STEREOCHEMISTRY OF 1,3-DIPOLAR CYCLOADDITION REACTION OF AZOMETHINE YLIDES DERIVED FROM N-ALKYL-N-(4-TOLUENESULPHONYL) CARBAMOYLMETHYL PHENANTHRIDINIUM WITH OLEFINIC DIPOLAROPHILES

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Abstract
A series of prepared N-alkyl-N-(p-toluenesulphonyl) bromoacetamides 1a-1b afforded with phenanthridine quaternary phenanthridinium salts 2a-2b. These, when treated with triethylamine in dichloromethane, form azomethine ylides that udergo cycloaddition reaction with present activated olefinic C=C double bond. This way pyrrolidino[1,2-f] phenanthridines 3-5 can be obtained. Their stereochemistry was studied by means of NMR spectroscopy. This family of phenanthridinium based ylides reacts very willingly with common olefinic dipolarophiles (dimethyl fumarate, dimethyl maleate or fumaronitrile) more or less stereoselectively. Some of the prepared racemic cycloadducts 3-5 were separated by HPLC on non-racemic cellulose-based sorbents with CD detection.

Introduction

Phenanthridinium based azomethine ylides (1,3-dipoles) stabilised by carbonyl exhibit their versatility in 1,3-dipolar cycloadditions with a series of activated dipolarophiles (dimethyl fumarate, dimethyl maleate and fumaronitrile) and this way new five-membered rings can be fused to the phenanthridine moiety to form pyrrolidino[1,2-f]phenanthridines (1)-(6). Such 1,3-dipolar cycloaddition reactions have been observed to proceed stereoselectively accordingly to the concerted transition structure (1)-(5). In our laboratory we are interested in stereochemistry of prepared pyrrolidino[1,2-f]phenanthridines. In addition, we have revealed that the reactivity of these ylides and hence stereoselectivity of the obtained cycloadducts are strongly dependent upon the group attached to the stabilising carbonyl group.

In the case of alkoxycarbonyl derivatives (esters) high reactivity and relatively low selectivity are observed (1)-(5). Moreover dehydrogenated products of primarily formed cycloadducts were often isolated. On the other hand, we could observe a very poor reactivity of aminocarbonyl derivatives (amides) (6) and a variety of applicable dipolarophiles is restricted to fumaronitrile save for the only exception of 1-adamantyl group (6).

In our present communication we want to bring further results contributing to the study of reactivity of phenanthridinium azomethine ylides bearing a N-alkyl-N-(p-toluenesulphonyl) amino group attached to the carbonyl because such arrangements are known in chiral auxiliaries (although bound mainly to dipolarophiles) (e. g. refs. (7)-(9)) to govern the stereochemistry of the cycloaddition and can be introduced to the ylide in future. Therefore, we were interested in how such a group alters the reactivity of phenanthridinium azomethine ylides and chiefly we were going for stereochemistry of formed cycloadducts.

Mixtures of cycloadducts (if formed) were separated by preparative column chromatography and the stereochemistry of products was studied under ^{1}H-NMR spestroscopy. For the prepared cycloadducts they are racemates we present here confirmation by separation of enantiomers by HPLC on non-racemic sorbents (10) based on derivatives of cellulose (11)-(13).

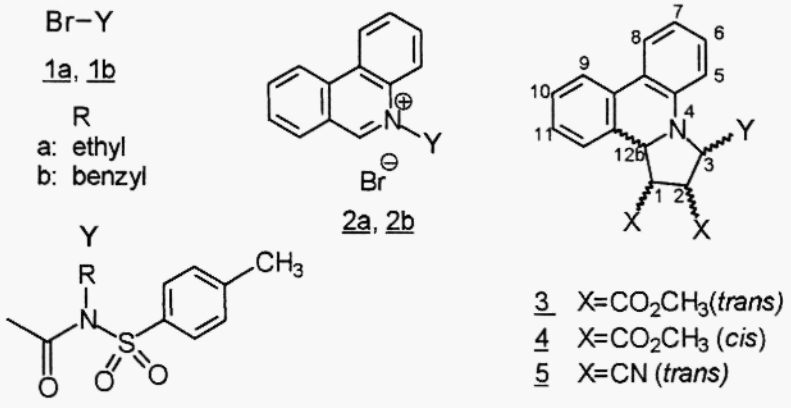
Discussion

N-Ethyl-N-(p-toluenesulphonyl) bromacetamide 1a and N-benzyl-N-(p-toluenesulphonyl) bromacetamide 1b (Scheme 1) were prepared from appropriate N-alkyl-p-toluene-sulphonamide by a new approach using $ZnCl_2$ as a catalyst (details in refs. (14)). Here $CHCl_3$ application at reflux afforded comparable reaction rates and yields to toluene or benzene. In this solvent the reaction took place in a homogenous phase.

Bromacetamide 1a and 1b (Scheme 1) show in FTIR spectra a characteristic stretching vibration of carbonyl group around 1690 cm^{-1} in addition to the pair of bands for SO_2 group at 1360 and 1170 cm^{-1}. A chemical shift of C=O group in 1a and 1b corresponds to the value for amide carbonyl being at 165 ppm. In MS one can find following principal peaks: molecular ion M^+ with its fellow M^++2, further M^+-HBr, M^+-N(R)COCH$_2$Br. Other characteristics are given in refs. (14).

Prepared bromoacetamides 1a and 1b (Scheme 1) undergo a nucleophilic substitution reaction with the phenanthridine nitrogen atom. Again (as in refs. (5-6)) we used acetonitrile as a solvent because of acceptable reaction time.

A CH=N$^+$ group of quaternary phenanthridinium salts 2a and 2b (Scheme 1) gives in FTIR spectra a band at 1629 cm^{-1} and in ^{13}C NMR spectrum an often hardly detectable peak at δ=157 ppm. In mass spectra we can find only a peak M^+-79 corresponding to the cationic part of salts 2a and 2b (Scheme 2). The parent peak in MS is at m/z=192 (phenathridine moiety), important is also one at 91.



Scheme 1

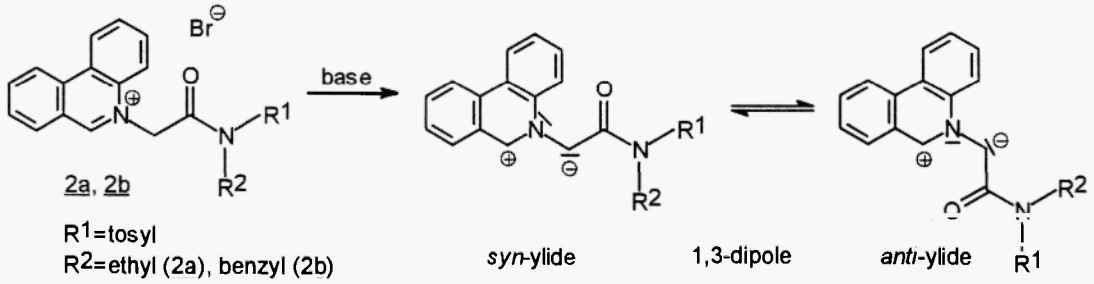
When quaternary phenanthridinium salts 2a-2b are treated with a base (in our case triethylamine) proton is abstracted from the methylene attached to carbonyl to form 1,3-dipol (azomethine ylide) (Scheme 2). This can react in a cycloaddition reaction adding onto an activated multiple bond to form a five-memberd ring (Scheme 1). As known, such reactions can proceed *via* two extreme mechanisms (15), (16), a concerted one

with the retention of the dipolarophile configuration or two-step zwitterionic mechanism where the obtained products lose the previous diploarophiie configuration. Moreover, phenanthridine based azomethine ylides can undergo a conformation change between *syn-* and *anti-* forms through possible rotation on partial double bond (Scheme 2).

Each of these ylide conformations affords a different stereoisomer at the same approach of dipolarophile. Therefore, we were interested in stereochemistry of cycloadducts 3-5 because we can reconstruct a transition structure arrangement and thus we can make some conclusions about ylide conformation.

Relative configurations of hydrogen atoms on C12b, C1, C2 and C3 can be evaluated from vicinal coupling constants $^3J_{1,12b}$ and $^3J_{2,3}$ under condition of remaining configuration on C1-C2. It is known that *trans*-constants are 0-5 Hz and *cis*-constants 6-9 Hz (6, 17). The assignement of the signal for C12b and C3 has been done obviously from H,H-COSY or HMBC experiments.

All the stereoisomers 3-5 formed in cycloaddition reactions must obviously be racemates. Therefore, we attempted to separate enantiomers. We chose an HPLC approach and tried to find the best combination of stationary and mobile phase. As stationary phases (sorbents) we used some of comercially available non-racemic sorbents based on derivatives of cellulose (18): triacetyl cellulose – methanol, tribenzoyl cellulose – ethanol and carbamate – ethanol. We separated compounds 3aA, 4a, 5aB, 3bA, 4b and 5bB. For detection of the separated enantiomers we applied a novel JASCO on-line CD detector (19 - 22). By its application we are able to obtain further information about chiral properties of our sample not recordable by a common UV detector.



Scheme 2

Results

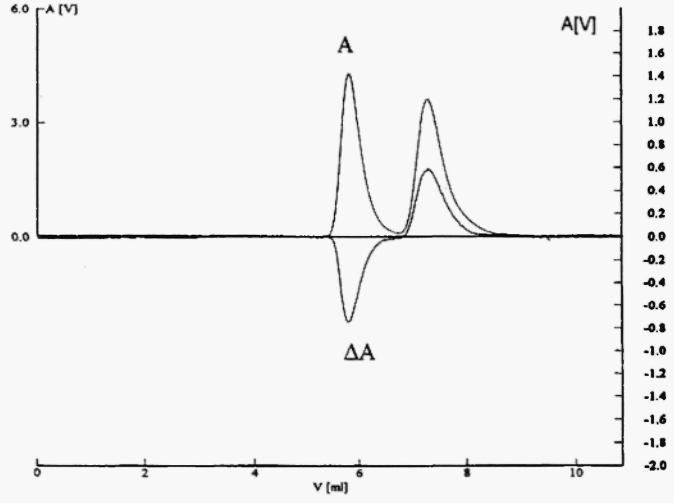
The generation of azomethinylides from 2a and 2b takes place under very mild conditions: to a mixture of suspended quaternary phenanthridinium salt 2a and 2b, respectively, and dipolarophile dissolved in CH_2Cl_2 triethylamine is added in one portion at ambient temperature under argon atmosphere in darkness. Once TEA is added pink hue of the ylide appears that disappears within few minutes, the reaction mixture turns dark yellow and the triethylammonium bromide deposit precipitates. The reaction outcome can be followed by TLC (in appropriate solvent mixture – see Experimental) and reaction usually ends within 1 hour. The crude reaction mixture was analysed by TLC and ^{1}H-NMR spectroscopy. The results are given in Table 1. In all the cases we obtained enantiomeric separation but the most representative results and good separation were made on tris(phenylcarbamoyl)cellulose (commercial column CHIRALCEL OC) in ethanol. We present

below an example of UV/CD detection for compound 3b (Figure 1) where one can see that 3b really consists of two enantiomers, between which we are not able to distinguish without CD information.

Product	Relative configuration			Ylide configuration
	1,2-	2,3-	1,12b-	
3aA	*trans*	*trans*	*trans*	*anti*
3aB	*trans*	*cis*	*cis*	*anti*
3b	*trans*	*trans*	*cis*	*syn*
4a	*cis*	*trans*	*trans*	*syn*
4b	*cis*	*trans*	*trans*	*syn*
5aA	*trans*	*cis*	*cis*	*anti*
5aB	*trans*	*cis*	*trans*	*syn*
5bA	*trans*	*cis*	*trans*	*syn*
5bB	*trans*	*trans*	*cis*	*syn*

In Table 1, **A** means less polar isomer, **B** means more polar isomer

Table 1



The curve A represents response of the UV detector at 260 nm, the curve ΔA is response of CD detector.

Figure 1

All solvents and reagents used for cycloaddition have to be thoroughly dried. Nevertheless, even then the reactions have to be carried out under argon and moreover in darkness. Employing argon is crucial for reproducibility of experiments and omitting it leads to the formation of ultimately other products and products of the dehydrogenation on C1-C12b bond are often isolated then. Therefore, it has turned out that phenanthdridinium based azomethine ylides are sensitive to molecular oxygen dissolved in reaction medium in addition to moisture. The latter can give rise to the formation of N-substituted-6-phenanthridones (3, 5, 6). Darkness is favourable, too. Such findings stand entirely in inconsistence to the reaction conditions in papers (23-26) concerning reactions of ylides derived from isoquinolinium or pyridinium salts where even water is used. The reason may be the presence of another fused benzene ring for phenanthridine derivatives.

Some results and experimental conditions of enantiomer separations are given in Table 2.

Compound	F	p	V	c	V_1	V_2	k_1	k_2	α
3aA	0.50	70	50	0.2	5.1 (-)	5.8 (+)	0.6	0.8	1.4
4a	0.50	70	100	0.5	6.3 (+)	7.1 (-)	1.0	1.3	1.3
5aB	0.50	70	150	0.2	13.2 (+)	19.7 (-)	3.2	5.3	1.7
3bA	0.25	34	15	0.5	5.8 (-)	7.3 (+)	0.9	1.3	1.6
4b	0.50	68	50	0.2	7.0 (+)	9.1 (-)	1.2	1.9	1.6
5bB	1.00	140	100	0.2	8.9 (-)	13.3 (+)	1.9	3.2	1.8

Column temperature 22°C. Column CHIRACEL OC. Eluent ethanol. F = flow [ml/min]; V = injected volume [μl]; c = sample concentration [mg/ml]; dead volume = 3.13 ml; V_1, V_2 = retention volumes of the first or the second peak [ml] with signs of circular dichroism detection at 260 nm; k_1, k_2 = capacity factors of first or second peak; α = relative retention; p = pressure [bar].

Table 2

Conclusion

We can conclude that the structure and bulkiness of substituent both at nitrogen atom of sulfonamide group and the substituent at double bond of dipolarophile play important role upon the stereochemical picture of 1,3-dipolar addition product. Ylide with R=Et reacts both in its *anti-* and *syn*-form according to the dipolarophile configuration. When dipolarophile possesses *trans*-configuration and at the same time the bulkier ethoxycarbonyl group is present the ylid is forced to react in its *anti*-conformation. In case this group is substituted by linear cyano group ylid reacts in both conformations. As soon as the substituent R is bulkier than ethyl group (R=benzyl) ylid reacts in its *syn*-conformation. When dipolarophile has got *cis*-configuration (samples 4) ylid reacts in conformation *syn*-. We noticed in ^{1}H NMR spectra that methylene protons both in ethyl and benzyl group of all the cycloadducts 3-5 are not equivalent giving complex spectra of higher order and each of them has different chemical shift. Thus, e.g. methylene protons couple with one of aromatic hydrogen atoms which is markedly shifted upfield (δ about 5.5 ppm). Values of coupling constants $J_{2,3}$ and $J_{1.12b}$ in products 3 - 5 were in full coincidence with those in ref. (23-26) and our previous observations (1-6). Less polar isomers 5aA and 5bA could not be unfortunately isolated as chemical individuals therefore we recorded neither mass spectra nor melting points, yet structure elucidation could unambiguously be carried out from NMR spectra. We observed that isomers 5aA, 5aB and 5bA, 5bB, respectively, were formed in ratio cca 2:1, isomers 3aA and 3aB in ratio cca 1:1.

We would like to state here that HPLC method of enantiomeric separation of fused pyrrolidino derivatives by CD JASCO detector was developed. But we have not succeeded to separate samples 3b and 4b.

It is of importance to emphasise that sulphonamide derivatives of phenanthridine azomethine ylides are comparable to ester series in their reactivity as for the choise of applicable dipolarophiles and as for the reaction rates.

Experimental

Melting points were measured on a Kofler hot stage VEB Wagetechnik Rapido 79/2106 and are incorrected. IR spectra were recorded on a FTIR ATI MATTSON spectrophotometer in KBr pellets. NMR spectra were recorded on a Bruker Avance 500 Varian apparatus with working frequency 500 MHz for ^{1}H and 125 MHz for ^{13}C in $CDCl_3$ (unless given otherwise) with TMS as an internal standard. Mass spectra were recorded on a FISONS INSTRUMENTS TRIO 1000 spectrometer in positive mode with EI ionization. TLC was carried out

on commercial silica plates Silufol Kavalier, Czech Republic. Column chromatography was carried out on Merck silica (63-100)μm. HPLC was performed on columns CHIRALCEL Series, detector: UV (260 nm) and JASCO CD 995 (260 nm).

CH_2Cl_2 (product of Onex, Czech Republic) was dried over CaH_2 and distilled from it. Triethylamine was dried over KOH and rectificated through a column with BaO. Commercially available CH_2Cl_2 (product of Onex, Czech Republic) and diethylether (product of Onex, Czech Republic) for column chromatography as well as acetonitrile (product of Lachema, Czech Republic) of pure grade were used. Phenanthridine, dimethyl fumarate, dimethyl maleate and fumaronitrile were products of Aldrich.

General method for quarternary phenanthridinium salts 2a-2b:

To a hot solution of 16.7 mmol appropriate bromacetamide (1a-1b) in 50 ml acetonitrile a chloroform solution of 3.0 g (16.7 mmol) phenanthridine was added and solution was refluxed under condenser for 5 days. During the heating period yellowish solid precipitated and solution turned to orange. Reaction mixture was concentrated in vacuum, deposit was collected, washed with chloroform and diethylether and dried at room temperature in air.

{[*N*-Ethyl-*N*-(*p*-toluenesulphonyl)carbamoyl]methyl}phenanthridinium bromide 2a.

Yield 7.51g (91%) of yellowish needles, m.p. 215-217 °C. For $C_{24}H_{23}BrN_2O_3S$ calculated 499.42 g mol^{-1}. EI-MS, m/z (%): 422 (1), 420 (M^+-79, 1), 322 (3), 320 (3), 270 (3), 255 (3), 240 (3), 180 (11), 179 (100), 178 (25), 155 (28), 150 (51), 148 (49), 139 (5), 122 (5), 120 (5), 91 (51), 65 (22). IR: 2974 m, 2992 s, 2888 m, 1694 s (ν C=O), 1629 s (ν CH=N^+), 1597 m (ν C=C), 1536 w, 1450 m, 1345 s (ν_{as} SO_2), 1266 w, 1239 s, 1166 s (ν_s SO_2), 1081 s, 1067 m, 858 m, 811 s, 755 s, 684 m. ^{1}H NMR spectrum (DMSO-d^6): 1.31 t, 3H, J=6.9 (**CH_3**CH_2); 2.44 s, 2H (**CH_3**Ph); 3.93 q, 2H, J=6.9 (CH_3**CH_2**); 6.59 s, 2H (CH_2C=O); 7.50 – 9.19 m, 14H (CH_{ar}); 10.50 s, 1H, CH=N^+. ^{13}C NMR spectrum (DMSO-d^6): 14.99 (**CH_3**CH_2); 21.50 (**CH_3**Ph); 42.24 (CH_3**CH_2**); 60.69 (CH_2C=O); 123.46; 125.76; 134.18; 135.28; 135.44; 145.91 (6 x $C_{q\ ar}$); 120.00; 123.82; 125.35; 128.51; 130.46; 130.77; 131.11; 132.43; 133.65; 139.48 (10 x CH_{ar}); 158.02 (CH=N^+); 165.48 (C=O).

{[*N*-Benzyl-*N*-(*p*-toluenesulphonyl)carbamoyl]methyl}phenanthridinium bromide 2b:

Yield 8.06 g (86%) of yellowish needles, m.p: 212-215 °C. For $C_{29}H_{25}BrN_2O_3S$ calculated 561.15 g mol^{-1}. EI-MS, m/z (%): 482 (M^+-79, 1), 322 (2), 246 (5), 228 (15), 226 (13), 180 (19), 179 (100), 178 (34), 155 (22), 151 (27), 108 (27), 106 (80), 91 (92), 65 (15). IR: 2929 m, 2848 s, 1706 s (ν C=O), 1625s (ν CH=N^+), 1598 m (ν C=C), 1456 m, 1353 s (ν_{as} SO_2), 1222 w, 1161 s (ν_s SO_2), 1088 s, 1011 m, 966 m, 802 s, 758 s, 655 m. ^{1}H NMR (DMSO-d^6): 2.58 s, 3H (**CH_3**Ph); 5.27 s, 2H (**CH_2**Ph); 6.66 s, 2H (CH_2C=O); 7.45 – 9.23 m, 17H (CH_{ar}); 10.80 s, 1H (CH=N^+). ^{13}C NMR (DMSO-d^6): 24.89 (**CH_3**Ph); 53.45 (**CH_2**Ph); 64.29 (CH_2C=O); 122.84; 123.19; 125.95; 133.71; 135.29; 135.88; 149.64 (7 x $C_{q\ ar}$); 121.11; 123.91; 124.72; 125.42; 127.43; 128.75; 130.66; 130.69; 130.97; 131.15; 132.72; 133.85; 141.59 (10 x CH_{ar}); 161.66 (CH=N^+); 169.31 (C=O).

General method for pyrrolidino[1,2-f]phenanthridines 3-5:

To a mixture of phenanthridinium salt 2a, 2b (0.5 g, 1.0 mmol for 2a, 0.89 mmol for 2b) suspended in dried CH_2Cl_2 and an equivalent of dissolved dipolarofile in dried CH_2Cl_2 argon was introduced for 5 minutes at

room temperature under stirring. Then equivalent of dried triethylamine was added in one portion under argon atmosphere with stirring in darkness. The reaction mixture was stirred for 3 hours at room temperature in darkness under inert. Then the solvent was evaporated in vacuum, the residue was extracted with benzene, the filtrate was concentrated under reduced pressure and the remainder was chromatographed on silica gel in appropriate solvent mixture. The combined fractions afforded product on evaporation.

(1R*, 2R*, 3R*, 12bR*)-Dimethyl-3-[*N*-ethyl-*N*-(*p*-toluenesulphonyl)]aminocarbonyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-1,2-dicarboxylate 3aA:

Yield 0.27 g (48%) of yellowish prisms (ethanol). Elution with CH_2Cl_2:Et_2O 60:1. m.p.: 155-157 °C. For $C_{30}H_{30}N_2O_7S$ calculated 562.63 g mol^{-1}. EI-MS, m/z, (%): 564 (M^++2, 1); 563 (M^++1, 1); 562 (M^+, 2); 410 (4); 409 (17); 408 (100); 375 (8); 336 (12); 304 (22); 302 (19); 277 (19); 276 (66); 275 (23); 251 (42); 244 (44); 219 (21); 218(39); 217 (64); 193 (10); 180 (13); 179 (22); 178 (6); 156 (12); 155 (13); 140 (10); 139 (12); 92 (36); 91 (71); 65 (18). IR: 3071 w, 3036 w, 2959 m, 2838 w, 1741 s (v C=O, ester), 1695 s (v C=O, amide), 1600 m (v C=C), 1497 m, 1450 m, 1367 s (v SO_2), 1310 m, 1261 m, 1180 s, 1171 s (v SO_2), 1091 m, 1022 s, 963 w, 802 m, 750 s, 717 w. ^{1}H NMR: 1.34 t, 3H, J=6.9 (**CH_3**CH_2); 2.46 s, 3H (CH_3Ph); 3.73 s, 3H (OCH_3); 3.78 dd, 1H, J(1,2)=4.1, J(2,3)=1.8 (H-2); 3.80 s, 3H (OCH_3); 3.91 dd, 1H, J(1,2)=4.1, J(1,12b)=1.5 (H-1); 3.94 and 4.04 m, 2H (CH_3**CH_2**); 5.34 d, 1H, J(2,3)=1.8 (H-3); 5.35 d, 1H, J=7.3 (CH_{ar}); 5.36 d, 1H, J(1,12b)=1.5 (H-12b); 6.72-7.94 m, 11H (CH_{ar}). ^{13}C NMR: 14.84 (**CH_3**CH_2); 21.52 (CH_3Ph); 42.57 (CH_3**CH_2**); 49.85 (C-1); 52.06; 52.14 (2 x OCH_3); 52.71 (C-2); 62.73 (C-3); 63.16 (C-12b); 112.01; 118.82; 122.9; 123.48; 124.08; 127.41; 127.53; 127.62; 128.35; 130.03; 130.26 (11 x CH_{ar}); 122.69; 131.27; 134.66; 136.66; 141.84; 145.30 (6 x $C_{q\,ar}$); 171.08; 171.92; 172.36 (3 x C=O).

(1S*, 2S*, 3R*, 12bR*)-Dimethyl-3-[*N*-ethyl-*N*-(*p*-toluenesulphonyl)]aminocarbonyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-1,2-dicarboxylate 3aB:

Yield 0.18 g (32%) of yellow powder. Elution with CH_2Cl_2:Et_2O 60:1. m.p.: 172-175 °C. For $C_{30}H_{30}N_2O_7S$ calculated 562.63 g mol^{-1}. EI-MS, m/z (%): 564 (M^++2, 1), 563 (M^++1, 1), 562 (M^+, 2), 410 (7), 409 (19), 408 (100), 375 (13), 336 (20), 304 (25), 302 (11), 277 (17), 276 (59), 275 (30), 251 (52), 244 (61), 219 (28), 218 (31), 217 (62), 193 (15), 180 (9), 179 (25), 178 (5), 156 (14), 155 (18), 140 (10), 139 (12), 92 (48), 91 (82), 65 (22). IR: 3067 w, 3033 w, 2957.7 m, 2854 w, 1737 s (v C=O, ester), 1700 s (v C=O, amide), 1602 m (v C=C), 1498 m, 1446 m, 1361 s (v SO_2), 1262 m, 1205 s, 1173 s (v SO_2), 1086 m, 1023 s, 957 w, 805 m, 749 s. ^{1}H NMR: 1.35 t, 3H, J=7.0 (**CH_3**CH_2); 2.40 s, 3H (CH_3Ph); 3.21 s, 3H (OCH_3); 3.65 s, 3H (OCH_3); 3.80-3.96 m, 4H (H-1 + H-2 + CH_3**CH_2**); 5.45 d, 1H, J(2,3)=6.6 (H-3); 5.68 d, 1H, J(1,12b)=6.6 (H-12b); 6.25 d, 1H, J=8.2, (CH_{ar}); 6.74-7.87 m, 11H (CH_{ar}). ^{13}C NMR: 14.56 (**CH_3**CH_2); 21.40 (CH_3Ph); 42.53 (CH_3**CH_2**); 47.97 (C-1); 51.42; 52.14 (2 x OCH_3); 52.19 (C-2); 63.15 (C-3); 65.95 (C-12b); 111.42; 118.92; 119.98; 122.97; 126.76; 127.32; 127.68; 127.97; 129.04; 129.58 (10 x CH_{ar}); 121.58; 129.12; 130.17; 136.19; 141.43; 144.83 (6 x $C_{q\,ar}$); 170.30; 170.70; 172.09 (3 x C=O).

(1R*, 2R*, 3R*, 12bS*)-Dimethyl-3-[*N*-benzyl-*N*-(*p*-toluenesulphonyl)]aminocarbonyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-1,2-dicarboxylate 3b:

Yield 0.32 g (58%) of yellowish powder. Elution with CH_2Cl_2:Et_2O 10:1. m.p.: 176-178 °C. For $C_{35}H_{31}N_2O_7S$ calculated 623.70 g mol^{-1}. EI-MS, m/z (%): 623 (M^+, 1), 597 (3), 536 (3), 431 (2), 426 (3), 406 (2), 368 (2), 363 (2), 339 (3), 337 (3), 320 (2), 276 (8), 262 (9), 207 (13), 180 (14), 179 (13), 158 (8), 157 (100), 156 (24), 141 (25), 140 (35), 139 (57), 125 (50), 124 (27), 123 (39), 107 (9), 106 (20), 105 (13), 93 (19), 92 (48), 91 (97), 79 (7), 65 (47). IR: 3065 w, 3033 w, 2958 m, 2851 w, 1743 s (v C=O, ester), 1708 s (v C=O, amide), 1598 m (v C=C), 1498 m, 1452 m, 1358 s (v SO_2), 1298 w, 1258 m, 1208 m, 1153 s (v SO_2), 1092 m, 1030 m, 928 w, 872 m, 744 m. ^{1}H NMR: 2.41 s, 3H (CH_3); 3.68 s, 3H (OCH_3); 3.74 dd, 1H, J(1,12b)=7.2, J(1,2)=4.3 (H-1); 3.75 s, 3H (OCH_3); 3.85 dd, 1H, J(1,2)=4.3, J(2,3)=1.5 (H-2); 5.02 and 5.44 AB quartet, 2H, J=15.3 (CH_2Ph); 5.04 d, 1H, J=9.7 (CH_{ar}); 5.23 d, 1H, J(2,3)=1.5 (H-3); 5.35 d, 1H, J(1,12b)=7.2 (H-12b); 6.57-7.64 m, 16H (CH_{ar}). ^{13}C NMR: 21.51 (CH_3); 49.22 (CH_2Ph); 49.73 (C-1); 52.04 (C-2); 52.63; 52.81 2xOCH_3; 62.42 C-3; 63.09 C-12b; 112.18; 118.89; 122.61; 123.46; 124.09; 127.45; 127.54; 127.91; 128.19; 128.25; 128.70; 129.83 12xCH_{ar}; 122.78; 131.25; 134.68; 136.21; 136.51; 141.72; 145.35 7x$C_{q\ ar}$; 171.70; 171.96; 172.15 3xC=O.

(1S*, 2R*, 3R*, 12bS*)-Dimethyl-3-[*N*-ethyl-*N*-(*p*-toluenesulphonyl)]aminocarbonyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-1,2-dicarboxylate 4a:

Yield 0.20 g (36%) of yellow powder. Elution with CH_2Cl_2:Et_2O 10:1. m.p.: 77-80 °C. For $C_{30}H_{30}N_2O_7S$ calculated 562.63 g mol^{-1}. EI-MS, m/z (%): 564 (M^++2, 1), 563 (M^++1, 1), 562 (M^+, 2), 409 (8), 408 (31), 407 (92), 375 (15), 336 (43), 302 (41), 277 (21), 276 (84), 275 (42), 251 (52), 244 (78), 219 (38), 218 (61), 217 (83), 193 (22), 180 (44), 179 (22), 178 (13), 156 (21), 155 (21), 140 (17), 139 (16), 92 (52), 91 (100), 65 (30). IR: 3066 w, 3034 w, 2953 m, 2854 w, 1743 s (v C=O, ester), 1695 s (v C=O, amide), 1600 m (v C=C), 1498 m, 1447 m, 1360 s (v SO_2), 1296 w, 1257 m, 1206 s, 1171 s (v SO_2), 1084 m, 1024 m, 962 w, 813 m, 749 m, 717 w. ^{1}H NMR: 1.43 t, 3H, J=7.0 (**CH_3**CH_2); 2.42 s, 3H (CH_3Ph); 3.28 s, 3H (OCH_3); 3.59 dd, 1H, J(1,2)=8.0, J(2,3)=5.7 (H-2); 3.73 s, 3H (OCH_3); 3.86 dd, 1H, J(1,2)=8.0, J(1,12b)=5.5 (H-1); 4.05 and 4.20 m, 2H (CH_3**CH_2**); 5.42 d, 1H, J(2,3)=5.7 (H-3); 5.71 d, 1H, J(1,12b)=5.5 (H-12b); 5.82 d, 1H, J=8.1 (CH_{ar}); 6.64-7.90 m, 11H (CH_{ar}). ^{13}C NMR: 15.37 (**CH_3**CH_2); 21.54 (CH_3Ph); 42.15 (CH_3**CH_2**); 50.11 (C-1); 51.49; 51.64 (2 x OCH_3); 52.56 (C-2); 62.38 (C-3); 63.68 (C-12b); 111.15; 118.00; 119.73; 123.03; 125.85; 126.93; 127.85; 128.21; 129.66; 130.66 (10 x CH_{ar}); 121.85; 128.78; 130.62; 136.16; 141.60; 144.99 (6 x $C_{q\ ar}$); 170.36; 170.57; 173.64 (3 x C=O).

(1S*, 2R*, 3R*, 12bS*)-Dimethyl-3-[*N*-benzyl-*N*-(*p*-toluenesulphonyl)]aminocarbonyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-1,2-dicarboxylate 4b:

Yield 0.34 g (62%) of yellow powder. Eluting with CH_2Cl_2:Et_2O 10:1. m.p.: 73-76 °C. For $C_{35}H_{31}N_2O_7S$ calculated 623.70 g mol^{-1}. EI-MS, m/z (%): 623 (M^+, 1), 471 (8), 470 (20), 336 (22), 302 (18), 277 (8), 276 (29), 275 (15), 251 (20), 244 (39), 218 (33), 217 (43), 193 (17), 180 (21), 179 (12), 156 (15), 139 (8), 133 (10), 106 (15), 92 (34), 91 (100), 77 (14), 65 (17). IR: 3064 w, 3033 w, 2957 m, 2851 w, 1742 s (v C=O, ester), 1698 s (v C=O, amide), 1602 m (v C=C), 1498 m, 1450 m, 1361 s (v SO_2), 1298 w, 1260 m, 1208 m, 1166 s (v SO_2), 1089 m, 1030 m, 924 w, 865 m, 807 m, 746 m. ^{1}H NMR: 2.42 s, 3H (CH_3); 3.23 s, 3H (OCH_3); 3.37 dd, 1H, J(1,2)=8.2, J(1,12b)=5.4 (H-1); 3.71 s, 3H (OCH_3); 3.78 dd, 1H, J(1,2)=8.2, J(2,3)=5.5 (H-2); 5.30 m, 2H (CH_2); 5.40 d, 1H, J(2,3)=5.5 (H-3); 5.42 d, 1H, J=9.7 (CH_{ar}); 5.65 d, 1H, J(1,12b)=5.4 (H-

12b); 6.56-7.80 m, 16H (CH_{ar}). ^{13}C NMR: 21.54 (CH_3); 49.24 (CH_2); 49.92 (C-1); 51.45 (OCH_3); 51.58 (C-2); 52.56 (OCH_3); 62.52 (C-3); 63.57 (C-12b); 111.18; 117.82; 121.77; 122.80; 125.88; 126.79; 127.80; 127.91; 128.51; 128.75; 128.80; 129.58 (12 x CH_{ar}); 119.30; 130.02; 130.59; 135.87; 136.20; 141.39; 145.08 (7 x $C_{q\ ar}$); 170.46; 170.52; 174.01 (3 x C=O).

(1S*, 2S*, 3R*, 12bR*)-[*N*-ethyl-*N*-(*p*-toluenesulphonyl)]-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide 5aA:

Yield 0.20 g (mixture 5aA+5aB of yellowish powder. Elution with CH_2Cl_2:Et_2O 40:1. IR: 3065 w, 3037 w, 2979 m, 2248 w (v CN), 1696 s (v C=O), 1601 m (v C=C), 1497 m, 1449 m, 1365 s (v SO_2), 1211 s, 1178 s (v SO_2), 1088 m, 1017 s, 961 m, 888 s, 814 m, 750 m. ^1H NMR: 1.32 t, 3H, J=7.0 (**CH_3**CH_2); 2.47 s, 3H (CH_3); 3.70 dd, 1H, J(2,3)=8.3, J(1,2)=5.7 (H-2); 3.80 dd, 1H, J(1,12b)=7.4, J(1,2)=5.7 (H-1); 3.86-4.03 m, 2H (CH_3**CH_2**); 5.44 d, 1H, J=9.3 (CH_{ar}); 5.48 d, 1H, J(2,3)=8.3 (H-3); 5.68 d, 1H, J(1,12b)=7.4 (H-12b); 6.74-7.95 m, 11H (CH_{ar}). ^{13}C NMR: 14.50 (**CH_3**CH_2); 21.60 (CH_3Ph); 36.24 (C-1); 38.36 (C-2); 43.21 (CH_3**CH_2**); 63.74 (C-3); 64.13 (C-12b); 112.18; 119.61; 122.29; 124.00; 125.49; 127.30; 127.54; 128.15; 128.92; 129.04; 130.22 (11 x CH_{ar}); 117.45; 118.20 (2 x CN); 120.78; 128.79; 131.34; 135.84; 139.86; 146.09 (6x$C_{q\ ar}$); 169.27 (C=O).

(1S*, 2S*, 3R*, 12bS*)-[*N*-Ethyl-*N*-(*p*-toluenesulphonyl)]-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide 5aB:

Yield 0.08 g (16%) of yellowish powder (ethanol). Elution with CH_2Cl_2:Et_2O 40:1.m.p.: 237-239 °C. For $C_{28}H_{24}N_4O_3S$ calculated 496.58 g mol^{-1}. EI-MS, m/z (%): 498 (M^++2, 1), 496 (M^+, 1), 344 (4), 343 (21), 342 (100), 284 (8), 283 (35), 282 (32), 270 (32), 268 (32), 244 (8), 243 (36), 242 (21), 220 (7), 219 (12), 218 (64), 193 (13), 180 (28), 179 (38), 165 (13), 92 (20), 91 (47), 65 (22). IR: 3067 w, 2983 m, 2956 m, 2926 m, 2249 w (v CN), 1695 s (v C=O), 1602 m (v C=C), 1498 m, 1450 m, 1368 s (v SO_2), 1212 s, 1183 s (v SO_2), 1089 m, 1023 s, 963 m, 813 s, 746 m. ^1H NMR spectrum: 1.30 t, 3H, J=7.0 (**CH_3**CH_2); 2.51 s, 3H (CH_3Ph); 3.84-3.96 m, 3H (CH_3**CH_2** +H-1); 4.25 dd, 1H, J(2,3)=9.0, J(1,2)=1.1 (H-2); 5.42 d, 1H, J=7.5 (CH_{ar}); 5.48 d, 1H, J(2,3)=9.0 (H-3); 5.80 d, 1H, J(1,12b)=4.5 (H-12b); 6.74-7.79 m, 11H (CH_{ar}). ^{13}C NMR spectrum: 14.11 (**CH_3**CH_2); 21.63 (CH_3Ph); 35.86 (C-1); 40.15 (C-2); 43.40 (CH_3**CH_2**); 62.02 (C-3); 62.78 (C-12b); 111.19; 119.61; 122.75; 123.54; 125.45; 127.54; 128.12; 128.88; 129.04; 130.48 (10 x CH_{ar}); 116.31; 116.68 (2 x CN); 120.49; 128.73; 130.61; 135.73; 139.80; 146.18 (6 x $C_{q\ ar}$); 169.03 C=O.

(1R*, 2S*, 3R*, 12bR*)-[*N*-Benzyl-*N*-(*p*-toluenesulphonyl)]-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide 5bA:

Yield 0.08 g (16%) of yellowish powder (ethanol). Elution with CH_2Cl_2:Et_2O 100:1. m.p.: 113-115 °C. For $C_{33}H_{26}N_4O_3S$ calculated 558.65 g mol^{-1}. EI-MS, m/z (%): 558 (M^+, 1), 406 (7), 405 (28), 404 (93), 336 (22), 283 (28), 270 (48), 243 (33), 218 (45), 193 (13), 180 (19), 179 (30), 155 (10), 132 (11), 106 (22), 92 (29), 91 (100), 77 (9), 65 (11). IR: 3064 w, 3035 w, 2927 m, 2855 w, 2249 w (v CN), 1696 s (v C=O), 1601 m (v C=C), 1495 m, 1449 m, 1365 s (v SO_2), 1262 w, 1161 s (v SO_2), 1089 m, 1027 s, 866 m, 803 s, 747 m. ^1H NMR: 2.43 s, 3H (CH_3Ph); 3.93 dd, 1H, J(1,12b)=4.7, J(1,2)=1.5 (H-1); 4.20 dd, 1H, J(2,3)=8.9, J(1,2)=1.5 (H-2); 4.90 and 5.33 AB quartet, 2H, J=15.0 (CH_2); 5.19 d, 1H, J=7.9 (CH_{ar}); 5.42 d, 1H, J(2,3)=8.9 (H-3);

5.77 d, 1H, J(1,12b)=4.7 (H-12b); 6.70-7.53 m, 16H (CH_{ar}). ^{13}C NMR: 21.55 (CH_3Ph); 35.90 (C-1); 40.13 (C-2); 50.05 (CH_2); 62.33 (C-3); 62.76 (C-12b); 111.42; 119.70; 122.77; 123.52; 125.41; 126.13; 127.77; 128.02; 128.14; 128.50; 129.24; 129.65; 130.23 (13 x CH_{ar}); 116.29; 116.65 (2 x CN); 120.62; 130.64; 135.36; 139.60; 143.44; 146.15 (6 x $C_{q\,ar}$); 169.05 (C=O).

(1R*, 2R*, 3R*, 12bS*)-[*N*-Benzyl-*N*-(*p*-toluenesulphonyl)]-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide 5bB:

Yield 0.20 g (mixture 5bA+5bB) of yellowish powder. Elution with CH_2Cl_2:Et_2O 100:1. IR: 3063 w, 3034 w, 2963 s, 2943 m, 2855 w, 2249 w (v CN), 1697s (v C=O), 1600 m (v C=C), 1496 m, 1499 m, 1365 s (v SO_2), 1262 w, 1159 s (v SO_2), 1090 s, 1028 s, 971 w, 806 s, 745 m. ^{1}H NMR: 2.47 s, 3H (CH_3Ph); 3.63 dd, 1H, J(1,12b)=8.4, J(1,2)=5.8 (H-1); 3.70 dd, 1H, J(1,2)=8.4, J(2,3)=2.1 (H-2); 4.98 and 5.37 AB quartet, 2H, J=15.1 (CH_2); 5.27 d, 1H, J(2,3)=2.1 (H-3); 5.35 d, 1H, J=6.2 (CH_{ar}); 5.39 d, 1H, J(1,12b)=8.4 (H-12b); 6.64-7.51 m, 16H (CH_{ar}). ^{13}C NMR: 21.53 (CH_3Ph); 35.81 (C-1); 40.12 (C-2); 49.44 (CH_2); 62.35 (C-3); 62.81 (C-12b); 111.28; 119.71; 122.76; 123.81; 125.45; 126.33; 127.83; 128.00; 128.30; 128.57; 129.44; 130.97; 131.75 (13 x CH_{ar}); 116.36; 116.59 (2 x CN); 120.88; 130.21; 135.41; 139.41; 143.42; 146.28 (6 x $C_{q\,ar}$); 169.23 C=O.

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