poor reactivity of aminocarbonyl derivatives (amides), was observed,[6,7] the

only reactive dipolarophile was fumaronitrile.

Natural products with phenanthridinium skeleton (phenanthridinium alkaloids) represent a broad group of biologically active compounds.[8–12] Compounds with an adamantyl-substituted amino group are known for their biological activity as well.[13-15] We wanted to study the influence of relatively bulky N-substituents on the stereochemical course of the reaction and the formation of stereoisomers, and in addition, the preparation of products with the above mentioned structures was carried out in anticipation of their biological activity.

Results and Discussion

The reaction of phenanthridine **1** with N-substituted α-bromoacetamides **2** furnished the phenanthridinium bromides **3** as starting materials for the subsequent triethylamine-induced conversion into *in situ* formed azomethine ylides **4**.

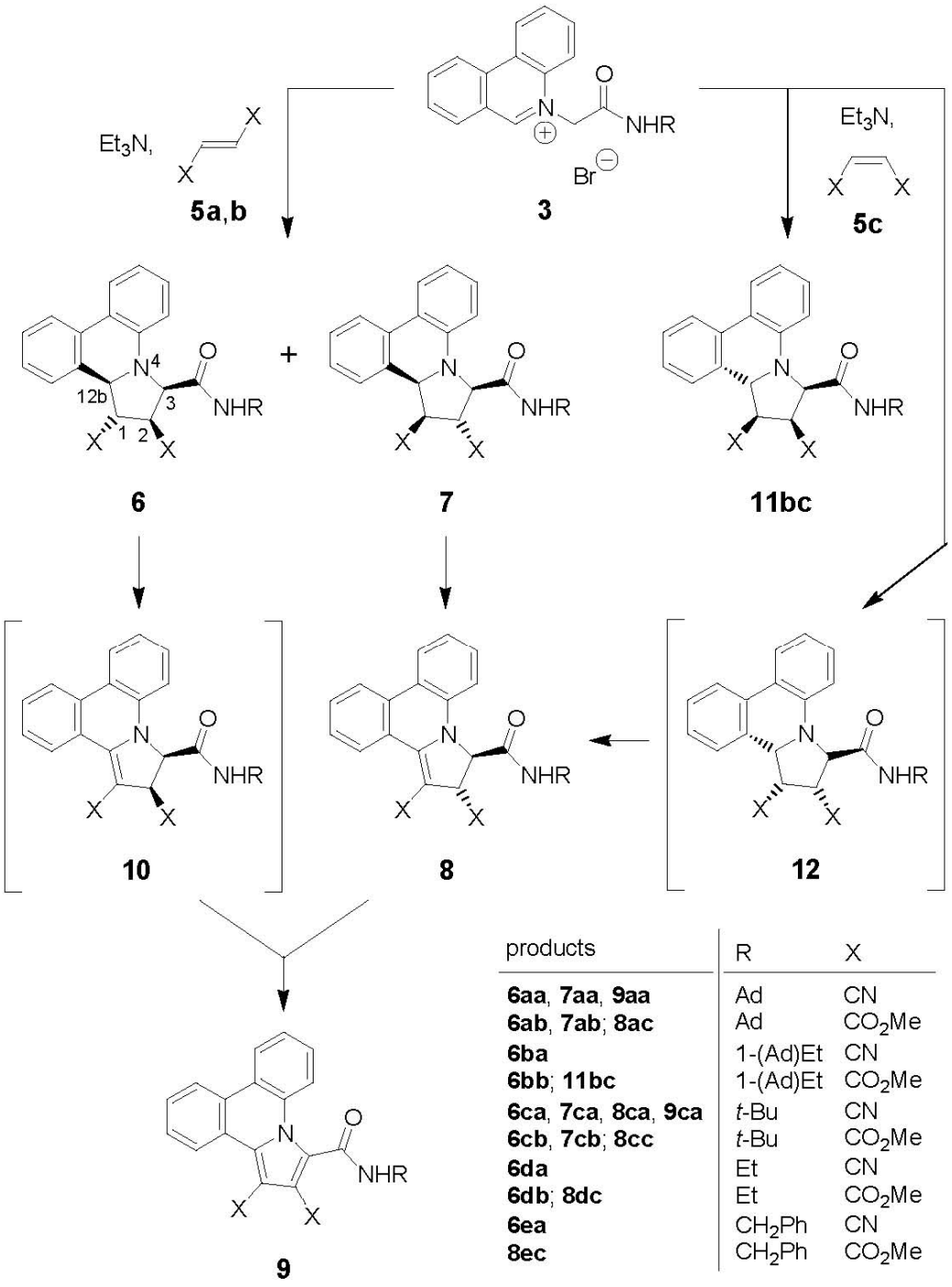


Scheme 1

The products obtained from azomethine ylides **4** reacting with symmetrically disubstituted dipolarophiles fumaronitrile **5a**, dimethyl fumarate **5b**, and dimethyl maleate **5c** indicate the existence of two ylide conformers *syn*-**4** and *anti*-**4** (Scheme 1) as reflected by the stereochemistry of the cycloadducts **6, 7,** and **11** (Scheme 2).

The cycloaddition reactions were carried out in an inert atmosphere. The cycloadducts formed in the reaction with the *E*-configurated dipolarophiles **5a** and **5b** were influenced by two

factors, the temperature and the bulkiness of the substituent at the carbamoyl nitrogen atom. With a bulky group directly attached to the nitrogen atom (as in **3a**, **3c**) two stereoisomeric cycloadducts **6** and **7** were obtained. In case the substituent at the nitrogen atom is not sterically demanding (**3d, 3e**) or if there is a spacer between the bulky group and the nitrogen atom (**3b**) only one stereoisomer was formed (Table 1).



Scheme 2

Table 1. Products **6–9** from the reaction of salts **3** with fumaronitrile **5a** or dimethyl fumarate **5b** in the presence of triethylamine as determined by the reaction conditions: inert atmosphere; solvent (dry) and reaction temperature (Methods 1, 2 and 3), and reaction time.

Entry	**3**	**5**	Solvent	Temp.	Method	Time	Product(s) (ratio)	Yield [%]
1	**3a**	**5a**	CH_2Cl_2	ambient	1	2 days	-	<5
2	**3a**	**5a**	CH_2Cl_2	ambient	1	2 months	**6aa, 7aa** (79:21)	49
3	**3a**	**5a**	CH_2Cl_2	reflux	2	2 days	**6aa, 7aa** (79:21)	95
4	**3a**	**5a**	$CHCl_3$	reflux	3	2 days	**9aa**	94
5	**3a**	**5b**	CH_2Cl_2	ambient	1	2 months	**6ab, 7ab** (56:44)	47
6	**3a**	**5b**	$CHCl_3$	reflux	3	2 days	**6ab, 7ab** (91:9)	89
7	**3b**	**5a**	CH_2Cl_2	ambient	1	2 days	**6ba**	52
8	**3b**	**5a**	CH_2Cl_2	reflux	2	2 days	**6ba**	26
9	**3b**	**5b**	CH_2Cl_2	ambient	1	2 days	**6bb**	48
10	**3c**	**5a**	CH_2Cl_2	ambient	1	2 days	**-**	<5
11	**3c**	**5a**	CH_2Cl_2	ambient	1	2 months	**6ca, 7ca** (67:33)	48
12	**3c**	**5a**	CH_2Cl_2	reflux	2	2 days	**6ca, 7ca** (67:33)	80
13	**3c**	**5a**	$CHCl_3$	reflux	3	2 days	**8ca, 9ca** (71:29)	62
14	**3c**	**5b**	CH_2Cl_2	ambient	1	2 months	**6cb, 7cb** (54:46)	47
15	**3c**	**5b**	$CHCl_3$	reflux	3	2 days	**6cb**	36
16	**3d**	**5a**	CH_2Cl_2	ambient	1	2 days	**6da**	52
17	**3d**	**5a**	CH_2Cl_2	reflux	2	2 days	**6da**	73
18	**3d**	**5b**	CH_2Cl_2	ambient	1	2 days	**6db**	45
19	**3e**	**5a**	CH_2Cl_2	ambient	1	2 days	**6ea**	49
20	**3e**	**5a**	CH_2Cl_2	reflux	2	2 days	**6ea**	75

The yields of cycloadducts **6** and **7** isolated from the reaction of salts **3** with fumaronitrile **5a** vary sensibly with temperature at a reaction time of two days (Table 1: Methods 1 and 2, entries 2 and 3; 7 and 8; 11 and 12; 16 and 17; 19 and 20); the slightly increased temperature of boiling dichloromethane (Method 2) significantly increased the cycloadduct yields (except for **6ba**). The reactions of salts **3a** and **3c** (R = bulky N-substituents) with fumaronitrile **5a** at ambient temperature (Method 1) barely provided any cycloaddition products after two days (Table 1, entries 1 and 10) but required a rather prolonged reaction period of two months to yield cycloadducts as a mixture of stereoisomers **6** and **7** (Table 1, entries 2 and 11). When the cycloaddition reactions of **3a** and **3c** with **5a** were carried out in boiling chloroform (Method 3), dehydrogenated products **8** and/or **9** were obtained instead of the expected cycloadducts **6** and **7** (Table 1, entries 4 and 13). Remarkably, no partially dehydrogenated products **10** (derived from cycloadducts **6**) have been found in these reactions (Method 3) though cycloadducts **6** are the

major products at lower reaction temperatures (Methods 1 and 2, vide supra). Obviously, dehydrogenation of **10** (*cis*-2,3-dihydro structure) and the conversion into the completely unsaturated products **9** occurs faster than the further dehydrogenation of **8** (the *trans*-2,3-dihydro isomer) into **9**.

The reaction of dimethyl fumarate **5b** with **3a** and **3c** (R = bulky N-substituents) at ambient temperature (Method 1) and after a prolonged reaction time of two months furnished the respective cycloadducts **6** and **7** (Table 1, entries 5, 14); at elevated reaction temperature (Method 3) the formation of cycloadducts **6** was strongly favored or was the exclusive product (Table 1, entries 6 and 15, respectively). The salts **3b** and **3d** (with sterically less demanding N-substituents) at ambient reaction temperature (Method 1) gave rise to the formation of cycloadducts **6** exclusively (Table 1, entries 9, 18).

Table 2. Temperature-dependent formation of products **8** and **11bc** from the reaction of salts **3** with dimethyl maleate **5c** (in dichloromethane in inert atmosphere after 2 days)

3	Temperature	Method	Product	Yield [%]
3a	ambient	1	–	<5
3a	reflux	2	**8ac**	34
3b	ambient	1	**11bc**	47
3b	reflux	2	**11bc**	15
3c	ambient	1	–	<5
3c	reflux	2	**8cc**	31
3d	ambient	1	**8dc**	45
3d	reflux	2	**8dc**	20
3e	ambient	1	**8ec**	48
3e	reflux	2	**8ec**	25

The primarily formed cycloadducts resulting from the reaction of salts **3** with dimethyl maleate **5c** appear to be very sensitive to dehydrogenation. With the exception of salt **3b** giving rise to the formation of cycloadduct **11bc** (reflecting the *anti*-conformation of the azomethine ylide intermediate **4b**) all other salts **3a**,**c-e** afforded partially dehydrogenated products **8ac**, **8cc**, **8dc**, and **8ec**, respectively (Table 2). Apparently, these products are formed *via* structure **12** featuring *cis*-orientation of H-1 and H-12b[1,2] very easily undergo dehydrogenation to the isolated products **8ac**, **8cc**, **8dc**, and **8ec.** Product **11bc** with *trans* configuration at C-1, C12b resists dehydrogenation thus enabling its isolation. Obviously, the bulky groups R of the starting materials **3a** and **3c** retard the cycloaddition reaction with dimethyl maleate **5c** at ambient temperature (Method 1), and a slightly higher temperature (Method 2) is required for the reaction to proceed. On the other hand, the reaction of the starting materials **3b** and **3d** (with sterically

less demanding groups R attached to the amide nitrogen atom) reacted already at ambient temperature (Method 1) affording products **8**. However, a slightly higher reaction temperature (Method 2) caused a significant decrease in product yield probably because of decomposition.

Table 3. Experimental coupling constants ($^3J_{exp}$) and coupling constants calculated ($^3J_{calc}$) with the Karplus equation using dihedral angles (Φ) obtained by the semi-empirical AM1 method (SPARTAN program) for cycloadducts **6, 7** and **11bc**

Product	H-12b–H-1		H-1–H-2			H-2–H-3			
$^3J_{exp}$ [Hz]	Φ[°] (AM1)	$^3J_{calc}$ [Hz]	$^3J_{exp}$ [Hz]	Φ[°] (AM1)		$^3J_{calc}$ [Hz]	$^3J_{exp}$ [Hz]	Φ[°] (AM1)	$^3J_{calc}$ [Hz]
6aa	4.7	136.2	4.8	9.7	172.3	9.1	10.0	0.5	8.2
7aa	8.3	2.0	7.9	0.0	102.4	0.2	4.2	134.2	4.2
6ba	4.6	134.9	4.6	9.9	179.5	9.2	10.0	1.1	8.2
6ca	4.7	135.6	4.7	9.9	176.2	9.2	9.9	2.1	7.9
7ca	8.7	1.4	8.2	0.0	99.2	0.0	3.5	128.4	6.5
6da	4.7	135.9	4.7	9.9	177.3	9.2	9.9	1.5	8.2
6ea	4.0	131.9	4.1	9.9	176.4	9.2	9.9	2.7	7.9
6ab	5.2	139.5	5.3	9.5	169.3	9.1	9.5	3.2	7.8
7ab	9.1	1.3	8.1	0.0	100.2	0.1	5.7	142.6	5.8
6bb	5.0	137.6	5.0	9.4	168.4	9.0	9.4	3.0	7.8
6cb	5.3	140.2	5.4	9.3	168.1	9.0	9.3	4.1	7.7
7cb	9.4	1.1	8.2	0.0	99.4	0.0	5.7	141.8	5.7
6db	5.2	139.8	5.2	9.4	169.7	9.1	9.4	2.9	7.8
11bc	4.7	136.4	4.7	0.0	87.2	0.2	9.4	3.2	7.8

The assignment of the relative configuration at C-1, C-2, C-3, and C-12b is based on the coupling constants ^3J under the premise that the reaction proceeds with preservation of dipolarophile configuration. The vicinal coupling constants $^3J_{1,12b}$ and $^3J_{2,3}$ have been found in the following ranges: $^3J_{cis}$ = 8.5–11.5 Hz and $^3J_{trans}$ = 2.5–5.5 Hz.[1-6] However, these values $^3J_{cis}$ and $^3J_{trans}$ are not applicable to $^3J_{1,2}$.[16] The values reflect conformation of the five-membered ring. Unfortunately, we were not able to obtain a suitable crystal for X-ray analysis to support the assignments; therefore, we tried to support the structure with data from quantum chemical calculations. The semi-empirical AM1 method (SPARTAN program) was employed for the calculation and optimization of the space arrangement of adducts **6, 7**, and **11b**. Based on the dihedral angles of the hydrogen atoms attached to the five-membered ring the coupling constants were calculated by application of the Karplus equation;[17] the calculated values together with the

experimental coupling constants are listed in Table 3. All calculated results are in a good agreement with experimental data and the structure elucidation by 2D NMR experiments. The value of the coupling constant depends on the conformation of the five-membered ring resulting from the cycloaddition reaction, and therefore, $^3J_{1,2}$ values differ from those found for $^3J_{1,12b}$ and $^3J_{2,3}$. With the dihedral angle H-1–C-1–C-2–H-2 close to 180° $^3J_{1,2}$ is relatively large (compounds 6); when the dihedral angle approaches 90°, the coupling constant $^3J_{1,2}$ is negligible (compounds 7). The experimental coupling constants are in very good agreement with the theoretical values obtained on the basis of the calculated dihedral angle. Differences between experimental and calculated ^3J values are observed only in those cases where the dihedral angle between neighboring hydrogen atoms is very close to zero (Table 3) and C-2 and C-3 are bearing different substituents. This causes divergent values of $^3J_{2,3}$ reflecting the fact that the Karplus equation does not consider electronic effect of adjacent groups.

The ^{1}H NMR spectra of compounds **6ba** and **11bc** exhibit duplicate sets of pyrrolidine ring signals owing to mixtures of diastereomers because the starting material **3a** was a racemic mixture; integration of the proton signals revealed a 1:1 ratio of the diastereomers.
Some adamantly-substituted compounds have been described earlier;[7] the experiments were repeated, the product structures were reinvestigated, and the results are included in order to put them into perspective with those of the other products described herein.

Experimental Section

General Procedures. Melting points were measured on a Kofler hot stage VEB Wägetechnik Rapido 79/2106. IR spectra were recorded as KBr pellets on a FTIR ATI MATTSON spectrophotometer. NMR spectra were recorded on a Bruker Avance DPX 300 apparatus with working frequency 300 MHz for ^{1}H and 75 MHz for ^{13}C in $CDCl_3$ or DMSO-d_6 solution with TMS as an internal standard. Mass spectra were recorded on a FISONS INSTRUMENTS TRIO 1000 spectrometer in positive mode with EI ionization (20eV). TLC was carried out on commercial silica plates Silufol Kavalier, Czech Republic. Column chromatography was carried out on Merck silica (63-100 μm). Dichloromethane (product of Onex, Czech Republic) was dried over CaH_2 and distilled from it. Triethylamine was dried over KOH and rectified through a column with BaO.

General method for the preparation of N-substituted 2-bromoacetamides 2a-e
To a solution of amine (90.98 mmol) in dry dichloromethane (50 mL) cooled to –20 to –30 °C bromoacetyl bromide (9.18 g, 45.49 mmol) was added dropwise under stirring and cooling of the strong exothermic reaction while a white precipitate was formed. The reaction temperature during the addition of bromoacetyl bromide should not exceed –10 °C. After all bromoacetyl

bromide was added stirring was continued for another 20 min at the same temperature. Finally, the reaction mixture was filtered, the filtrate was evaporated *in vacuo*, and the residue was crystallized from an appropriate solvent.

***N*-(1-Adamantyl)-2-bromoacetamide**[7] **(2a).** Colorless crystals (from benzene) (7.8 g, 63%), mp 124–126 °C; IR (KBr): 3266 (NH), 3081, 2904, 2856, 1656 (C=O), 1563 (NH), 1454, 1402, 1305, 1211, 1093, 998, 914, 750, 696, 565 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.69 (s, 6H, 3 $CH_{2\ Ad}$), 2.02 (s, 6H, 3 $CH_{2\ Ad}$), 2.10 (s, 3H, 3 CH_{Ad}), 3.77 (s, 2H, CH_2Br), 6.15 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 30.01 (CH_{Ad}), 36.35 ($CH_{2\ Ad}$), 41.31 ($CH_{2\ Ad}$), 52.68 (CH_2Br), 164.24 (C=O). Anal. Calcd. for $C_{12}H_{18}BrNO$ (272.18): C, 52.95; H, 6.67; N, 5.15. Found: C, 52.60; H, 6.70; N, 5.13.

***N*-[(1*RS*)-1-(1-Adamantyl)ethyl]-2-bromoacetamide**[7] **(2b).** Colorless crystals (from benzene) (8.19 g, 60%), mp 128–129 °C; IR (KBr): 3294 (NH), 3044, 2902, 2847, 1647 (C=O), 1559 (amide II), 1449, 1383, 1160, 722, 555 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.04 (d, 3H, J = 6.9 Hz, CH_3), 1.36 (q, J = 6.9 Hz, 1H, HC-N), 1.53–1.62 (m, 12H, 6 $CH_{2\ Ad}$), 1.99 (br, 3H, 3 CH_{Ad}), 3.63 (br s, 1H, NH), 3.89 (s, 2H, CH_2Br); ^{13}C NMR ($CDCl_3$): δ 14.12 (CH_3), 28.13 (CH_{Ad}), 34.70 (CH_2Br). 36.86 ($CH_{2\ Ad}$), 38.21 ($CH_{2\ Ad}$), 53.90 (CH-N), 164.46 (C=O). Anal. Calcd. for $C_{14}H_{22}BrNO$ (300.23): C, 56.01; H, 7.39; N, 4.67. Found: C, 55.99; H, 7.30; N, 4.55.

***N*-(*tert*-Butyl)-2-bromoacetamide (2c).** Colorless crystals (from benzene) (5.29 g, 60%), mp 111–112 °C; IR (KBr): 3309 (NH), 3074, 2973, 2888, 1679 (C=O), 1551 (NH), 1454, 1402, 1305, 1212, 1093, 998, 933, 750, 696, 573 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.38 [s, 9H, 3 CH_3), 1.52 (s, 1H, NH), 3.79 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ: 28.38 (CH_3), 29.82 (CH_2), 164.43 (C=O). Anal. Calcd. for $C_6H_{12}BrNO$ (194.07): C, 37.13; H, 6.23; N, 7.22. Found: C, 36.80; H, 6.00; N, 7.32.

***N*-Ethyl-2-bromoacetamide (2d).** Colorless oil (4.22 g, 56%), bp 80 °C/5 mm Hg; IR (KBr): 3278 (NH), 3073, 2976, 2878, 1657 (C=O), 1551 (NH), 1443, 1308, 1208, 1151, 796, 549 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.78 (t, 3H, CH_3), 3.29 (q, 2H, CH_2N), 3.93 (s, 2H, CH_2Br), 7.78 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 14.17 (CH_3), 28.10 (CH_2N), 35.64 (CH_2Br), 167,26 (C=O). Anal. Calcd. for C_4H_8BrNO (166.01): C, 28.94; H, 4.86; N, 8.44. Found: C, 28.67; H, 4.57; N, 8.20.

***N*-Benzyl-2-bromoacetamide**[7] **(2e)**. Colorless oil (5.49 g, 53%), bp 125–127 °C; IR (KBr): 3277 (NH), 3069, 3016, 2952, 2853, 1646 (C=O), 1553 (NH), 1453, 1420, 1322, 1210, 1145, 1059, 1005, 895, 748, 698, 495 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.43 (d, 2H, CH_2N), 3.86 (s, 2H, CH_2Br), 7.97 (br, 1H, NH), 7.2–7.55 (m, 5H, C_6H_5); ^{13}C NMR ($CDCl_3$): δ 39.15 (CH_2N), 44.29 (CH_2Br), 127.84–137.49 (C_6H_5), 165.81 (C=O). Anal. Calcd. for $C_9H_{10}BrNO$ (228.08): C, 47.39; H, 4.42; N, 6.14. Found: C, 47.00; H, 4.22; N, 5.89.

5-[2-(Alkylamino)-2-oxoethyl]phenantridinium bromides 3. General procedure

To a hot solution (65 ^oC) of corresponding bromoacetamide **2a**–**2e** (14.7 mmol) in acetonitrile (50 mL) a solution of phenanthridine **1** (2.63 g, 14.7 mmol) in chloroform was added, and the mixture was refluxed for 3 days. A yellowish solid precipitated, and the solution turned orange.

The reaction mixture was concentrated *in vacuo*, the precipitate was collected, washed with chloroform and diethyl ether, and air-dried at room temperature.

5-[2-(1-Adamantylamino)-2-oxoethyl]phenantridinium bromide[7] **(3a)**. Green-grey crystals (from toluene) (4.64 g, 70%); 228–230 °C; IR (KBr): 3187 (NH), 3037 (CH_{arom}), 2904, 2848, 1683 (C=O), 1625 ($C=N^+$), 1552, 1450, 1359, 1259, 1089, 750, 713 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.61–2.01 (m, 12H, 6 $CH_{2\ Ad}$), 3.30 (br, 3H, 3 CH_{Ad}), 5.94 (s, 2H, CH_2), 8.10–9.19 (m, 9H, CH_{arom}), 10.40 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 30.72 (CH_{Ad}), 37.79 ($CH_{2\ Ad}$), 42.75 ($CH_{2\ Ad}$), 54.03 (C_{Ad}), 120.96–140.47 (CH_{arom} and C_{arom}), 155.35 ($C=N^+$), 164.52 (C=O). Anal. Calcd. for $C_{25}H_{27}BrN_2O$ (451.40): C, 66.52; H, 6.03; N, 6.21. Found: C, 66.22; H, 6.00; N, 5.93.

5-[2-[(1*RS*)-1-(1-Adamantyl)-1-ethylamino]-2-oxoethyl]phenantridinium bromide[7] **(3b).** Slightly green grey crystals (from toluene) (4.72 g, 67%), mp 175–177 °C; IR (KBr): 3416 (NH), 3206, 2901, 2847, 1683 (C=O), 1626 ($C=N^+$), 1451, 758.5 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.04 (d, 3H, J = 6.9 Hz, CH_3), 1.36 (q, 1H, J = 6.9, HC-N), 1.53–1.62 (m, 12H, 6 $CH_{2\ Ad}$), 1.99 (s, 3H, 3 CH_{Ad}), 6.07 (br, 2H, CH_2N), 8.19–9.27 (m, 9H, CH_{arom}), 10.48 (br, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.43 (CH_3), 27.81 (CH_{Ad}), 34.45 (CH_2N), 36.07 ($CH_{2\ Ad}$), 36.53 ($CH_{2\ Ad}$), 53.90 (CH-N), 59.61 (C_{Ad}), 119.45–139.00 (CH_{arom} and C_{arom}), 155.35 ($C=N^+$), 163.58 (C=O). Anal. Calcd. for $C_{27}H_{31}BrN_2O$ (479.45): C, 67.64; H, 6.52; N, 5.84. Found: C, 67.34; H, 6.32; N, 5.60.

5-[2-(*tert*-Butylamino)-2-oxoethyl]phenantridinium bromide (3c). Green-grey crystals (from toluene) (3.84 g, 70%), mp 173–175 °C; IR (KBr): 3208 (NH), 3052 (CH_{arom}), 2961, 2865, 1680 (C=O), 1626 ($C=N^+$), 1545, 1452, 1363, 1223, 1157, 754, 716 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.31 (s, 9H, 3 CH_3), 5.87 (s, 2H, CH_2), 8.09–9.22 (m, 9H, CH_{arom}), 10.37 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 28.38 (CH_3), 51.44 (C-N), 119.11–138.74 (CH_{arom} and C_{arom}), 157.31 ($C=N^+$), 163.08 (C=O). Anal. Calcd. for $C_{19}H_{21}BrN_2O$ (373.29): C, 61.13; H, 5.67; N, 7.50. Found: C, 60.99; H, 5.45; N, 7.26.

5-[2-(Ethylamino)-2-oxoethyl]phenantridinium bromide (3d). Light grey crystals (from toluene) (3.14 g, 62%), mp 152–154 °C; IR (KBr): 3189 (NH), 3048 (C-H arom), 2936, 2889, 1678 (C=O), 1625 ($C=N^+$), 1556, 1450, 1354, 1274, 1224, 1151, 926, 761, 714 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.10 (t, 3H, CH_3), 3.19 (q, 2H, CH_2N), 5.95 (s, 2H, CH_2N^+), 8.06–9.19 (m, 9H, CH_{arom}), 10.46 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.31 (CH_3), 34.03 (CH_2N), 59.06 (CH_2N^+), 119.15–138.52 (CH_{arom} and C_{arom}), 157.11 ($C=N^+$), 163.54 (C=O). Anal. Calcd. for $C_{17}H_{17}BrN_2O$ (345.23): C, 59.14; H, 4.96; N, 8.11. Found: C, 59.00; H, 4.74; N, 7.99.

5-[2-(Benzylamino)-2-oxoethyl]phenantridinium bromide[7] **(3e).** Green-grey crystals (from toluene) (3.41 g, 57%), mp 165–168 °C; IR (KBr): 3447 (N-H), 3000 (C-H_{arom}), 2689, 1679 (C=O), 1626 ($C=N^+$), 1542, 1455, 1364, 1228, 1159, 751, 715 cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.38 (d, 2H, CH_2N), 6.00 (s, 2H, CH_2N^+), 7.25–7.34 $CH_{arom\text{-}Bn}$), 8.08–9.35 (m, 9H, CH_{arom}), 10.37 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 42.82 (CH_2N), 59.24 (CH_2N^+), 119.15–138.78 (CH_{arom} and C_{arom}), 157.20 ($C=N^+$), 164.12 (C=O). Anal. Calcd. for $C_{22}H_{19}BrN_2O$ (407.30): C, 64.87; H, 4.70; N, 6.88. Found: C, 64.54; H, 4.52; N, 6.68.

1,2,3,12b-Tetrahydropyrrolo[1,2-*f*]phenanthridine derivatives. General procedure. To a suspension of salt **3a–e** (2.22 mmol) in dry dichloromethane (20 mL; Method 1 and 2) or dry $CHCl_3$ (20mL, Method 3) the dipolarophile 5 (2.22 mmol) was added, and argon was introduced under stirring at ambient temperature. After 5 minutes dry triethylamine (224 mg, 2.22 mmol) was added under argon. The reaction mixture was left at ambient temperature (Method 1) or was refluxed for 2 days (Methods 2 and 3). Then the solvent was removed in vacuo, and the residue was analyzed by TLC and ^{1}H NMR. Products were separated by column chromatography on silica. Yields are listed in Table 1 (products with 5a,b) and Table 2 (products with 5c).

Products from the reaction of salts 3a-e with fumaronitrile 5a. *N*3-(1-Adamantyl)-(1*R,2*R**,3*S**,12b*R**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide[7] (6aa)**

Yellowish crystals (from chloroform/ether), mp 133–135 °C; R_f = 0.85 (silica; dichloromethane/ether 4:1); IR (KBr): 3342 (N-H), 3061 (C-H arom), 2908, 2851, 2364, (C≡N), 2344 (C≡N), 1678 (C=O), 1602, 1519, 1444, 1263, 1094, 755 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.66–1.97 (m, 12H, 6 $CH_{2\ Ad}$), 2.07 (s, 3H, 3 CH_{Ad}), 3.19 (dd, *J* = 9.7 Hz, *J* = 9.7 Hz, 1H, H-2), 3.93 (dd, *J* = 9.5 Hz, *J* = 4.7 Hz, 1H, H-1), 4.62 (d, *J* = 10.0 Hz, 1H, H-3), 4.85 (d, *J* = 5.2 Hz, 1H, H-12b), 6.39 (s, 1H, NH), 6.79–7,87 (m, 8H, C-H_{arom}); ^{13}C NMR ($CDCl_3$): δ 29.25 (CH_{Ad}), 33.54 (C-2), 36.01 ($CH_{2\ Ad}$), 41.05 (C-1), 41.33 ($CH_{2\ Ad}$), 52.56 (C_{Ad}), 64.20 (C-3), 69.53 (C-12b), 113.31–140.74 (CH_{arom} and C_{arom}), 116.28 (C≡N), 117.87 (C≡N), 166.70 (C=O); EI-MS, *m/z* (%): 448 (M^+, 1), 421 (2), 419 (3), 370 (1), 313 (1), 270 (12), 219 (22), 218 (96), 180 (12), 135 (16). Anal. Calcd. for $C_{29}H_{28}N_4O$ (448.56): C, 77.65; H, 6.29; N, 12.49. Found: C, 77.37; H, 6.11; N, 12.25.

***N*3-(1-Adamantyl)-(1*R**,2*R**,3*R**,12b*S**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide[7] (7aa)**. Dark yellow crystals (from chloroform/ether), mp 157–159 °C; R_f = 0.68 (silica; dichloromethane/ether 4:1); IR (KBr): 3361 (NH), 3064 (C-H arom), 2907, 2851, 2354 (C≡N), 2339 (C≡N), 1674 (C=O), 1603, 1522, 1444, 1263, 1094, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.68–2.06 (m, 12 H, 6 $CH_{2\ Ad}$), 2.09 (s, 3 H, 3 CH_{Ad}), 3.67 (d, *J* = 4.1 Hz, 1H, H-2), 3.99 (d, *J* = 8.3 Hz, 1H, H-1), 4.57 (d, *J* = 8.3 Hz, 1H, H-12b), 5.54 (d, *J* = 4.2 Hz, 1H, H-3), 6.48 (s, 1H, NH), (6.93–7.92) (m, 8 H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 29.28 (CH_{Ad}), 35.65 (C-2), 36.06 ($CH_{2\ Ad}$), 41.26 ($CH_{2\ Ad}$), 42.96 (C-1), 52.59 (C_{Ad}), 62.94 (C-12b), 68.81 (C-3), 113.01–142.09 (CH_{arom} and C_{arom}), 115.00 (C≡N), 115.98 (C≡N), 166.08 (C=O); EI-MS, *m/z* (%): 448 (M^+, 1), 421 (2), 419 (3), 370 (1), 313 (1), 270 (12), 219 (22), 218 (96), 180 (12), 135 (16). Anal. Calcd. for $C_{29}H_{28}N_4O$ (448.56): C, 77.65; H, 6.29; N, 12.49. Found: C, 77.45; H, 6.12; N, 12.22.

***N*3-(1-Adamantyl)-1,2-dicyanopyrrolo[1,2-*f*]phenanthridine-3-carboxamide (9aa).** White crystals (insoluble in most solvents), mp >350 °C; R_f = 0.73 (silica; dichloromethane/ether 25:4);

IR (KBr): 3344 (NH), 3069 (CH_{arom}), 2910, 2852, 2217 (C≡N), 1672 (C=O), 1525, 1444, 1364, 1296, 1092, 754 cm^{-1}; EI-MS, *m/z* (%): 444 (M^+, 100), 420 (2), 419 (2), 387 (41), 309 (21), 294 (65), 281(7), 267 (19), 266 (26), 265 (27), 239 (7), 216 (16), 199 (4), 135 (54). Anal. Calcd. for $C_{29}H_{24}N_4O$ (444.53): C, 78.36; H, 5.44; N, 12.60; Found: C, 78.13, H, 5.36; N, 12.45.

***N*3-[(1*RS*)-1-(1-Adamantyl)-1-ethyl]-(1*R**,2*R**,3*S**,12b*R**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide[7] (6ba)**. Yellowish crystals (from chloroform/ ether), mp 195–197 °C; R_f = 0.74 (silica; ethyl acetate); IR (KBr): 3299 (NH), 3061 (C-Harom), 2903, 2847, 2247 (C≡N), 1674 (C=O), 1603, 1522, 1495, 11447, 1383, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.04 (d, *J* = 6.9 Hz, 3H, CH_3), 1.36 (q, *J* = 6.9 Hz, 1H, HC-N), 1.53–1.62 (m, 12H, 6 $CH_{2\ Ad}$), 1.99 (s, 3H, 3 CH_{Ad}), 3.23 (dd, *J* = 9.9, *J* = 9.9, Hz, 1H, H-2), 3.27 (dd, *J* = 10.0 Hz, *J* = 10.0 Hz, 1H, H-2), 3.94 (dd, *J* = 9.9 Hz, *J* = 4.6 Hz, 1H, H-1), 4.01 (dd, *J* = 10.0 Hz, *J* = 4.5 Hz, 1H, H-1), 4.70 (d, *J* = 9.9 Hz, 1H, H-3), 4.72 (d, *J* = 10.0 Hz, 1H, H-3), 4.95 (d, *J* = 4.6 Hz, 1H, H-12b), 5.00 (d, *J* = 4.5 Hz, 1H, H-12b), 6.48 (br, 1H, N-H), 6.82–7.90 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 14.45 (CH_3), 28.13 (CH_{Ad}), 33.89 (C-2), 34.06 (C-2), 36.10 (C_{Ad}), 36.88 ($CH_{2\ Ad}$), 38.60 ($CH_{2\ Ad}$), 40.84 (C-1), 41.22 (C-1), 53.69 (C-3), 53.78 (C-3), 64.05 (CH-N), 64.80 (CH-N), 69.03 (C-12b), 69.06 (C-12b), 113.21140.82 (CH_{aro} and C_{arom}), 116.23, 116.31, 117.76 (C≡N), 117.94 (C≡N), 167.17 (C=O); EI-MS: *m/z* (%)476 (M^+, 3), 449 (1), 423 (1), 313 (2), 270 (19), 243 (11), 219 (20), 218 (100), 193 (8), 180 (25), 179 (18), 165 (7), 135 (11), 79 (18), 67 (7), 41 (6). Anal. Calcd. for $C_{31}H_{32}N_4O$ (476.62): C, 78.12; H, 6.77; N, 11.75. Found: C, 77.98; H, 6.55; N, 11.55.

***N*3-(*tert*-Butyl)-(1*R**,2*R**,3*S**,12b*R**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide (6ca)**. Yellowish crystals (from chloroform/ether), mp 136–138 °C; R_f = 0.61 (silica; dichloromethane/ethyl acetate 5:1); IR (KBr): 3350 (N-H), 3069 (C-Harom), 2968, 2932, 2249 (C≡N), 2184 (C≡N), 1676 (C=O), 1632, 1523, 1448, 1260, 1097, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.39 (s, 9 H, 3 CH_3), 3.23 (dd, *J* = 9.9 Hz, *J* = 9.9 Hz, 1H, H-2), 3.98 (dd, *J* = 9.9 Hz, *J* = 4.7 Hz, 1H, H-1), 4.64 (d, *J* = 9.9 Hz, 1H, H-3), 4.90 (d, *J* = 4.7 Hz, 1H, H-12b), 6.57 (s, 1H, NH), 6.82–7.91 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 27.64 (CH_3), 32.61 (C-2), 40.15 (C-1), 51.02 (C-N), 63.37 (C-3), 68.69 (C-12b), 112.39–139.83 (CH_{arom} and C_{arom}), 115.35 (C≡N), 116.94 (C≡N), 166.15 (C=O); EI-MS: *m/z* (%) 370 (M^+, 1), 343 (1), 313 (1), 277 (1), 271 (3), 270 (17), 268 (7), 243 (6), 219 (17), 218 (100), 193 (33), 179 (22), 58 (5), 41 (4). Anal. Calcd. for $C_{23}H_{22}N_4O$ (370.45): C, 74.57; H, 5.99; N, 15.12. Found: C, 74.33; H, 5.61; N, 15.22.

***N*3-(*tert*-Butyl)-(1*R**,2*R**,*3R**,12b*S**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide (7ca).** Light yellow crystals (from chloroform/ether), mp 156–157 °C; R_f = 0.32 (silica; dichloromethane/ethyl acetate 5:1); IR (KBr): 3365 (N-H), 3070 (CH_{arom}), 2971, 2941, 2252 (C≡N), 2189 (C≡N), 1678 (C=O), 1638, 1523, 1449, 1261, 1099, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.41 (s, 9H, 3 CH_3), 3.68 (d, *J* = 3.5 Hz, 1H, H-2), 4.01 (d, *J* = 8.7 Hz, 1H, H-1), 4.59 (d, *J* = 8.7 Hz, 1H, H-12b), 5.55 (d, *J* = 3.5 Hz, 1H, H-3), 6.57 (s, 1H, N-

H), 6.82–7.91 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 27.63 (CH_3), 34.68 (C-2), 42.06 (C-1), 51.07 [$\underline{C}(CH_3)_3$], 62.05 (C-12b), 67.88 (C-3), 112.03–144.52 (CH_{arom} and C_{arom}), 114.12 (C≡N), 115.07 (C≡N), 166.15 (C=O); EI-MS: *m/z* (%) 370 (M^+, 1), 343 (1), 313 (1), 277 (1), 271 (3), 270 (17), 268 (7), 243 (6), 219 (17), 218 (100), 193 (33), 179 (22), 58 (5), 41 (4). Anal. Calcd. for $C_{23}H_{22}N_4O$ (370.45): C, 74.57; H, 5.99; N, 15.12. Found: C, 74.40; H, 5.88; N, 15.01.

***N*3-(*tert*-Butyl)-(2*R*,3R**)-1,2-dicyano-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide (8ca)**. Yellow crystals (from chloroform/ether), mp 279–281 °C; R_f = 0.68 (silica; petroleum ether/ethyl acetate 5:1); IR (KBr): 3315 (N-H), 3067 (CH_{arom}), 2906, 2847, 2249 (C≡N), 2186 (C≡N), 1657 (C=O), 1602, 1547, 1448, 1383, 1094, 748 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.39 (s, 9H, 3 CH_3), 5.23 (d, *J* = 4.9 Hz, 1H, H-2), 5.97 (d, *J* = 4.9 Hz, 1H, H-3), 6.59 (s, 1H, NH), 6.82–7.91 (m, 8 H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 27.64 (CH_3), 51.02 [$\underline{C}(CH_3)_3$], 59.61 (C-2), 65.28 (C-3), 93.54 (C-1), 112.39–139.83 (CH_{arom} and C_{arom}), 115.35 (C≡N), 116.94 (C≡N), 166.15 (C=O); EI-MS: *m/z* (%) 368 (M^+, 15), 343 (12), 313 (5), 270 (77), 241 (7), 216 (100), 193 (33), 178 (22), 58 (5), 41 (4). Anal. Calcd. for $C_{23}H_{20}N_4O$ (368.43): C, 74.98; H, 5.47; N, 15.21. Found: C, 74.82; H, 5.15; N, 15.03.

***N*3-(*tert*-Butyl)-1,2-dicyanopyrrolo[1,2-*f*]phenanthridine-3-carboxamide (9ca)**. Pale pink crystals (insoluble in common solvents), mp >350 °C; R_f = 0.62 (silica; dichloromethane/ether 15:1); IR (KBr): 3358 (NH), 3069 (C-H_{arom}), 2968, 2927, 2220 (C≡N), 1670 (C=O), 1601, 1566, 1447, 1365, 1217, 1085, 750 cm^{-1}; EI-MS: *m/z* (%) 366 (M^+, 100), 310 (19), 309 (90), 294 (95), 267 (35), 242 (19), 239 (18), 218 (11), 57 (18), 41 (12). Anal. Calcd. for $C_{23}H_{18}N_4O$ (366.42): C, 75.39; H, 4.95; N; 15.29. Found: C, 75.32; H, 5.06; N, 15.32.

***N*3-Ethyl-(1*R**,2*R**,3*S**,12b*R**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide (6da)**. Yellowish crystals (from chloroform/ether), mp 227–228 °C; R_f = 0.72 (silica; ethyl acetate); IR (KBr): 3390 (N-H), 3065 (CH_{arom}), 2976, 2934, 2239 (C≡N), 2185 (C≡N), 1669 (C=O), 1601, 1532, 1445, 1261, 961, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.18 (t, 3H, CH_3), 3.24 (dd, *J* = 9.9 Hz, *J* = 9.9 Hz, 1H, H-2), 3.45 (q, 2H, CH_2), 3.97 (dd, *J* = 9.9 Hz, *J* = 4.7 Hz, 1H, H-1), 4.70 (d, *J* = 9.9 Hz, 1H, H-3), 4.98 (d, *J* = 4.7 Hz, 1H, H-12b), 6.48 (s, 1H, N-H), 6.82–7.94 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 14.61 (CH_3), 33.76 (C-2), 34.89 (CH_2N), 41.06 (C-1), 64.28 (C-3), 69.00 (C-12b), 116.28–141.98 (CH_{arom} and C_{arom}), 116.28 (C≡N), 117.92 (C≡N), 167.99 (C=O); EI-MS: *m/z* (%) 341 (M^+, 1), 294 (1), 270 (12), 219 (18), 218 (100), 204 (3), 193 (6), 180 (10), 179 (9), 165 (8), 135 (8), 106 (3), 93 (8), 79 (10), 67 (5), 55 (3), 41 (3). Anal. Calcd. for $C_{21}H_{18}N_4O$ (342.40): C, 73.67; H, 5.30; N, 16.36. Found: C, 73.55; H, 5.11; N, 16.09.

***N*3-Benzyl-(1*R**,2*R**,3*S**,12b*R**)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-3-carboxamide (6ea)**. Dark yellow crystals (from chloroform/ether), mp 238–239 °C; R_f = 0.71 (silica; ethyl acetate/petroleum ether 2.5:1); IR (KBr): 3325 (N-H), 3066 (CH_{arom}), 3032, 2889, 2178 (C≡N), 2177 (C≡N), 1652 (C=O), 1603, 1563, 1449, 1365, 1233, 1175, 749 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.29 (dd, *J* = 9.9 Hz, *J* = 9.9 Hz, 1H, H-2), 4.37 (dd, *J* =

9.9 Hz, *J* = 4.0 Hz, 1H, H-1), 4.43 (d, 2H, CH_2N), 4.78 (d, *J* = 9.9 Hz, 1H, H-3), 5.29 (d, *J* = 4.0 Hz, 1H, H-12b), 6.48 (s, 1H, N-H), 6.81–8.98 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 37.60 (C-2), 38.85 (C-1), 43.61 (CH_2N), 66.13 (C-3), 68.10 (C-12b), 113.36–144.12 (CH_{arom} and C_{arom}), 117.28 (C≡N), 117.63 (C≡N), 166.50 (C=O); EI-MS: *m/z* (%) 404 (M^+, 3), 294 (30), 267 (20), 218 (100), 193 (12), 180 (14). Anal. Calcd. for $C_{26}H_{20}N_4O$ (404.47): C, 77.21; H, 4.98; N, 13.85. Found: C, 77.02; H, 4.69; N, 13.77.

Products from the reaction of salts 3a-d with dimethyl fumarate 5b

Dimethyl (1*R,2*R**,3*S**,12b*R**)-3-(1-adamantyl)aminocarbonyl-1,2,3,12b-tetrahydropyrrolo-[1,2-*f*]phenanthridine-1,2-dicarboxylate[7] (6ab)**. Dark orange crystals (from chloroform/ether), mp 191–193 °C; R_f = 0.83 (silica; dichloromethane/ether 5:1); IR (KBr): 3300 (N-H), 3030 (CH_{arom}), 2908, 2849, 1730, (C=O), 1675 (C=O), 1149, 1167, 741 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.67–1.97 (m, 12H, 6 $CH_{2\ Ad}$), 2.07 (s, 3H, 3 CH_{Ad}), 3.38 (dd, *J* = 9.5 Hz, *J* = 9.5 Hz, 1H, H-2), 3.73 (s, 3H, OCH_3), 3.75 (dd, *J* = 9.4 Hz, *J* = 5.1 Hz, 1H, H-1), 3.80 (s, 3H, OCH_3), 4.79 (d, *J* = 5.2 Hz, 1H, H-12b), 4.97 (d, *J* = 9.5 Hz, 1H, H-3), 6.44 (s, 1H, N-H), 6.69–8.65 (m, 8 H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 29.32 (CH_{Ad}), 36.17 ($CH_{2\ Ad}$), 41.41 ($CH_{2\ Ad}$), 50.37 (C-2), 51.87 (C_{Ad}), 54.2 (OCH_3), 55.18 (C-1), 55.7 (OCH_3), 64.02 (C-3), 68.53 (C-12b), 113.5–142.97 (CH_{arom} and C_{arom}), 169.53, 171.81, 172.05 (3 C=O); EI-MS: *m/z* (%) 514 (M^+, 1), 398 (5), 374 (5), 304 (5), 251 (40), 219 (12), 194 (31), 180 (100), 135 (22). Anal. Calcd. for $C_{31}H_{34}N_2O_5$ (514.62): C, 72.35; H, 6.66; N, 5.44. Found: C, 72.22; H, 6.46; N, 5.15.

Dimethyl (1*R,2*R**,*3R**,12b*S**)-3-(1-adamantyl)aminocarbonyl-1,2,3,12b-tetrahydropyrrolo-[1,2-*f*]phenanthridine-1,2-dicarboxylate[7] (7ab).** Yellowish crystals (from chloro-form/ether), mp 208–210 °C; R_f = 0.72 (silica; dichloromethane/ether 5:1); IR (KBr): 3399 (N-H), 3035 (C-H_{arom}), 2909, 2855, 1729 (C=O), 1647 (C=O), 1450, 1168, 741 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.68–1.97 (m, 12H, 6 $CH_{2\ Ad}$), 2.08 (s, 3H, 3 CH_{Ad}), 3.38 (d, *J* = 5.6 Hz, 1H, H-2), 3.67 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.75 (d, *J* = 9.2 Hz, 1H, H-1), 4.72 (d, *J* = 9.1 Hz, 1H, H-12b), 5.70 (d, *J* = 5.7 Hz, 1H, H-3), 6.54 (s, 1H, N-H), 6.81–8.64 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 29.45 (CH_{Ad}), 36.32 ($CH_{2\ Ad}$), 41.38 ($CH_{2\ Ad}$), 46.17 (C-2), 51.0 (OCH_3), 53.7 (OCH_3), 55.79 (C-1), 52.39 (C_{Ad}), 63.30 (C-12b), 71.36 (C-3), 112.75–144.42 (CH_{arom} and C_{arom}), 166.08, 172.49, 172.90 (3 C=O); EI-MS: *m/z* (%) 514 (M^+, 1), 398 (5), 374 (5), 304 (5), 251 (40), 219 (12), 194 (31), 180 (100), 135 (22). Anal. Calcd. for $C_{31}H_{34}N_2O_5$ (514.62): C, 72.35; H, 6.66; N, 5.44. Found: C, 71.99; H, 6.24; N, 5.14.

Dimethyl (1*R,2*R**,3*S**,12b*R**)-3-[(1*RS*)-1-(1-adamantyl)-1-ethylaminocarbonyl]-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-1,2-dicarboxylate (6bb)**. White-yellow crystals (from chloroform/ether), mp 250–252 °C; R_f = 0.66 (silica; ethyl acetate); IR (KBr): 3418 (NH), 3075, 2903, 2847, 1736 (C=O), 1673 (C=O), 1516, 1447, 1314, 1163, 1011, 750 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.04 (d, *J* = 6.9 Hz, 3H, CH_3), 1.36 (q, *J* = 6.9, 1H, HC-N), 1.53–1.62 (m, 12H, 6 $CH_{2\ Ad}$), 1.99 (s, 3H, 3 CH), 3.23 (dd, *J* = 9.4 Hz, *J* = 9.4 Hz, 1H, H-2), 3.75 (dd, *J* = 9.4 Hz, *J* =

5.0 Hz, 1H, H-1), 3.82 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.91 (d, *J* = 5.0 Hz, 1H, H-12b), 4.99 (d, *J* = 9.4 Hz, 1H, H-3); 6.68 (br s, 1H, NH), 6.82–7.90 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 15.92 (CH_3), 29.72 (CH_{Ad}), 37.10 (C_{Ad}), 39.88 ($CH_{2\ Ad}$), 39.97 ($CH_{2\ Ad}$), 51.86 (C-2), 53.59 (C-1), 54.65 (OCH_3), 56.46 (CH-N), 65.32 (C-12b), 69.27 (C-3), 114.99–145.82 (CH_{arom} and C_{arom}), 167.08, 171.41, 173.30 (3 C=O); EI-MS: *m/z* (%) 542 (M^+, 1), 325 (1), 374 (1), 304 (2), 251 (42), 219 (10), 194 (29), 180 (100), 135 (22). Anal. Calcd. for $C_{33}H_{38}N_2O_5$ (542.67): C, 73.04; H, 7.06; N, 5.16. Found: C, 72.92; H, 7.01; N, 4.93.

Dimethyl (1*R,2*R**,3*S**,12b*R**)-3-(*tert*-butylaminocarbonyl)-1,2,3,12b-tetrahydropyrrolo-[1,2-*f*]phenanthridine-1,2-dicarboxylate (6cb)**. Yellowish crystals (from chloroform /ether), mp 203–205 °C; R_f = 0.67 (silica; dichloromethane/ethyl acetate 5:1); IR (KBr): 3320 (N-H), 3035 (C-H_{arom}), 2928, 2862, 1732 (C=O), 1676 (C=O), 1528, 1260, 1149, 1167, 741 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (s, 9H, 3 CH_3), 3.43 (dd, *J* = 9.3 Hz, *J* = 9.3 Hz, 1H, H-2), 3.72 (s, 3H, OCH_3), 3.80 (dd, *J* = 9.3 Hz, *J* = 5.2 Hz, 1H, H-1), 3.82 (s, 3H, OCH_3), 4.83 (d, *J* = 5.3 Hz, 1H, H-12b), 5.01 (d, *J* = 9.3 Hz, 1H, H-3), 6.56 (s, 1H, NH), 6.70–7.84 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 28.77 (CH_3), 50.49 (C-2), 51.34 [C-NH], 52.80 (OCH_3), 53.72 (OCH_3), 55.25 (C-1), 64.13 (C-12b), 68.63 (C-3), 113.61–143.07 (CH_{arom} and C_{arom}), 169.91, 171.94, 172.26 (3 C=O); EI-MS: *m/z* (%) 437 (M^+, 5), 435 (4), 405 (2), 336 (7), 304 (15), 276 (28), 251 (100), 219 (41), 217 (35), 193 (15), 180 (15), 57 (8), 41 (3). Anal. Calcd. for $C_{25}H_{28}N_2O_5$ (436.50): C, 68.79; H, 6.47; N, 6.42. Found: C, 68.59; H, 6.52; N, 6.22.

Dimethyl (1*R,2*R**,3*R**,12b*S**)-3-(*tert*-butylaminocarbonyl)-1,2,3,12b-tetrahydropyrrolo-[1,2-*f*]phenanthridine-1,2-dicarboxylate (7cb).** Yellow crystals (from chloroform/ether), mp 213–215 °C; R_f = 0.52 (silica; dichloromethane/ethyl acetate 5:1); IR (KBr): 3385.6 (N-H), 3039 (C-H_{arom}), 2929, 2865, 1731 (C=O), 1646 (C=O), 1526, 1450, 1168, 741 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.39 (s, 9H, 3 CH_3), 3.39 (d, *J* = 5.7 Hz, 1H, H-2), 3.75 (s, 3H, OCH_3), 3.76 (d, *J* = 9.2 Hz, 1H, H-1), 3.82 (s, 3H, OCH_3), 4.75 (d, *J* = 9.4 Hz, 1H, H-12b), 5.71 (d, *J* = 5.8 Hz, 1H, H-3), 6.68 (s, 1H, NH), 6.54–7.81 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 28.58 (CH_3), 46.08 (C-2), 51.08 (C-NH), 55.78 (C-1), 63.30 (C-12b), 71.34 (C-3), 112.65–144.42 (CH_{arom} and C_{arom}), 169.33, 171.16, 172.91 (3 C=O); EI-MS: *m/z* (%) 437 (M^+, 5), 435 (4), 405 (2), 336 (7), 304 (15), 276 (28), 251 (100), 219 (41), 217 (35), 193 (15), 180 (15), 57 (8), 41 (3). Anal. Calcd. for $C_{25}H_{28}N_2O_5$ (436.50): C, 68.79; H, 6.47; N, 6.42. Found: C, 68.58; H, 6.52; N, 6.63.

Dimethyl (1*R,2*R**,3*S**,12b*R**)-3-(ethylaminocarbonyl)-1,2,3,12b-tetrahydropyrrolo-[1,2-*f*]phenanthridine-1,2-dicarboxylate (6db)**. Pale red crystals (from chloroform/ether), mp 228–230 °C; R_f = 0.75 (silica; ethyl acetate); IR (KBr): 3424 (NH), 3075, 2979, 2946, 1778 (C=O), 1704 (C=O), 1541, 1443, 1360, 1204, 1092, 744 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (t, 3H, CH_3), 3.52 (q, 2H, CH_2N), 3.23 (dd, *J* = 9.4 Hz, *J* = 9.4 Hz, 1H, H-2), 3.65 (dd, *J* = 9.3 Hz, *J* = 5.2 Hz, 1H, H-1), 3.75 (s, 6H, OCH_3), 4.91 (d, *J* = 5.3 Hz, 1H, H-12b), 4.99 (d, *J* = 9.5 Hz, 1H, H-3), 6.68 (s, 1H, NH), 7.06–7.98 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 12.95 (CH_3), 34.71 (CH_2N), 48.77 (C-2), 51.71 (OCH_3), 52.86 (OCH_3), 53.59 (C-1), 56.46 (C-12b), 69.27 (C-3), 114.99–

151.19 (CH_{arom} and C_{arom}), 165.60, 173.11, 175.48 (3 C=O); EI-MS: *m/z* (%) 408 (M^+, 1), 376 (70), 343 (22), 316 (28), 276 (51), 244 (100), 217 (39), 191 (20), 122 (15), 108 (29), 94 (28), 56 (5), 44 (3). Anal. Calcd. for $C_{23}H_{24}N_2O_5$ (408.45): C, 67.63; H, 5.92; N, 6.86. Found: C, 67.77; H, 5.62; N, 6.62.

Products from the reaction of salts 3a-e with dimethyl maleate 5c

Dimethyl (2*R*,3R)-3-(1-adamantyl)aminocarbonyl-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-1,2-dicarboxylate[7] (8ac)**. Pale orange crystals (from chloroform/ether), mp 189–192 °C; R_f = 0.81 (silica; dichloromethane/ether 2:1); IR (KBr): 3342 (N-H), 3061 (C-H_{arom}), 2908, 2851, 1740 (C=O),1678 (C=O), 1602, 1519, 1444, 1263, 1094, 755 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.60–1.88 (m, 12H, 6 $CH_{2\ Ad}$); 1.99 (s, 3H, 3 CH_{Ad}), 3.73 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.21 (d, *J* = 5.0 Hz, 1H, H-2), 4.79 (d, *J* = 5.0 Hz, 1H, H-3), 6.15 (s, 1H, NH), 6.82–8.53 (m, 8H, CH_{aro}); ^{13}C NMR ($CDCl_3$): δ 29.25 (CH_{Ad}), 34.22 (C-2), 36.01 ($CH_{2\ Ad}$), 41.05 (C-1), 41.24 ($CH_{2\ Ad}$), 51.30 (OCH_3), 52.82 (OCH_3), 52.58 (C_{Ad}), 65.52 (C-3), 95.27 (C-12b), 113.06–137.21 (CH_{arom} and C_{arom}), 173.49 (C=O); EI-MS: *m/z* (%) 512 (M^+, 1), 386 (4), 302 (3), 251 (5), 236 (5), 210 (10), 209 (100), 178 (15), 135 (11), 91 (18), 41 (3). Anal. Calcd. for $C_{31}H_{32}N_2O_5$ (512.60): C, 72.64; H, 6.29; N, 5.46. Found: C, 72.36; H, 6.00; N, 5.52.

Dimethyl (1*R,2*S**,3*R**,12b*R**)-3-[(1*RS*)-1-(1-adamantyl)-1-ethylaminocarbonyl]-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridine-1,2-dicarboxylate (11bc)**. Orange crystals (from chloroform/ether), mp 248–250 °C; R_f = 0.66 (silica; ethyl acetate); IR (KBr): 3294 (NH), 3061, 2902, 2847, 1738 (C=O), 1654 (C=O), 1543, 1439, 1163, 743 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.04 (d, *J* = 6.9 Hz, 3H, CH_3), 1.36 (q, *J* = 6.9 Hz, 1H, HC-N), 1.53–1.62 (m, 12H, 6 $CH_{2\ Ad}$), 1.99 (s, 3H, 3 CH_{Ad}), 3.41 (d, *J* = 9.4 Hz, 1H, H-2), 3.45 (d, *J* = 9.4 Hz, 1H, H-2), 4.25 (d, *J* = 3.95 Hz, 1H, H-1), 4.29 (d, *J* = 3.75 Hz, 1H, H-1), 4.92 (d, *J* = 5.0 Hz, 1H, H-12b); 4.95 (d, *J* = 4.7 Hz, 1H, H-12b), 5.00 (d, *J* = 9.3 Hz, 1H, H-3), 5.05 (d, *J* = 9.5 Hz, 1H, H-3), 6.59 (br, 1H, N-H), 6.70–7.80 (m, 8H, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 15.92 (CH_3), 29.72 (CH_{Ad}), 37.10 (C_{Ad}), 39.88 ($CH_{2\ Ad}$), 39.97 ($CH_{2\ Ad}$), 51.86 (C-2), 52.12 (OCH_3), 52.42 (OCH_3), 52.22 (C-2), 53.59 (C-1), 53.72 (C-1), 56.46 (C-12b), 56.61 (C-12b), 65.32 (CH-N), 65.90 (CH-N), 69.27 (C-3), 69.32 (C-3), 114.99–145.82 (CH_{arom} and C_{arom}), 166.80, 167.08, 171.21, 171.41, 173.30 (3 C=O); EI-MS: *m/z* (%) 542 (M^+, 1), 325 (1), 374 (1), 304 (2), 251 (42), 219 (10), 194 (29), 180 (100), 135 (22). Anal. Calcd. for $C_{33}H_{38}N_2O_5$ (542.67): C, 73.04; H, 7.06; N, 5.16. Found: C, 72.92; H, 7.16; N, 5.28.

Dimethyl (2*R,*3R)-3-(*tert*-butyl)aminocarbonyl-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-1,2-dicarboxylate (8cc)**. Yellow crystals (from chloroform/ether), mp 169.2–171.1 °C; R_f = 0.68 (silica; ethyl acetate/ dichloromethane 1:5); IR (KBr): 3368 (N-H), 3075 (C-H_{arom}), 2965, 1738 (C=O), 1671 (C=O), 1528, 1443, 1361, 1290, 1168, 1098, 753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (s, 9H, 3 CH_3), 3.75 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 4.23 (d, *J* = 4.97 Hz, 1H, H-2), 4.85 (d, *J* = 4.97 Hz, 1H, H-3), 5.64 (s, 1H, NH), 6.45–8.13 (m, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 28.44 (CH_3), 51.41 (OCH_3), 52.22 (C-2), 52.65 (OCH_3), 54.55 (C-N), 65.53 (C-3), 95.34 (C-1),

111.59–136.25 (CH_{arom} and C_{arom}), 169.91, 171.94, 172.26 (3 C=O), EI-MS: *m/z* (%) 434 (M^+, 1), 308 (11), 276 (2), 236 (9), 210 (12), 209 (100), 180 (38), 178 (50), 152 (22), 57 (12), 32 (9), 28 (31). Anal. Calcd. for $C_{25}H_{26}N_2O_5$ (434.49): C, 69.11; H, 6.03; N, 6.45. Found: C, 68.92; H, 6.12; N, 6.45.

Products from the reaction of salt 3d with dimethyl maleate 5c

Dimethyl (2*R*,*3*R)-3-(ethylaminocarbonyl)-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-1,2-dicarboxylate (8dc)**. Pale yellow crystals (from chloroform/ether), mp >350 °C; R_f = 0.35 (silica; ether/dichloromethane 1:5); IR (KBr): 3359 (NH), 3070, 2947, 1742 (C=O), 1665 (C=O), 1524, 1443, 1299, 1171, 1094, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.02 (t, 3H, CH_3), 3.25 (q, 2H,CH_2N), 3.73 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 4.23 (d, *J* = 4.39 Hz, 1H, H-2), 4.99 (d, *J* = 4.34 Hz, 1H, H-3), 5.59 (s, 1H, NH), 6.58–9.64 (m, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 14.76 (CH_3), 34.81 (CH_2N), 51.32 (C-2), 51.62 (OCH_3), 52.78 (OCH_3), 65.26 (C-3), 95.76 (C-1), 113.34–150.89 (CH_{arom} and C_{arom}), 165.92, 168.77, 173.62 (3 C=O); EI-MS: *m/z* (%) 408 (M^+, 1), 376 (70), 343 (22), 316 (28), 276 (51), 244 (100), 217 (39), 191 (20), 122 (15), 108 (29), 94 (28), 56 (5), 44 (3). Anal. Calcd. for $C_{23}H_{22}N_2O_5$ (406.43): C, 67.97; H, 5.46; N, 6.89. Found: C, 67.87; H, 5.26; N, 6.64.

Dimethyl (2*R*,*3*R)-3-(benzylaminocarbonyl)-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-1,2-dicarboxylate (8ec)**. White crystals (from chloroform/ether), mp >350 °C; R_f = 0.75 (silica; ethyl acetate/petroleum ether 1:3); IR (KBr): 3325 (NH), 3066 (C-H_{arom}), 3032, 2889, 1742 (C=O), 1665 (C=O), 1524, 1443, 1299, 1171, 1094, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.73 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 4.23 (d, *J* = 3.59 Hz, 1H, H-2), 4.48 (d, 2H, CH_2N), 4.99 (d, *J* = 3.68 Hz, 1H, H-3), 5.62 (s, 1H, NH), 6.58–9.64 (m, CH_{arom}); ^{13}C NMR ($CDCl_3$): δ 43.61 (CH_2N), 51.32 (C-2), 52.84 (OCH_3), 54.12 (OCH_3), 65.26 (C-3), 95.76 (C-1), 113.34–150.89 (CH_{arom} and C_{arom}), 165.92, 168.77, 173.62 (3 C=O); EI-MS: *m/z* (%) 471 (M^+, 1), 376 (50), 343 (12), 316 (28), 276 (51), 244 (100), 217 (35), 191 (21), 121 (15), 108 (29), 94 (28), 56 (5), 44 (3). Anal. Calcd. for $C_{28}H_{24}N_2O_5$ (468.50): C, 71.78; H, 5.16; N, 5.98. Found: C, 71.48; H, 4.92; N, 5.62.

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