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Domino Imine Condensation/Intramolecular Polar [4π⁺ + 2π]-Cycloaddition of Anilines and ω-Unsaturated Aldehydes: A Versatile Tool for the Highly Diastereoselective Synthesis of 1,2,3,4,4a,9,9a,10-Octahydroacridines

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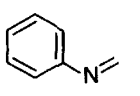
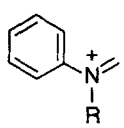
Abstract. The highly diastereoselective synthesis of substituted 1,2,3,4,4a,9,9a,10-octahydroacridines **7**, **8** with five stereogenic centers has been achieved by domino imine condensation/intramolecular polar [4π⁺ + 2π]-cycloaddition of anilines **3** and ω-unsaturated aldehydes **4**. The transformations which can be performed under mild reaction conditions using 0.3 eq. $BF_3{\cdot}Et_2O$ as a Lewis acid give the cycloadducts **7**, **8** with yields ranging from 63–76%. The relative configuration of **7**, **8** was assigned by ^1H- and ^{13}C-NMR spectroscopy. For **7a**, an X-ray crystal structure analysis was obtained. Experimental as well as semiempirical results support a polar [4π⁺ + 2π]-cycloaddition under kinetic control. It is assumed that the diastereoselectivity of the process is governed by decalin-like *exo-E-anti*-transition state structures **24**, **25** with equatorial arrangement of the bulky substituents R^2.

Despite their importance to pharmacological research and the synthesis of natural products only few methods are known for the efficient and stereoselective synthesis of partially unsaturated *N*-heterocycles like tetrahydroquinolines [1], tetrahydro- or octahydroacridines [2]. One way to gain access to partially unsaturated *N*-heterocycles is based on the cycloaddition of electron-poor neutral or cationic 2-azabutadienes with electron-rich dienophiles [3]. It is also possible to employ neutral 2-azabutadienes **1** as dienes in cycloaddition reactions, but these are known to be less reactive than their positively charged counterparts **2** and therefore need to be activated by Lewis acids and/or electron withdrawing groups [3, 4]. Cationic 2-azabutadienes can be generated *in situ* by imine condensation of aromatic amines with carbonyl compounds under acidic conditions. Reaction with a suitable dienophile then yields the corresponding cyclo-adducts [3, 5, 6]. A difficulty entailed is the tendency of the initially formed cycloadduct to undergo a second domino imine condensation/cycloaddition sequence [5, 6]. By employing suitable substituted aromatic amines this can be avoided [6]. Other efficient methods for the selective generation of cationic 2-azabutadienes include the heterolytic cleavage of 2-hetero-substituted α-aryl amines like *N,X*-acetals [7], *N*-alkyl-*N*-aryl-1*H*-ben- zo-triazole-1-methanamines [8] or hexahydro-1,3,5-triazines [9]. Recently, we have demonstrated that 1,2,3,4-tetrahydroquinolines can be prepared regio- and diastereoselectively by intermolecular polar [4π⁺ + 2π]-cycloaddition of cationic 2-azabutadienes generated by cleavage of *N,S*-acetals, α-aminosulfones and α-aminonitriles [7d,e]. Octahydroacridines have been obtained by intramolecular cyclization of cationic 2-aza- butadienes derived from oxime sulfonates *via Beckmann*-rearrangement [10] and Lewis acid catalyzed cyclizations of *N*-arylimines. The influence of Lewis acids, solvents or metal tricarbonyl fragments on the cyclizations has been studied [11]. So far little is known of the mechanism of such processes in general, and on the influence of the configuration of diene and dienophile on the stereochemical outcome of such cyclizations in particular. Other methods for the synthesis of the 1,2,3,4,4a,9,9a,10-octahydroacridine skeleton include the catalytic hydrogenation of acridines [12a] and the ring expansion of 4a-methoxy-amino-cyclohex[a] indanes [12b].



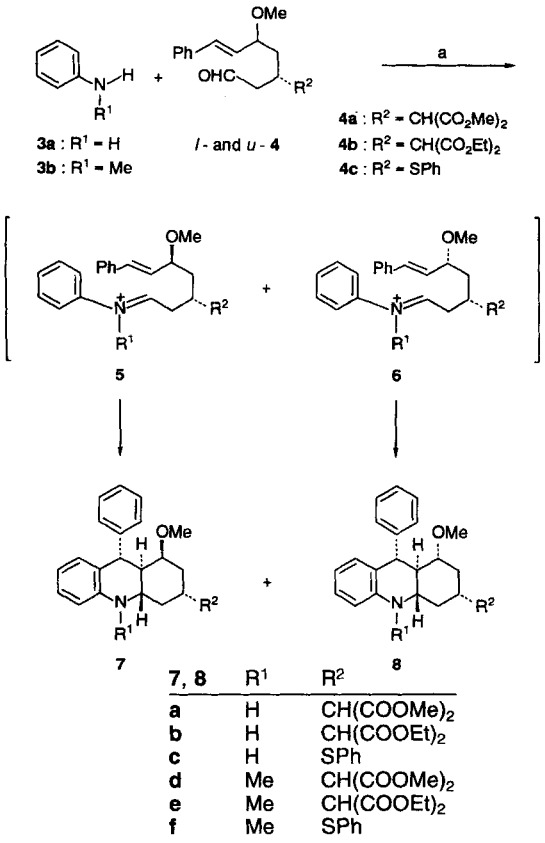
1



2

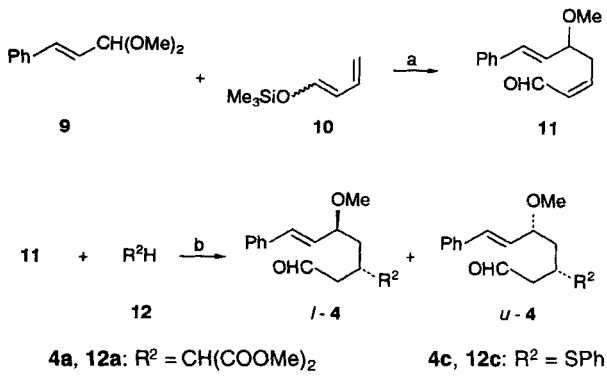
Here we give a full account on the intramolecular polar [4π⁺ + 2π]-cycloaddition of di- and trisubstituted α-aryliminium ions **5**,**6** generated *in situ* by imine condensation of anilines **3** and ω-unsaturated aldehydes **4** [13]. Using this domino process [14] the highly diastereoselective formation of *trans*-annulated octahydroacridines **7**,**8** with five stereogenic centers could be achieved (Scheme 1, Table 1).

For this purpose the w-unsaturated aldehydes **4a–c** and **19** were synthesized. **4a–c** were obtained straight

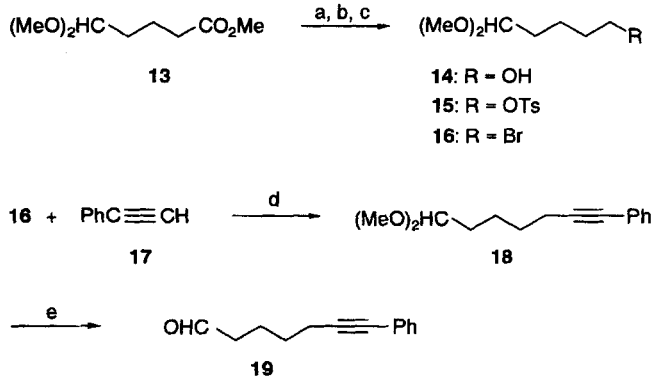


7, 8	R^1	R^2
a	H	$CH(COOMe)_2$
b	H	$CH(COOEt)_2$
c	H	SPh
d	Me	$CH(COOMe)_2$
e	Me	$CH(COOEt)_2$
f	Me	SPh

Scheme 1 a) **3** (1.0 equiv.), CH_2Cl_2, –78 °C. **4** (1.0 equiv.), –60 °C, 10 min, $BF_3{\cdot}Et_2O$ (0.3 equiv.), then room temp., 12–15 h.



Scheme 2 a) **9** (1.0 equiv.), THF, –78 °C, $TiCl_4$ (1.2 equiv.), **10** (1.2 equiv.), –78 °C, 2 h, 87%; b) for **4a**: KO*t*Bu (0.3 equiv.), THF, **12a** (2.0 equiv.), **11** (1.0 equiv.), room temp., 2 h, 55%; for **4b**: KO*t*Bu (0.3 equiv.), THF, **12b** (2.0 equiv.), **11** (1.0 equiv.), reflux, 2 h, 61%; for **4c**: **11** (1.0 equiv.), THF, 0 °C, **12c** (10.0 equiv.), *n* BuLi (0.1 equiv.), room temp., 15 h, 90%.



Scheme 3 a) $LiALH_4$, Et_2O, 0 °C, 6 h, then room temp., 12 h, 94%; b) *p*-TsCl, pyridine, –20 °C, 2h, 86%; c) LiBr, acetone, room temp., 2.5 h, 96%; d) *n* BuLi (1.0 equiv.), THF, DMSO, **17** (1.0 equiv.), –12 °C, 30 min, **16** (0.8 equiv.), –12 °C, 14 h, 80%; e) 9% HCl, THF, room temp., 20 min, 90%.

forward in only two steps as shown in scheme 2. The a,b-unsaturated aldehyde **11** was easily available in one step by *Mukaiyama* aldol reaction of the acetal **9** with the 1-silyloxybutadiene **10** in 87% yield [15]. The base catalyzed 1,4-addition of nucleophiles **12a–c** to **11** gave the desired w-unsaturated aldehydes **4a–c** with yields between 55 and 90% as mixtures of their *l*- and *u*-diastereoisomers (Scheme 2).

As outlined in scheme 3 the acetylenic aldehyde **19** was obtained in five steps from the easily available C_5-building block **13** [16]. Reduction of **13** yielded the primary alcohol **14** with 94%, which was transformed into the bromide **16** in high yields *via* the tosylate **15** using standard procedures. Deprotonation of phenylacetylene **17** with *n*-BuLi/DMSO [17] and then reaction with the bromide **16** gave the acetylenic acetal **18** with 80% yield.

Table 1 Diastereoselective formation of octahydroacridines **7, 8** by domino imine condensation/intramolecular polar $[4\pi^+ + 2\pi]$-cycloaddition

Entry	3	R^1	4	R^2	7, 8	Yield[a] 7+8 [%]	Yield[b] 7 [%]	Yield[b] 8 [%]
1	a	H	a	$CH(CO_2Me)_2$	a	76	38	29
2	a	H	b	$CH(CO_2Et)_2$	b	73	35	29
3	a	H	c	SPh	c	63	30	23 [c]
4	b	Me	a	$CH(CO_2Me)_2$	d	71	31	25
5	b	Me	b	$CH(CO_2Et)_2$	e	70	38	29
6	b	Me	c	SPh	f	67	31	23 [c]

[a] After column chromatography. [b] Yields refer to analytically pure compounds. [c] **8c** and **8f** could not be obtained pure due to decomposition upon purification.

In the last step of the sequence the acetal **18** was hydrolyzed with 9% hydrochloric acid to produce the desired aldehyde **19** with 90% [18].

The Lewis acid catalyzed domino reaction of aniline (**3a**) with aldehydes **4a** and **4b** exclusively gave the *trans*-annulated diastereomeric octahydroacridines **7a/8a** and **7b/8b** with 76 and 73% yield, respectively (Table 1, entries 1, 2). **7** and **8** only differ in the arrangement of the methoxy group at C-1: in compounds of type **7** the methoxy group occupies the *axial*, in compounds of type **8** the *equatorial* position. The same holds true for the transformations of *N*-methylaniline (**3b**) with **4a** and **4b**. Here also only *trans*-annulated octahydroacridines are obtained; **7d/8d** and **7e/8e** were isolated with 71 and 70% yield, respectively (Table 1, entries 4, 5). In all cases the diastereomers **7** and **8** could be separated by flash chromatography on silica gel (Table 1). Similar results were produced in the reactions of **3a** and **3b** with the aldehyde **4c** bearing a thiophenyl- substituent at C-3. With **4c**, though, just the octahydroacridines **7c** and **7f**, resp., with an *axial* methoxy group at C-1 could be isolated without decomposition (Table 1, entries 3, 6). It is interesting to note that in no case any products of a second domino imine condensation/cycloaddition sequence could be detected. In a typical experiment the aniline **3** was added to a solution of the aldehyde **4** in CH_2Cl_2 in the presence of molecular sieves (4 Å). To secure the formation of the iminium salts **5**, **6** the reaction mixture was kept at −60 °C for 10 min. Subsequently the Lewis acid was added at −60 °C, the reaction mixture was warmed up to room temp. and stirred until completion. Best chemical yields were observed when the transformations were performed with $BF_3{\cdot}Et_2O$ (0.3 equiv.) as Lewis acid in CH_2Cl_2. Usually the reactions were performed in the presence of molecular sieves (4 Å). In further experiments it was shown, however, that the addition of molecular sieves (4 Å) has no marked influence on the outcome of the cyclizations.

Analytically pure samples of **7** and **8** were obtained by flash chromatography on silica gel followed by recrystallization. The structure elucidation and the assignment of the relative configuration of all stereogenic centers in **7** and **8** was deduced from their NMR-spectra. As an example ^1H NMR-data are discussed which allowed an unambiguous configurational assignment of the dia- stereomeric octahydroacridines **7d** and **8d**.

The ^1H NMR-spectrum of **7d** shows characteristic and well resolved signals for 2-H_{ax}, 4-H_{ax}, 4a-H, 9-H and 9a-H amongst others. The signal for 9a-H appears at $\delta = 1.77$ ppm as a doublet of triplet with coupling constants of $J = 2.5$ ($^3J_{1,9a}$), 11.0 ($^3J_{4a,9a}$) and 11.0 Hz ($^3J_{9,9a}$). From the large vicinal coupling constants $^3J_{4a,9a} = 11.0$ Hz and $^3J_{9,9a} = 11.0$ Hz the *axial* positions of 4a-H, 9-H and 9a-H can be concluded. This proves the *trans*-arrangement of the rings B and C as well as

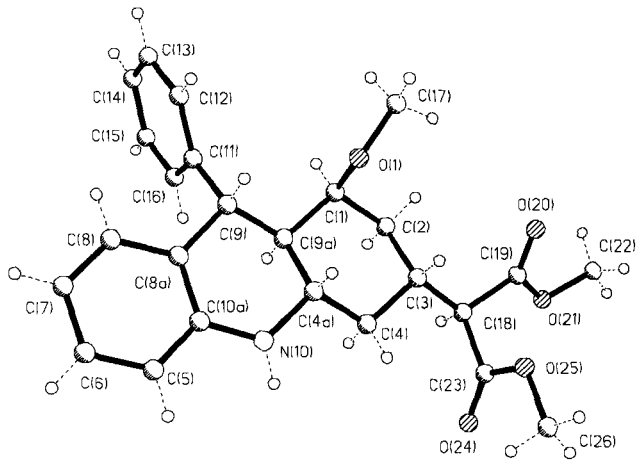


Fig. 1 X-ray structure and crystallographic numbering scheme of **7a**.

the *pseudoequatorial* position of the phenyl group at C-9. The small vicinal coupling constant $^3J_{1,9a} = 2.5$ Hz is typical for an *equatorial-axial* relationship and firmly establishes the *axial* methoxy group at C-1. The *equatorial* position of the malonic ester group at C-3 is deduced from the vicinal coupling constants $^3J_{2ax,3ax} = 14.0$ Hz and $^3J_{3ax,4ax} = 12.0$ Hz which indicate an *axial* orientation for 3-H. The arguments for the structure elucidation of the octahydroacridines **8** with an *equatorial* methoxy group at C-1 follow the same pattern. In the ^1H NMR-spectrum of **8d**, e.g., 9a-H resonates at $\delta = 2.18$ ppm as a doublet of triplet with coupling constants of $J = 8.5$ ($^3J_{1,9a}$), 10.5 ($^3J_{4a,9a}$ and 10.5 Hz ($^3J_{9,9a}$). The large vicinal coupling constant $^3J_{1,9a} = 10.5$ Hz unambiguously proves the *trans-diaxial* relationship of 1-H and 9a-H and with this the *equatorial* position of the methoxy group at C-1.

Further evidence for the structure assignments of **7** and **8** comes from an X-ray crystal structure analysis of **7a** [19]. Figure 1 clearly demonstrates the *trans* annulation of rings B and C, the *pseudoequatorial* arrangement of the phenyl group at C-9 as well as the *equatorial* malonic ester group at C-3 and the *axial* methoxy group at C-1.

We assume that the reactions proceed as domino imine condensation/intramolecular polar [$4\pi^+ + 2\pi$]-cy-

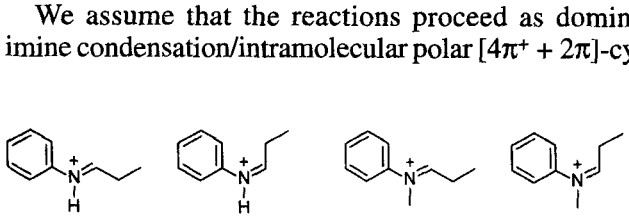
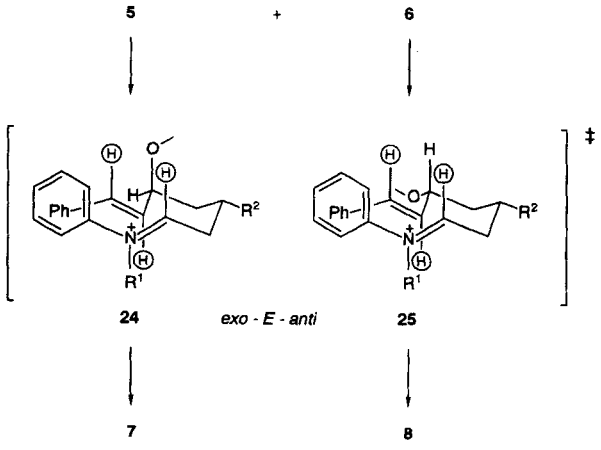
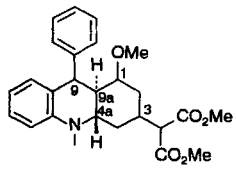
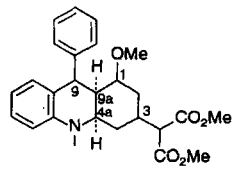


Fig. 2 PM3 Calculations on the stability of di- and trisubstituted aryliminium ions **20–23**.





7d, 8d, 26d - 31d



32d -39d

No.	Rel. configuration	E kcal mol^{-1}
7d	1*S*, 3*R*, 4a*S*, 9*S*, 9a*R*	−161.73
8d	1*R*, 3*R*, 4a*S*, 9*S*, 9a*R*	−157.65
26d	1*S*, 3*S*, 4a*S*, 9*S*, 9a*R*	−160.21
27d	1*R*, 3*S*, 4a*S*, 9*S*, 9a*R*	−155.93
28d	1*R*, 3*S*, 4a*S*, 9*R*, 9a*R*	−159.80
29d	1*R*, 3*R*, 4a*S*, 9*R*, 9a*R*	−161.66
30d	1*S*, 3*R*, 4a*S*, 9*R*, 9a*R*	−156.95
31d	1*S*, 3*S*, 4a*S*, 9*R*, 9a*R*	−155.75

No.	Rel. configuration	E [kcal mol^{-1}]
32d	1*S*, 3*R*, 4a*R*, 9*R*, 9a*R*	−154.82
33d	1*R*, 3*R*, 4a*R*, 9*R*, 9a*R*	−154.60
34d	1*R*, 3*S*, 4a*R*, 9*R*, 9a*R*	−153.67
35d	1*S*, 3*S*, 4a*R*, 9*R*, 9a*R*	−153.50
36d	1*S*, 3*S*, 4a*R*, 9*S*, 9a*R*	−155.00
37d	1*R*, 3*S*, 4a*R*, 9*S*, 9a*R*	−160.81
38d	1*R*, 3*R*, 4a*R*, 9*S*, 9a*R*	−159.60
39d	1*S*, 3*R*, 4a*R*, 9*S*, 9a*R*	−157.20

Scheme 4 AM1 Calculations on the stability of 1,2,3,4,4a, 9,9a,10-octahydroacridines **7d**, **8d**, **26d–39d**.

cloaddition. In the first step the condensation of **3** with *l*- or *u*-**4** yields the corresponding iminium ions **5** and ions **5** and **6**, respectively. From PM3 caclulations on model compounds **20–23** it is clear that not only di- but also trisubstituted imionium ions with an (*E*)-C=N$^+$-bond are considerab ly more stable than the corresponding (*Z*)-isomers (Figure 2). Based on these results we assume the (*E*)-configuration for the C=N$^+$-bond in all iminium ions **5** and **6**.

In the second step of the domino process **5** and **6** undergo an intramolecular cyclization with the formation of three new stereogenic centers in sequence to yield the cycloadducts **7** and **8**, respectively. These cyclizations may either proceed as a one step intramolecular [4π$^+$ + 2π]-cycloaddition [3] or as a two step intramolecular 1,2-C=N$^+$-addition [20]/intramolecular cationic cyclization [21] sequence.

It is remarkable that in all the cases studied so far only **7** and **8**, that is two out of 16 possible diastereomers, are formed selectively. These results can best be explained by assuming that both (*E*)-iminium ions **5** and **6** undergo kinetically controlled intramolecular polar [4π$^+$ + 2π]-cycloadditions. Passing the decalin-like *exo-E-anti*-transition state structures **24** and **25** the cycloadducts **7** and **8**, resp., are obtained highly diastereoselectively. The conformation of **24** and **25** is governed by the bulky substituents R^2 preferring an *equatorial* arrangement. This view is heavily supported by the fact that the *l*/*u*- ratio as well as the (*E*)-stereochemistry of the dienophilic double bond of the starting aldehydes **4** is being retained during the whole process. Furthermore, it was shown that **7d** and **8d** do not isomerize under reaction conditions. Further support for kinetically controlled cyclizations comes from AM1 calculations on the stability of all 16 possible diastereomeric cyclization products. From the comparison of the relative energies of the diastereomeric octahydroacridines **7d**, **8d**, **26d–39d** it follows that in the case of reactions under thermodynamic control complex mixtures of diastereomers would have been formed (Scheme 4).

To further explore the scope of the intramolecular polar [4π$^+$ + 2π]-cycloaddition with cationic 2-azabutadienes the acetylenic aldehyde **19** was treated with aniline (**3a**) under different acidic and Lewis acidic conditions. However, under no circumstances the expected hexahydroacridine could be detected. We assume that the low reactivity of the acetylenic dienophile is due to its low HOMO energy.

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Experimental

Reagents were used as obtained or purified if necessary [22]. Solvents were dried by standard procedures and distilled prior to use [22]. All reactions were carried out under an atmosphere of argon and monitored by TLC (Macherey & Nagel, Alugram SIL G/UV$_{254}$). For column filtration silica gel (Macherey & Nagel 50–200 μm) was used. Flash chromatography was performed with silica gel (Baker 30-60 μm).
Melting points (uncorrected): Mettler FP 61. UV: Perkin Elmer Lambda 9. IR: Bruker IFS 25. ^{1}H and ^{13}C NMR: Varian FT-80 A, XL-200, VXR-200, Bruker AMX-300, Varian XL-500; multiplicities were determined with APT pulse sequence. Asterisk marked assignments are interchangeable. MS: Varian MAT 311A, high resolution: Varian MAT 731. Elemental analyses: Microanalytical laboratory of the Institut für Organische Chemie der Universität, Göttingen. Calculations were performed using VAMP and MOPAC 6.0 packages. VAMP (T. Clark, Universität Erlangen–Nürnberg) is a vectorized version of AMPAC and MOPAC.

(E)-Dimethyl-2-[3-methoxy-1-(2-oxo-ethyl)-5-phenyl-pent-4-enyl]-malonate(**4a**)

245 mg (1.85 mmol) dimethyl malonate (**12a**) and 200 mg (0.93 mmol) of aldehyde **11** were added successively to a solution of 35.0 mg (0.31 mmol) potassium *t*-butoxide in 6 ml dry tetrahydrofuran, and the resulting solution was stirred for 2 h at room temp. The reaction mixture was poured into 30 ml satd. ammonium chloride solution, and the aqueous layer extracted twice with 30 ml pentane. The combined organic layers were dried over sodium sulfate and the volatiles removed under reduced pressure. Flash chromatography of the crude product on silica gel (acetone/petroleum ether 1 : 4) gave 178 mg (55%) of a 1.3 : 1.0 - mixture of two diastereomers (^{13}C NMR).

R_f 0.28 (acetone/petroleum ether 1 : 4). – IR: ν = 3058 cm^{-1}, 3026 (CH), 2954, 2848, 2826 (CH), 2728 (H-CO), 1734 (C=O), 1620 (C=C), 1438 (CH_2), 1198, 1160, 1096, 1024 (C-O-C), 972 (H-C=C-H), 752, 696 (CH). – UV (acetonitrile): λ_{max} (lg ε) = 195 nm (4.314), 250 (4.137), 282 (3.222), 291 (3.102). – ^{1}H NMR (200 MHz, C_6D_6): δ = 1.59–2.08 (m, 2H, 2'-H_2), 2.39–2.76 (m, 2H, H_2C-CHO), 3.06, 3.07 (s, 3H, OCH_3), 3.11–3.25 (m, 1H, 1'-H), 3.27, 3.29, 3.30, 3.31 (s, 2×, 3H, CO_2CH_3), 3.60–3.72 (m, 1H, 3'-H), 3.75, 3.80 (d, *J* = 5.5 Hz, 1H, 2-H), 5.93, 5.95 (dd, *J* = 7.5 Hz, *J* = 16.0 Hz, 1H, 4'-H), 6..38, 6.41 (d, *J* = 16.0 Hz, 1H, 5'-H), 7.00–7.25 (m, 5H, arom. H), 9.41–9.46 (m, 1H, CHO). – ^{13}C NMR (50 MHz, C_6D_6): δ = 30.14, 30.54 (C-1'), 38.87, 38.97 (C-2'), 46.37, 46.81 (CH_2CHO), 51.86, 51.91 (CO_2CH_3), 54.77, 55.08 (C-2), 55.74, 55.85 (OCH_3), 80.44, 81.30 (C-3'), 126.88 (C-2", C-6"), 128.00 (C-4'), 128.79 (C-3", C-5"), 130.09 (C-5'), 132.74 (C-4"), 136.85 (C-1"), 168.92, 169.07, 169.17 (CO_2CH_3), 199.77, 200.17 (CHO). – MS (70 eV); *m/z* (%): 348 (2) [M$^+$], 330 (4) [M$^+$–H_2O], 316 (2) [M$^+$–CH_3OH], 289 (1) [M$^+$–$C_2H_3O_2$], 216(18) [M$^+$–$H_2C(CO_2CH_3)_2$], 162 (11) [C_6H_5-$(CH)_2$-$CH(OCH_3)CH_3^+$], 147 (100) [162–CH_3], 132 (37) [$H_2C(CO_2CH_3)_2^+$], 115 (34) [C_6H_5-C≡C-CH_2^+], 91 (21) [$C_7H_7^+$]. – $C_{19}H_{24}O_6$ (348.4): calcd. C 65.50, H 6.94, found C 65.55, H 6.85.

(E)-Diethyl-2-[3-methoxy-1-(2-oxo-ethyl-5-phenyl-pent-4-enyl]-malonate (**4b**)

A solution of 1.02 g (4.72 mmol) aldehyde **11** in 10 ml dry tetrahydrofuran was added at room temp. to a stirred solution of 1.49 g (9.26 mmol) diethyl malonate (**12b**) and 153 mg (1.36 mmol) potassium *t*-butoxide in 20 ml dry tetrahydrofuran. The resulting solution was stirred for 2 h under reflux. After cooling to room temp. the reaction mixture was poured into 130 ml satd. ammonium chloride solution and extracted twice with 130 ml pentane. The combined organic phases were dried over sodium sulfate and the volatiles removed under reduced pressure. Flash chromatography of the crude product on silica gel (acetone/petroleum ether 1 : 4) gave 1.08 g (61%) of a 1.1 : 1.0 mixture of two diastereomers (^{13}C NMR).

R_f 0.24 (acetone/petroleum ether 1 : 4). – IR: ν = 3060 cm^{-1}, 3026 (C=CH), 2982, 2936 (CH), 1732 (C=O), 1602, 1494 (C=C), 1464, 1448, 1370 (CH_2, CH_3), 1098, 1034 (C-O), 752, 696 (CH). – UV (acetonitrile): λ_{max} (log ε) = 204 nm (4.368), 252 (4.845), 283 (3.215), 291 (3.082). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.0 Hz, 3H, OCH_2CH_3), 1.27 (dt, *J* = 1.0 Hz, *J* = 3.5 Hz, 3H, OCH_2CH_3), 1.60–1.90 (m, 2H, 2'-H_2), 2.52–2.82 (m, 2H, H_2CCHO), 2.90–3.08 (m, 1H, 1'H), 3.25, 3.26 (s, 3H, OCH_3), 3.6, 3.62 (d, *J* = 6.0 Hz, 1H, 2-H), 3.69–3.83 (m, 1H, 3'-H), 4.19 (q, *J* = 3.5 Hz, 2H, $CO_2CH_2CH_3$), 4.21 (dq, *J* = 1.0 Hz, *J* = 7.0 Hz, 2H, $CO_2CH_2CH_3$), 5.99, 6.03 (dd, *J* = 7.5 Hz, *J* = 16.0 Hz, 1H, 4'-H), 6.53, 6.55 (d, *J* = 16.0 Hz, 1H, 5'-H), 7.21–7.42 (m, 5H, arom. H), 9.72, 9.73 (s, 1H, CHO). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.05, 14.08 ($CO_2CH_2CH_3$), 29.50, 30.08 (C-1'), 38.50, 38.55 (C-2'), 46.01, 46.48 (H_2CCHO), 54.70, 54.94 (OCH_3), 55.89, 56.08 (C-2), 61.37, 61.46 ($CO_2CH_2CH_3$), 79.95, 81.04 (C-3'), 126.50 (C-2", C-6"), 127.86 (C-4'), 128.59 (C-3", C-5"), 129.37 (C-4"), 132.79 (C-5'), 136.27 (C-1"), 168.56, 168.67 ($CO_2CH_2CH_3$), 200.91, 201.28 (CHO). – MS (70 eV); *m/z* (%): 376 (0.1) [M$^+$], 358 (1) [M$^+$–H_2O], 331 (1) [M$^+$–C_2H_5O], 216 (9) [$C_{15}H_{20}$], 184 (13) [$C_{13}H_{12}O^+$], 147 (100) [$C_{11}H_{15}^+$], 115 (27) [$C_9H_7^+$], 91 (17) [$C_7H_7^+$]. – $C_{21}H_{28}O_6$ (376.4): calcd. C 67.00, H 7.50, found C 67.13, H 7.54.

(E)-5-Methoxy-7-phenyl-3-phenylsulfanyl-hept-6-enal (**4c**)

A solution of 571 mg (2.64 mmol) of aldehyde **11** in 5 ml dry tetrahydrofuran was cooled to 0 °C and added dropwise to a solution of 2.86 g (25.96 mmol) thiophenol (**12c**) and *n*-butyllithium (165 µl, 2.36 M in *n*-hexane, 0.04 mmol) in 10 ml dry tetrahydrofuran at 0 °C. The solution was warmed up to room temp. and stirred for 15 h. The reaction mixture was poured into 80 ml 5% sodium hydroxide solution and extracted twice with 80 ml diethyl ether. The combined organic layers were dried over sodium sulfate and the solvents removed under reduced pressure. Flash chromatography of the crude product on silica gel (acetone/petroleum ether 1:4) gave 779 mg (90%) of a 1.3 : 1.0 - mixture of two diastereomers (^{13}C NMR) as a slightly yellow liquid.

R_f 0.39 (acetone/petroleum ether 1:4). – IR: ν = 3058 cm^{-1}, 3026 (CH, arom.), 2980, 2932, 2900, 2822 (CH), 2726 (H-CO), 1598, 1582, 1494 (C=C), 1440 (CH_2), 1362 (CH_3), 1104, 1090, 1026 (C-O-C), 970 (H-C=C-H), 750, 694 (CH). – UV (acetonitrile): λ_{max} (lg ε) = 194 nm (4.687), 254 (4.351), 291 (3.240), 344 (2.280). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.70–2.18 (m, 2H, 4-H_2), 2.65–2.75 (m, 2H, 2-H_2), 3.22, 3.30 (s, 3H, OCH_3), 3.36–4.16 (m, 2H, 3-H, 5-H), 6.00, 6.04 (dd, *J* = 8.0 Hz, *J* = 16.0 Hz, 1H, 6-H), 6.54, 6.58 (d, *J* = 16.0 Hz, 1H, 7-H), 7.23–7.50 (m, 10H, arom. H), 9.75 (m_c, 1H, CHO). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 39.60, 40.10 (C-3), 40.44, 41.67 (C-4), 48.25, 49.23 (C-2), 56.10, 56.21 (OCH_3), 79.51, 79.79 (C-5), 126.49, 126.55 (C-2", C-6"), 127.69, 127.87 (C-4'), 127.93 (C-6), 128.61 (C-3", C-5"), 128.92 (C-6), 129.08, 129.11 (C-2', C-6'), 129.28, 132.62 (C-7), 133.01, 133.11 (C-3', C-5'), 133.28, 133.43 (C-1'), 133.55 (C-4"), 136.23, 136.31 (C-1"), 200.34, 200.46 (CHO). – MS (70 eV); *m/z* (%): 326 (5) [M$^+$], 294 (3) [M$^+$–CH_3OH], 235 (2) [M$^+$–C_7H_7], 217 (8) [M$^+$–C_6H_5S], 185 (75) [294–C_6H_5S], 147 (52) [C_6H_5-$(CH)_2$-$CHOCH_3^+$], 115 (98) [C_6H_5-C≡C-CH_2^+], 109 (90) [$C_6H_5S^+$], 91 (100) [$C_7H_7^+$], 77 (37) [$C_6H_5^+$], 65 (32) [$C_5H_5^+$], 51 (20) [$C_4H_3^+$]. – $C_{20}H_{22}O_2S$ (326.5): calcd. C 73.58, H 6.79, found C 73.65, H 6.84.

Synthesis of 7-Phenyl-hept-6-ynal (19)

5-Hydroxy-pentanal-dimethylacetal (**14**)

59.9 g (320 mmol) 5,5-dimethoxy-pentanoic acid methyl ester

(**13**) was added slowly to a suspension of 15.8 g (417 mmol) lithium aluminium hydride in 1100 ml dry diethyl ether at -78 °C. The reaction mixture was warmed up and stirred at 0 °C for 6 h. After 12 h stirring at room temp. the mixture was cooled to 0 °C, hydrolyzed carefully with brine, then adjusted to pH 8 and filtered. The filter cake was washed with 500 ml diethyl ether. The aqueous layer was extracted twice first at pH 8 and then at pH 6 with 150 ml diethyl ether. The combined organic layers were dried over sodium sulfate and the solvents removed under reduced pressure. The crude product was distilled *in vacuo* to yield 44.5 g (94%) **14** as a colourless liquid.

B.p. 74 °C/1 mbar (Ref. [23] 57–63 °C). – R_f 0.56 (acetone/petroleum ether 1 : 1). – IR: ν = 3416 cm^{-1} (OH), 2944, 2884, 2832 (CH), 1460 (CH_2), 1386 (CH_3), 1194, 1168, 1130, 1074, 1056 (C-O-C). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.34–1.72 (m, 6H, 2-H_2, 3-H_2, 4-H_2), 1.86 (s br, 1H, OH, H/D-exchange), 3.34 (s, 6H, OCH_3), 3.66 (t, *J* = 6.0 Hz, 2H, 5-H_2), 4.40 (t, *J* = 6.0 Hz, 1H, 1-H). – ^{13}C NMR (20 MHz, $CDCl_3$): δ = 21.02 (C-2), 32.33 (C-3), 32.49 (C-4), 52.60 (OCH_3), 62.09 (C-5), 104.64 (C-1). – MS (70 eV); *m/z* (%): 148 (0.03) [M^+], 147 (0.4) [M^+–H], 117 (9) [M^+–CH_3O], 85 (38) [117 –CH_3OH], 75 (100) [$HC(OCH_3)_2^+$], 71 (18) [$C_4H_7O^+$], 58 (16) [$C_3H_6O^+$], 57 (11) [$C_3H_5O^+$], 41 (34) [C_2HO^+]. – $C_7H_{16}O_3$ (148.2).

5-Tosyl-pentanal-dimethylacetal (**15**)

A stirred solution of 2.00 g (13.5 mmol) **14** in 10 ml dry pyridine was treated with 3.10 g (16.3 mmol) *p*-toluenesulfonyl chloride at –20 °C. The mixture was kept at –20 °C for 2 h and then warmed up to room temp., then 50 ml water was added, the mixture was extracted with 30 ml diethyl ether and the etheral layer was washed three times with 30 ml water. The organic phases were dried over sodium sulfate, and the diethyl ether was removed under reduced pressure. Complete removal of the pyridine by evaporation of the residue at 90 °C/0.005 mbar yielded 3.50 g (86%) **15** as a slightly yellow liquid, which crystallized upon cooling to 0 °C.

M.p. 0 °C (diethyl ether). – R_f 0.81 (acetone/petroleum ether 1: 1). – IR: ν = 3064 cm^{-1}, 3082 (C=C-H), 2950, 2832 (CH), 1598 (C=C), 1458 (CH_2), 1360 (CH_3), 1178 (O-SO_2-R), 1130, 1098, 1070, 1054 (C-O-C), 834, 818 (CH). – ^1H NMR (80 MHz, $CDCl_3$): δ = 1.15–1.85 (m, 6H, 2-H_2, 3-H_2, 4-H_2), 2.47 (s, 3H, aryl-CH_3), 3.27 (s, 6H, OCH_3), 4.00 (t, *J* = 6.0 Hz, 2H, 5-H_2), 4.27 (t, *J* = 6.0 Hz, 1H, 1-H), 7.30 (dd, *J* = 1.0 Hz, *J* = 8.0 Hz, 2H, 2'-H, 6'-H), 7.75 (dd, *J* = 1.0 Hz, *J* = 8.0 Hz, 2H, 3'-H, 5'-H). – ^{13}C NMR (20 MHz, $CDCl_3$): δ = 20.52 (C-2), 21.52 (aryl-CH_3), 28.60 (C-4), 31.83 (C-3), 52.79 (OCH_3), 70.46 (C-5), 104.31 (C-1), 127.82 (C-2', C-6'), 129.92 (C-3', C-5'), 133.21 (C-4'), 144.78 (C-1'). – MS (70 eV); *m/z* (%): 302 (1) [M^+], 271 (9) [M^+–CH_3O], 173 (2) [*p*-$TsOH_2^+$], 155 (4) [$C_7H_7SO_2^+$], 147 (2) [$C_4H_7SO_3^+$], 99 (16) [$C_6H_{11}O^+$], 91 (14) [$C_7H_7^+$], 75 (100) [$C_3H_7O_2^+$], 71 (14) [$C_4H_7O^+$], 58 (4) [$C_3H_6O^+$], 41 (8) [C_2HO^+]. – $C_{14}H_{22}O_5S$ (302.4): calcd. C 55.61, H 7.33, found C 55.70, H 7.28.

5-Brom-pentanal-dimethylacetal (**16**)

68.1 g (225 mmol) 5-tosyl-pentanal-dimethylacetal (**15**) was added to a solution of 101 g (1.16 mol) lithium bromide in 700 ml dry acetone. The resulting solution was stirred for 2.5 h at room temp. The solid was filtered and washed with 200 ml acetone. The organic layers were combined, and the solvent was removed under reduced pressure. The organic residue was diluted with 400 ml diethyl ether and washed three times with 100 ml brine. The combined aqueous layers were extracted with 100 ml diethyl ether and the combined organic layers dried over sodium sulfate. The diethyl ether was removed and the crude product was distilled *in vacuo* to yield 45.7 g (96%) **16** as a colorless liquid.

B.p. 87 °C (11 mbar). – R_f 0.56 (acetone/petroleum ether 1 : 2). – IR: ν = 2984 cm^{-1}, 2948, 2830 (CH), 1458 (CH_2), 1366 (CH_3), 1192, 1126, 1072, 1056 (C-O-C), 644 (C-Br). – ^1H NMR (80 MHz, $CDCl_3$): δ = 1.30–2.10 (m, 6H, 2-H_2,3-H_2, 4-H_2), 3.30 (s, 6H, OCH_3), 3.40 (t, *J* = 6.0 Hz, 2H, 5-H_2), 4.35 (t, *J* = 6.0 Hz, 1H, 1-H). – ^{13}C NMR (20 MHz, $CDCl_3$): δ = 23.29 (C-2), 31.66 (C-3), 32.57 (C-4), 33.47 (C-5), 52.74 (OCH_3), 104.28 (C-1). – MS (70 eV); *m/z* (%): 211 (0.4) [M^+–1], 181 (26) [M^+–CH_3O], 149 (4) [$C_5H_9Br^+$], 147 (4) [$C_5H_9Br^+$], 99 (4) [$C_6H_{11}O^+$], 75 (100) [$HC(OCH_3)_2^+$], 71 (14) [$C_4H_7O^+$], 67 (17) [$C_5H_7^+$], 55 (10) [$C_4H_7^+$], 45 (58) [$C_2H_5O^+$], 41 (32) [C_2HO^+]. – $C_7H_{15}OBr$ (211.1): calcd. C 39.83, H 7.16, found C 39.91, H 7.16.

7-Phenyl-hept-6-ynal-dimethylacetal (**18**)

n-Butyllithium (36.7 ml, 1.6 M in *n*-hexane, 58.7 mmol) and 6.00 g (58.7 mmol) phenylacetylene (**17**) were added successively to a solution of 65 ml dry dimethylsulfoxide and 400 ml dry tetrahydrofuran at –12 °C. After stirring for 30 min at –12 °C 10.0 g (47.4 mmol) **16** was slowly added and the reaction mixture stirred for 14 h at –12 °C. The solution was warmed up to room temp. and the tetrahydrofuran removed *in vacuo*. The residue was diluted with 400 ml diethyl ether and then washed with 75% sodium chloride solution. The aqueous layer was extracted with 80 ml diethyl ether and the combined organic layers were dried over sodium sulfate. The volatiles were removed under reduced pressure and the residue was submitted to column filtration on silica gel (acetone/petroleum ether 1 : 3) to remove the dimethylsulfoxide. Further purification was achieved by fractional destillation *in vacuo* to yield 8.82 g (80%) **18** as a colorless liquid.

B.p. 90–95 °C (0.01 mbar). – R_f 0.56 (aceton/petroleum ether 1 : 3). – IR: ν = 3080 cm^{-1}, 3056, 3032, 3020 (C=C-H), 2944, 2864, 2830 (CH), 2234 (C≡C), 1598, 1572, 1490 (C=C), 1460, 1442 (CH_2), 1386 (CH_3), 1162, 1128, 1074, 1052 (C-O-C), 758, 692 (CH). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.42–1.74 (m, 6H, 2-H_2, 3-H_2, 4-H_2), 2.42 (t, *J* = 7.0 Hz, 2H, 5-H_2), 3.30 (s, 6H, OCH_3), 4.39 (t, *J* = 6.0 Hz, 1H, 1-H), 7.23–7.31 (m, 3H, 4'-H, 3'-H, 5'-H), 7.32–7.44 (m, 2H, 2'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.20 (C-5), 23.80 (C-2), 28.43 (C-4), 31.89 (C-3), 52.46 (OCH_3), 80.66 (C-6), 89.83 (C-7), 104.23 (C-1), 123.87 (C-1'), 127.35 (C-4'), 128.02 (C-2', C-6'), 131.37 (C-3', C-5'). – MS (70 eV); *m/z* (%): 232 (0.02) [M^+], 201 (19) [M^+–CH_3O], 200 (26) [201–H], 169 (14) [200 –CH_3O], 155 (26) [M^+–C_6H_5], 129 (18) [Ph-C≡C-$(CH_2)_2^+$], 115 (40) [Ph-C≡C-CH_2^+], 101 (11) [Ph-C≡C^+], 91 (20) [$C_7H_7^+$], 89 (7) [$C_4H_9O_2^+$], 75 (100) [$C_3H_7O_2^+$], 41 (14) [C_2HO^+]. – $C_{15}H_{20}O_2$ (232.3): calcd. 232.1463, found 232.1463 (MS).

7-Phenyl-hept-6-ynal (**19**)

30 ml 9% hydrochloric acid was added to a stirred solution of 2.00 g (8.61 mmol) **18** in 90 ml tetrahydofuran at room temp. After stirring for 20 min at this temperature the reaction

mixture was neutralized with 2*N* sodium hydroxide solution and then extracted with 70 ml diethyl ether. The organic layer was washed three times with 30 ml water, with 30 ml brine and finally dried over sodium sulfate. The solvent was removed under reduced pressure and the crude product purified by flash chromatography on silica gel (acetone/petroleum ether 1:3) to yield 1.44 g (90%) **19** as a slightly yellow liquid.
R_f 0.55 (acetone/petroleum ether 1: 4). – IR: ν = 3078 cm^{-1}, 3058, 3034 (C=C-H), 2940, 2866, 2832 (CH), 2722 (H-CO), 2234 (C≡C), 1724 (C=O), 1598, 1572, 1490 (C=C), 1456, 1442 (CH_2), 758, 694 (CH). – ^1H NMR (80 MHz, $CDCl_3$): δ = 1.45–2.00 (m, 4H, 3-H_2, 4-H_2), 2.20–2.65 (m, 4H, 2-H_2, 5-H_2), 7.15–7.50 (m, 5H, arom. H), 9.75 (t, *J* = 3.0 Hz, 1H, 1-H). – ^{13}C NMR (20 MHz, $CDCl_3$): δ = 19.14 (C-5), 21.27 (C-3), 28.07 (C-4), 43.29 (C-2), 81.12 (C-6), 89.44 (C-7), 123.87 (C-1'), 127.60 (C-4'), 128.19 (C-2', C-6'), 131.51 (C-3', C-5'), 202.26 (C-1). – MS (70 eV); *m/z* (%): 186 (16) [M^+], 185 (12) [M^+–H], 157 (16) [M^+–CHO], 143 (15) [M^+–CH_2CHO], 129 (48) [M^+–C_4H_7O], 115 (84) [M^+–C_5H_9O], 102 (100) [Ph-C CH^+], 91 (26) [$C_7H_7^+$], 77 (24) [$C_6H_5^+$], 52 (52) [$C_4H_4^+$], 51 (44) [$C_4H_3^+$], 43 (52) [$C_2H_3O^+$]. – $C_{13}H_{14}O$ (186.3): calcd. 186.1045, found 186.1045 (MS).

General procedure for the domino imine condensation/ intramolecular polar [4π⁺+2π]-cycloaddition sequence of 3 with with 4

1.0 mmol aldehyde **4** and 1.0 mmol aniline **3** were added successively to a suspension of powdered molecular sieves (4Å) and dry dichloromethane at – 78 °C. The suspension was stirred at – 78 °C for 10 min and then treated dropwise with 0.3 mmol $BF_3{\cdot}Et_2O$, the reaction mixture warmed up to room temp. and stirred until completion (TLC). 15 ml water was added, the phases were separated and the aqueous phase was extracted twice with 15 ml dichloromethane each. The com- bined organic phases were dried over sodium sulfate and the solvent was removed under reduced pressure. Column filtration of the residue yielded a mixture of the diastereomers **7** and **8**, which were separated by flash chromatography. Analytically pure samples were obtained by crystallization.

Reaction of 3a with 4a

Reaction of 568 mg (1.63 mmol) aldehyde **4a** and 152 mg (1.63 mmol) aniline (**3a**) with 69 mg (0.49 mmol) boron trifluoride diethyl etherate for 12 h and column filtration (ethyl acetate/petroleum ether 1:3) gave 527 mg (76%) as a mixture of diastereomers. **7a** and **8a** were separated by flash chromatography (ethyl acetate/petroleum ether 1:4) for **7a** and then acetone/petroleum ether 1:2 for **8a**). Crystallization from diethyl ether yielded 261 mg (38%) **7a** and 201 mg (29%) **8a** in analytically pure form.

(±)-(1S,3R,4aS,9S,9aR)-Dimethyl-2-(1-methoxy-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3yl)-malonate (**7a**)
M.p. 138 °C (diethyl ether). – R_f 0.26 (ethyl acetate/petroleum ether 1:4). – IR (KBr): ν = 3378 cm^{-1} (NH), 3052, 3028 (C=CH), 2984, 2928, 2900 (CH), 1754, 1732 (C=O), 1598, 1490 (C=C), 1454, 1430, 1378 (CH_2, CH_3), 1314, 1232 (C-O), 755, 704 (CH). – UV (acetonitrile): λ_{max} (log ε) = 191 nm (4.721), 211 (4.511), 252 (3.974), 303 (3.455). – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 (dt, *J* = 2.0 Hz, *J* = 11.0 Hz, 1H, 2-H_{ax}), 1.26 (q, *J* = 11.0 Hz, 1H, 4-H_{ax}), 1.58 (s br, 1H, NH), 1.70 (dt, *J* = 2.5 Hz, *J* = 11.0 Hz, 1H, 9a-H), 1.92 (ddd, *J* = 2.0 Hz, *J* = 6.0 Hz, *J* = 11.0 Hz, 1H, 2-H_{eq}), 2.10 (ddd, *J* = 2.5 Hz, *J* = 4.0 Hz, *J* = 11.0 Hz, 1H, 4-H_{eq}), 2.53–2.70 (m, 1H, 3-H), 3.06 (m_c, 1H, 1-H), 3.22 (s, 3H, OCH_3), 3.26 (d, *J* = 8.5 Hz, 1H, 3-CH), 3.53 (dt, *J* = 4.0 Hz, *J* = 11.0 Hz, 1H, 4a-H), 3.73 (s, 3H, CO_2CH_3), 3.76 (s, 3 H, CO_2CH_3), 4.28 (d, *J* = 11.0 Hz, 1H, 9-H), 6.46–6.60 (m, 3H, 5-H, 7-H, 8-H), 6.93 (ddt, *J* = 1.0 Hz, *J* = 2.5 Hz, *J* = 7.5 Hz, 1H, 6-H), 7.12–7.34 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 30.09 (C-3), 31.65 (C-2), 37.31 (C-4), 44.39 (3-CH), 48.76 (C-9), 49.74 (C-9a), 52.37 (CO_2CH_3), 52.44 (CO_2CH_3), 56.06 (OCH_3), 56.77 (C-4a), 74.02 (C-1), 113.75 (C-5), 117.39 (C-7), 126.19 (C-8a), 126.34 (C-8), 126.66 (C-6), 128.33 (C-2', C-6'), 129.62 (C-3', C-5'), 130.26 (C-4'), 144.24 (C-1')*, 144.39 (C-10a)*, 168.76 (CO_2CH_3), 168.84 (CO_2CH_3). – MS (70 eV); *m/z* (%): 423 (100) [M^+], 392 (5) [M^+–OCH_3], 314 (13) [M^+–C_7H_5O], 260 (28) [$C_{19}H_{18}N^+$], 182 (2) [$C_{13}H_{12}N^+$]. – $C_{25}H_{29}NO_5$ (423.5): calcd. C 70.90, H 6.90, N 3.31, found C 70.72, H 7.06, N 3.41.

(±)-(1R,3R,4aS,9S,9aR)-Dimethyl-2-(1-methoxy-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3-yl)-malonate (**8a**)
M.p. 150 °C (diethyl ether). – R_f 0.20 (ethyl acetate/petroleum ether 1: 4). – IR (KBr): ν = 3374 cm^{-1} (NH), 3082, 3054, 3024 (C=CH), 2950, 2926 (CH), 1752, 1734 (C=O), 1602, 1494 (C=C), 1316, 1254 (C-O), 750, 702 (CH). – UV (acetonitrile): λ_{max} (log ε) = 192 nm (4.699), 210 (4.500), 249 (3.962), 300 (3.417). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.11 (dt, *J* = 10.5 Hz, *J* = 11.0 Hz, 1H, 4-H_{ax}), 1.36 (q, *J* = 11.5 Hz, 1H, 2-H_{ax}), 1.65 (s br, 1H, NH), 1.90 (ddd, *J* = 3.5 Hz, *J* = 5.0 Hz, *J* = 12.0 Hz, 1H, 2-H_{eq}), 2.05 (dt, *J* = 10.0 Hz, *J* = 11.0 Hz, 1H, 9a-H), 2.06–2.13 (m, 1H, 4-H_{eq}), 2.25–2.41 (m, 1H, 3-H), 3.08 (dt, *J* = 3.5 Hz, *J* = 11.0 Hz, 1H, 1-H), 3.14 (dt, *J* = 4.0 Hz, *J* = 11.0 Hz, 1H, 4a-H), 3.31 (d, *J* = 8.5 Hz, 1H, 3-CH), 3.90 (d, *J* = 10.0 Hz, 1H, 9-H), 6.49-6.61 (m, 3H, 5-H, 7-H, 8-H), 6.93 (dt, *J* = 2.5 Hz, *J* = 7.5 Hz, 1H, 6-H), 7.08–7.23 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 32.93 (C-3), 34.71 (C-4), 36.64 (C-2), 51.40 (C-9), 52.49 (CO_2CH_3), 52.53 (CO_2CH_3), 54.00 (C-1), 55.89 (C-9a), 56.78 (3-CH), 65.81 (C-4a), 83.20 (OCH_3), 114.31 (C-5), 118.61 (C-7), 125.47 (C-6), 126.55 (C-8), 127.37 (C-8a), 127.86 (C-2', C-6'), 128.76 (C-3', C-5'), 130.76 (C-4'), 144.48 (C-1'), 147.94 (C-10a), 168.59 (CO_2CH_3), 168.65 (CO_2CH_3). – MS (70 eV); *m/z* (%): 423 (100) [M^+], 392 (1) [M^+–OCH_3], 314 (1) [M^+–C_7H_5O], 260 (7) [$C_{19}H_{18}N^+$], 180 (4) [$C_{13}H_{11}N^+$]. – $C_{25}H_{29}NO_5$ (423.5): calcd. C 70.90, H 6.90, N 3.31, found C 70.75, H 6.92, N 3.25.

Reaction of 3a with 4b

Reaction of 424 mg (1.13 mmol) aldehyde **4b** and 105 mg (1.13 mmol) aniline (**3a**) with 48 mg (0.34 mmol) boron trifluoride diethyl etherate for 15 h and column filtration (diethyl ether/petroleum ether 1:2) gave 373 mg (73%) as a mixture of diastereomers. **7b** and **8b** were separated by flash chromatography (diethyl ether/petroleum ether 1:6). Crystallization from diethyl ether yielded 179 mg (35%) **7b** and 148 mg (29%) **8b** in analytically pure form.

(±)-(1S,3R,4aS,9S,9aR)-Diethyl-2-(1-methoxy-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3-yl)-malonate (**7b**)

M.p. 118–120 °C (diethyl ether). – R_f 0.23 (diethylether/petroleum ether 1:2). – IR (KBr): = 3378 cm^{-1} (NH), 3078, 3062, 3024 (C=CH), 2986, 2930 (CH), 1730 (C=O), 1600, 1478 (C=C), 1450, 1370, 1320 (CH_2, CH_3), 1092 (C-O), 762, 700 (CH). – UV (acetonitrile): λ_{max} (log ε) = 192 nm (4.700), 210 (4.519), 249 (3.955), 300 (3.419). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (dd, *J* = 2.0 Hz, *J* = 12.5 Hz, *J* = 14.0 Hz, 1H, 2-H_{ax}), 1.15–1.30 (m, 1H, 4-H_{ax}), 1.26 (t, *J* = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 1.28 (t, *J* = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 1.60 (s br, 1H, NH), 1.71 (dt, *J* = 3.0 Hz, *J* = 11.5 Hz, 1H, 9a-H), 1.94 (ddd, *J* = 3.5 Hz, *J* = 6.0 Hz, *J* = 12.5 Hz, 1H, 2-H_{eq}), 2.12 (ddd, *J* = 3.5 Hz, *J* = 6.5 Hz, *J* = 13.5 Hz, 1H, 4-H_{eq}), 2.55-2.64 (m, 1H, 3-H), 3.05 (m_c, 1H, 1-H), 3.21 (d, *J* = 8.5 Hz, 1H, 3-CH), 3.23 (s, 3H, OCH_3), 3.53 (dt, *J* = 3.5 Hz, *J* = 11.5 Hz, 1H, 4a-H), 4.19 (q, *J* = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 4.21 (q, *J* = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 4.28 (d, *J* = 11.5 Hz, 1H, 9-H), 6.46–6.59 (m, 3H, 5-H, 7-H*, 8-H), 6.90–6.97 (m, 1H, 6-H*), 7.10–7.36 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.15 ($CO_2CH_2CH_3$), 29.95 (C-3), 31.66 (C-2), 37.40 (C-4), 44.42 (3-CH), 48.81 (C-9), 49.77 (C-9a), 56.08 (OCH_3), 57.16 (C-4a), 61.29 ($CO_2CH_2CH_3$), 61.35 ($CO_2CH_2CH_3$), 74.07 (C-1), 113.72 (C-5), 117.39 (C-7), 126.22 (C-8a), 126.34 (C-8), 126.67 (C-6), 128.36 (C-2', C-6'), 129.64 (C-3', C-5'), 130.28 (C-4'), 144.26 (C-1'), 144.44 (C-10a), 168.38 ($CO_2CH_2CH_3$), 168.47 ($CO_2CH_2CH_3$). – MS (70 eV); *m/z* (%): 451 (100) [M^+], 406 (8) [$M^+ - OCH_2CH_3$], 342 (16) [$M^+ - C_7H_9O$], 260 (38) [$C_{19}H_{18}N^+$], 232 (12) [$C_{17}H_{14}N^+$], 130 (10) [$C_{10}H_{10}^+$], 91 (4) [$C_7H_7^+$]. – $C_{27}H_{33}NO_5$ (451.6): calcd. C 71.82, H 7.37, N 3.10, found C 71.69, H 7.42, N 3.03.

(±)-(1R,3R,4aS,9S,9aR)-Diethyl-2-(1-methoxy-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3-yl)-malonate (**8b**)

M.p. 124 °C (diethyl ether). – R_f 0.41 (diethyl ether/petroleum ether 1:2). – IR (KBr): ν = 3378 cm^{-1} (NH), 3080, 3060, 3024 (C=CH), 2986, 2930 (CH), 1730 (C=O), 1600, 1548, 1492 (C=C), 1478, 1450, 1370 (CH_2, CH_3), 1166, 1124, 1092 (C-O), 762, 700 (CH). – UV (acetonitrile): λ_{max} (log ε) = 192 nm (4.646), 210 (4.466), 250 (3.997), 300 (3.425). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (dt, *J* = 10.0 Hz, *J* = 11.5 Hz, 1H, 4-H_{ax}), 1.21 (t, *J* = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 1.23 (t, *J* = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 1.33 (q, *J* = 11.5 Hz, 1H, 2-H_{ax}), 1.90 (ddd, *J* = 2.0 Hz, *J* = 3.5 Hz, *J* = 11.5 Hz, 1H, 2-H_{eq}), 2.03 (q, *J* = 10.0 Hz, 1H, 9a-H), 2.08 (ddd, *J* = 3.5 Hz, *J* = 5.0 Hz, *J* = 11.5 Hz, 1H, 4-H_{eq}), 2.25–2.34 (m, 1H, 3-H), 2.91(s, 3H, OCH_3), 3.06 (dt, *J* = 3.5 Hz, *J* = 10.5 Hz, 1H, 1-H), 3.12 (dt, *J* = 3.5 Hz, *J* = 10.5 Hz, 1H, 4a-H), 3.22 (d, *J* = 8.5 Hz, 1H, 3-CH), 3.68 (s br, 1H, NH), 3.88 (d, *J* = 10.0 Hz, 1H, 9-H), 4.18 (q, *J* = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 4.22 (q, *J* = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 6.43–6.59 (m, 3H, 5-H, 7-H, 8-H), 6.92 (dt, *J* = 2.5 Hz, *J* = 7.5 Hz, 1H, 6-H), 7.09–7.30 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.12 ($CO_2CH_2CH_3$), 32.81 (C-3), 34.65 (C-4), 36.72 (C-2), 49.65 (3-CH), 50.64 (C-9), 54.04 (C-1), 55.88 (C-9a), 57.10 (C-4a), 61.45 ($CO_2CH_2CH_3$), 83.29 (OCH_3), 114.32 (C-5), 118.58 (C-7), 125.47 (C-6), 126.55 (C-8), 127.38 (C-8a), 127.86 (C-2', C-6'), 128.77 (C-3', C-5'), 130.77 (C-4'), 144.51 (C-1'), 147.98 (C-10a), 168.23 ($CO_2CH_2CH_3$), 168.26 ($CO_2CH_2CH_3$). – MS (70 eV); *m/z* (%): 451 (100) [M^+], 406 (3) [$M^+ - OCH_2CH_3$], 374 (1) [M^+ – Ph], 290 (3) [$C_{20}H_{20}NO^+$], 260 (11) [$C_{19}H_{18}N^+$], 206 (8) [$C_{15}H_{12}N^+$], 130 (8) [$C_{10}H_{10}^+$], 109 (3) [$C_8H_{13}^+$], 91 (2) [$C_7H_7^+$]. – $C_{27}H_{33}NO_5$ (451.6): calcd. C 71.82, H 7.37, N 3.10, found C 71.72, H 7.46, N 3.29.

Reaction of 3a with 4c

Reaction of 485 mg (1.49 mmol) aldehyde **4c** and 138 mg (1.48 mmol) aniline (**3a**) with 63 mg (0.44 mmol) boron trifluoride diethyl etherate for 12 h and column filtration (ethyl acetate/petroleum ether 1:3) gave 376 mg (63%) as a mixture of diastereomers. Separation by flash chromatography (acetone/petroleum ether 1:4) yielded 179 mg (30%) **7c** and 137 mg (23%) **8c**. Due to decomposition **8c** could not be obtained in pure form.

(±)-(1S,3R,4aS,9S,9aR)-1-Methoxy-9-phenyl-3-phenylsulfanyl-1,2,3,4,4a,9,9a,10)octahydroacridine (**7c**)

R_f 0.30 (acetone/petroleum ether 1:4). – IR (Film): ν = 3410 cm^{-1} (NH), 3058, 3026, 3002 (C=CH), 2974, 2928 (CH), 1598, 1494 (C=C), 1312, 1246 (C-O), 1090 (C-S-C), 746, 696 (CH). – UV (acetonitrile): λ_{max} (log ε) = 191 nm (4.829), 254 (4.231), 292 (3.612). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20 (dt, *J* = 2.5 Hz, *J* = 12.0 Hz, 1H, 2-H_{ax}), 1.44 (q, *J* = 11.5 Hz, 1H, 4-H_{ax}), 1.72 (dt, *J* = 2.5 Hz, *J* = 11.5 Hz, 1H, 9a-H), 2.19 (ddd, *J* = 2.5 Hz, *J* = 5.5 Hz, *J* = 12.0 Hz, 1H, 2-H_{eq}), 2.34 (ddd, *J* = 2.5 Hz, *J* = 5.5 Hz, *J* = 11.5 Hz, 1H, 4-H_{eq}), 3.06 (m_c, 1H, 1-H), 3.20 (s, 3H, OCH_3), 3.38–3.60 (m, 2H, 3-H_{ax}, 4a-H), 3.72 (s br, 1H, NH), 4.29 (d, *J* = 11.5 Hz, 1H, 9-H), 6.43–6.55 (m, 3H, 5-H, 7-H, 8-H), 6.93 (dt, *J* = 2.0 Hz, *J* = 7.5 Hz, 1H, 6-H), 7.00–7.30 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – MS (70 eV); *m/z* (%): 401 (39) [M^+], 293 (5) [M^+–SPh], 260 (17) [$C_{19}H_{18}N^+$], 208 (20) [$C_{15}H_{14}N^+$], 180 (7) [$C_{13}H_{10}N^+$], 130 (20) [$C_9H_8N^+$], 109 (100) [SPh$^+$], 77 (76) [$C_6H_5^+$], 65 (46) [$C_5H_5^+$]. – $C_{26}H_{27}NOS$ (401.6): calcd. 401.1813, found 401.1813 (MS).

Reaction of 3b with 4a

Reaction of 172 mg (0.49 mmol) aldehyde **4a** and 52.9 mg (0.49 mmol) *N*-methylaniline (**3b**) with 21.0 mg (0.15 mmol) boron trifluoride diethyl etherate for 12 h and column filtration (diethyl ether/petroleum ether 1:2) gave 153 mg (71%) as a mixture of diastereomers. **7d** and **8d** were separated by flash chromatography (diethyl ether/petroleum ether 1:4). Crystallization from diethyl ether yielded 67 mg (31%) **7d** and 53 mg (25%) **8d** in analytically pure form.

(±)-(1S,3R,4aS,9S,9aR)-Dimethyl-2-(1-methoxy-10-methyl-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3-yl)-malonate (**7d**)

R_f 0.20 (diethyl ether/petroleum ether 1:6). – IR (KBr): ν = 3058 cm^{-1}, 3024 (C=CH), 2988, 2952, 2928, 2896 (CH), 1756 (C=O), 1598, 1496 (C=C), 1454, 1434 (CH_3, CH_2), 1318, 1248 (C-O), 756, 706 (CH). – UV (acetonitrile): λ_{max} (lg ε) = 191 nm (4.769), 211 (4.449), 262 (4.032), 305 (4.470). – ^{1}H NMR (300 MHz, C_6D_6): δ = 0.74 (dt, *J* = 2.0 Hz, *J* = 14.0 Hz, 1H, 2-H_{ax}), 1.12 (dt, *J* = 11.0 Hz, *J* = 12.0 Hz, 1H, 4-H_{ax}), 1.77 (dt, *J* = 2.5 Hz, *J* = 11.0 Hz, 1H, 9a-H), 1.94 (ddd, *J* =

2.0 Hz, J = 4.0 Hz, J = 14.0 Hz, 1H, 2-H_{eq}), 2.36 (ddd, J = 2.5 Hz, J = 3.5 Hz, J = 12.0 Hz, 1H, 4-H_{eq}), 2.60–2.70 (m, 1H, 3-H_{ax}), 2.70 (s, 3H, NCH_3), 2.90–2.98 (m, 1H, 1-H), 2.95 (s, 3H, OCH_3), 3.22 (d, J = 7.5 Hz, 1H, 3-CH), 3.28 (s, 3H, CO_2CH_3), 3.31 (s, 3H, CO_2CH_3), 3.43 (dt, J = 3.5 Hz, J = 11.0 Hz, 1H, 4a-H), 4.24 (d, J = 11.0 Hz, 1H, 9-H), 6.60 (dt, J = 1.0 Hz, J = 8.0 Hz, 1H, 7-H), 6.64 (dd, J = 1.0 Hz, J = 8.0 Hz, 1H, 5-H), 6.73 (dt, J = 8.0 Hz, J = 1.5 Hz, 1H, 8-H), 7.04–7.24 (m, 6H, 8-H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 30.09 (C-2), 30.25 (C-3), 35.37 (C-4), 36.22 (NCH_3), 44.43 (3-CH), 47.86 (C-9), 52.06 (CO_2CH_3), 52.13 (CO_2CH_3), 55.48 (1-OCH_3), 55.71 (C-9a), 56.43 (C-4a), 74.43 (C-1), 112.79 (C-5), 115.90 (C-7), 126.36 (C-8), 126.73 (C-6), 127.72 (C-8a), 128.04 (C-4'), 128.32 (C-2', C-6'), 129.31 (C-3', C-5'), 142.94 (C-1'), 146.87 (C-10a), 168.44 (CO_2CH_3), 168.54 (CO_2CH_3). – MS (70 eV); *m/z* (%): 437 (100) [M^+], 406 (9) [M^+-OCH_3], 378 (2) [$M^+-C_2H_3O_2$], 360 (30) [$C_6H_5^+$], 288 (2) [$M^+-C_5H_9O_5$], 184 (34) [$C_{13}H_{14}N^+$], 97 (14) [$C_7H_{13}^+$], 91 (22) [$C_7H_7^+$], 85 (23) [$C_6H_{13}^+$], 57 (32) [$C_4H_9^+$]. – $C_{26}H_{31}NO_5$ (437.5): calcd. C 71.37, H 7.14, N 3.20, found C 71.21, H 7.17, N 3.22.

(±)-(1R,3R,4aS,9S,9aR)-Dimethyl-2-(1-methoxy-10-methyl-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3-yl)-malonate (**8d**)

R_f 0.14 (diethyl ether/petroleum ether 1: 6). – IR (KBr): ν = 3058 cm^{-1}, 3028 (C=CH), 2954, 2928, 2896, 2824 (CH), 1752 (C=O), 1598, 1494 (C=C), 1452, 1436 (CH_3, CH_2), 1318, 1254 (C-O), 752, 702 (CH). – UV (acetonitrile): λ_{max} (lg ε) = 253 (3.928), 296 (3.337). – ^{1}H NMR (500 MHz, C_6D_6): δ = 1.02 (dt, J = 10.5 Hz, J = 12.0 Hz, 1H, 4-H_{ax}), 1.12 (q, J = 11.5 Hz, 1H, 2-H_{ax}), 2.10 (m_c, 1H, 4-H_{eq}), 2.18 (dt, J = 8.5 Hz, J = 10.5 Hz, 1H, 9a-H), 2.16–2.25 (m, 2H, 2-H_{eq}, 3-H), 2.43 (ddd, J = 3.2 Hz, J = 10.5 Hz, J = 11.5 Hz, 1H, 1-H), 2.60 (s, 3H, OCH_3), 2.80 (s, 3H, NCH_3), 2.80 (dt, J = 4.0 Hz, J = 10.5 Hz, 1H, 4a-H), 3.23 (d, J = 7.0 Hz, 1H, 3-CH), 3.30 (s, 3H, CO_2CH_3), 3.32 (s, 3H, CO_2CH_3), 3.85 (d, J = 8.5 Hz, 1H, 9-H), 6.66–6.70 (m, 2H, 5-H, 7-H), 6.95 (ddd, J = 1.0 Hz, J = 1.5 Hz, J = 8.0 Hz, 1H, 8-H), 6.99–7.08 (m, 2H, 4'-H, 6-H), 7.10–7.15 (m, 2H, 3'-H, 5'-H), 7.23–7.26 (m, 2H, 2'-H, 6'-H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 33.50 (C-3), 34.44 (C-4), 34.71 (NCH_3), 34.90 (C-2), 49.60 (C-9), 51.83 (CO_2CH_3), 52.77 (C-9a), 55.52 (C-4a), 57.09 (3-CH), 60.38 (C-1), 83.22 (OCH_3), 113.76 (C-5), 119.16 (C-7), 125.53 (C-8), 126.85 (C-6), 128.07 (C-2', C-6'), 128.29 (C-8a), 129.28 (C-3', C-5'), 130.74 (C-4'), 149.34 (C-1'), 149.46 (C-10a), 168.61 (CO_2CH_3), 168.67 (CO_2CH_3). – MS (70 eV); *m/z* (%): 437 (100) [M^+], 406 (7) [$M^+ - OCH_3$], 360 (7) [$M^+-C_6H_5$], 85 (7) [C_6H_{13}]. – $C_{26}H_{31}NO_5$ (437.5): calcd. C 71.37, H 7.14, found C 71.45, H 7.24.

Reaction of 3b with 4b

Reaction of 453 mg (1.20 mmol) aldehyde **4b** and 130 mg (1.21 mmol) *N*-methylaniline (**3b**) with 51.3 mg (0.36 mmol) boron trifluoride diethyl etherate for 12 h and column filtration (diethyl ether/petroleum ether 1: 2) gave 406 mg (70%) as a mixture of diastereomers. **7a** and **8a** were separated by flash chromatography (diethyl ether/petroleum ether 1: 6). Crystallization from diethyl ether yielded 213 mg (38%) **7e** and 160 mg (29%) **8e** in analytically pure form.

(±)-(1S,3R,4aS,9S,9aR)-Diethyl-2-(1-methoxy-10-methyl-9-phenyl-1,2,3,4,4a,9,9a,10-octahydroacridin-3-yl)-malonate (**7e**)

M.p. 108 °C (diethyl ether). – R_f 0.36 (diethyl ether/petroleum ether 1:2). – IR (KBr): ν = 3068 cm^{-1}, 3028 (C=CH), 2980, 2964, 2944, 2926 (CH), 1746, 1724 (C=O), 1598, 1494 (C=C), 1452, 1370, 1350 (CH_2, CH_3), 752, 702 (CH). – UV (acetonitrile): λ_{max} (log ε) = 191 nm (4.738), 213 (4.436), 262 (4.007), 305 (3.468). – ^{1}H NMR (300 MHz, C_6D_6): δ = 0.78 (dt, J = 2.0 Hz, J = 14.0 Hz, 1H, 2-H_{ax}), 0.92, (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 0.94 (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 1.16 (q, J = 11.5 Hz, 1H, 4-H_{ax}), 1.80 (dt, J = 2.5 Hz, J = 11.5 Hz, 1H, 9a-H), 2.00 (ddd, J = 2.0 Hz, J = 3.0 Hz, J = 14.0 Hz, 1H, 2-H_{eq}), 2.42 (ddd, J = 2.5 Hz, J = 3.5 Hz, J = 11.5 Hz, 1H, 4-H_{eq}), 2.70 (s, 3H, NCH_3), 2.70–2.83 (m, 2H, 1-H, 3-H), 2.97 (s, 3H, OCH_3), 3.26 (d, J = 8.0 Hz, 1H, 3-CH), 3.46 (dt, J = 3.5 Hz, J = 11.5 Hz, 1H, 4a-H), 3.85–4.05 (m, 4H, 2×$CO_2CH_2CH_3$), 3.98 (q, J = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 4.26 (d, J = 11.5 Hz, 1H, 9-H), 6.60 (dt, J = 1.0 Hz, J = 8.0 Hz, 1H, 7-H), 6.65 (dd, J = 1.0 Hz, J = 8.0 Hz, 1H, 5-H), 6.73 (ddd, J = 1.0 Hz, J = 1.5 Hz, J = 8.0 Hz, 1H, 8-H), 7.06–7.22 (m, 6H, 6-H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.11 ($CO_2CH_2CH_3$), 14.15 ($CO_2CH_2CH_3$), 30.64 (C-3), 31.08 (C-2), 36.41 (C-4), 36.99 (NCH_3), 44.89 (3-CH), 48.91 (C-9), 55.98 (OCH_3), 56.82 (C-9a), 57.16 (C-4a), 61.23 ($CO_2CH_2CH_3$), 61.27 ($CO_2CH_2CH_3$), 74.69 (C-1), 112.85 (C-5), 116.27 (C-7), 126.40 (C-8), 126.99 (C-6), 128.10 (C-8a), 128.35 (C-2', C-6'), 128.78 (C-4'), 129.73 (C-3', C-5'), 143.17 (C-1'), 147.17 (C-10a), 168.38 ($CO_2CH_2CH_3$), 168.47 ($CO_2CH_2CH_3$). – MS (70 eV); *m/z* (%): 465 (100) [M^+], 434 (1) [M^+-OCH_3], 420 (9) [$M^+-OCH_2CH_3$], 388 (12) [M^+ – Ph], 274 (11) [$C_{20}H_{20}N^+$], 264 (16) [$C_{19}H_{22}N^+$], 246 (5) [$C_{19}H_{18}^+$], 220 (16) [$C_{16}H_{14}N^+$], 144 (12) [$C_{11}H_{12}^+$], 85 (5) [$C_5H_{11}N^+$]. – $C_{28}H_{35}NO_5$ (465.6): calcd. C 72.23, H 7.58, found C 72.00, H 7.70.

(±)-(1R,3R,4aS,9S,9aR)-Diethyl-2-(1-methoxy-10-methyl-9-phenyl-1,2,3,4,4a,9,9a-10-octahydroacridin-3yl)-malonate (**8e**)

M.p. 84 °C (diethyl ether). – R_f 0.24 (diethyl ether/petroleum ether 1:2). – IR (KBr): = 3058 cm^{-1}, 3024 (C=CH), 2980, 2928, 2904 (CH), 1748, 1724 (C=O), 1604, 1586, 1494 (C=C), 1456, 1370, 1354 (CH_3, CH_2), 1312 (C-O), 1232 (C-O), 748, 706 (CH). – UV (acetonitrile): λ_{max} (log ε) = 192 nm (4.827), 211 (4.579), 252 (4.026), 304 (3.494). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (q, J = 11.5 Hz, 1H, 4-H_{ax}), 1.20–1.35 (m, 1H, 2-H_{ax}), 1.26 (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 1.28 (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 2.07–2.32 (m, 3H, 3-H_{ax}, 4-H_{eq}, 9a-H), 2.26 (ddd, J = 2.0 Hz, J = 3.5 Hz, J = 11.5 Hz, 1H, 2-H_{eq}), 2.79 (dt, J = 3.5 Hz, J = 11.5 Hz, 1H, 1-H), 2.86 (s, 3H, NCH_3), 3.00 (s, 3H, OCH_3), 3.15 (dt, J = 4.0 Hz, J = 11.5 Hz, 1H, 4a-H), 3.29 (d, J = 8.0 Hz, 1H, 3-CH), 3.94 (d, J = 9.0 Hz, 1H, 9-H), 4.21 (q, J = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 4.23 (q, J = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 6.60 (dt, J = 1.5 Hz, J = 7.5 Hz, 1H, 7-H), 6.69 (dd, J = 1.5 Hz, J = 7.5 Hz, 1H, 5-H)*, 6.76 (dd, J = 1.5 Hz, J = 7.5 Hz, 1H, 8-H)*, 7.05 (dt, J = 1.5 Hz, J = 7.5 Hz, 1H, 6-H), 7.08–7.24 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.12 ($CO_2CH_2CH_3$), 14.15 ($CO_2CH_2CH_3$), 33.27 (C-3), 34.11 (C-

4), 34.80 (C-2), 35.10 (NCH_3), 49.36 (C-9), 51.93 (C-9a), 56.00 (3-CH), 57.24 (C-4a), 60.17 (C-1), 61.41 ($CO_2CH_2CH_3$), 83.45 (OCH_3), 113.35 (C-5), 118.52 (C-7), 125.36 (C-8), 126.59 (C-6), 127.85 (C-2', C-6'), 128.61 (C-3', C-5'), 129.72 (C-8a), 130.19 (C-4'), 148.52 (C-1', C-10a), 168.19 ($CO_2CH_2CH_3$), 168.25 ($CO_2CH_2CH_3$).– MS (70 eV); *m/z* (%): 465 (100) [M^+], 434 (1) [$M^+ - OCH_3$], 420 (5) [$M^+ - OCH_2CH_3$], 388 (25) [M^+–Ph]), 274 (54) [$C_{20}H_{20}N^+$], 264 (58) [$C_{19}H_{22}N^+$], 220 (58) [$C_{16}H_{14}N^+$], 144 (50) [$C_{10}H_{10}N^+$], 85 (29) [$C_5H_{11}N^+$], 55 (7) [$C_4H_7^+$]. – $C_{28}H_{35}NO_5$ (465.6): calcd. C 72.23, H 7.58, N 3.01, found C 72.27, H 7.51, N 3.08.

Reaction of 3b with 4c

Reaction of 172 mg (0.53 mmol) aldehyde **4c** and 56 mg (0.53 mmol) *N*-methylaniline (**3b**) with 22 mg (0.16 mmol) boron trifluoride diethyl etherate for 12 h and column filtration (diethyl ether/petroleum ether 1:2) gave 147 mg (67%) as a mixture of diastereomers. Separation by flash chromatography (diethyl ether/petroleum ether 1:5) yielded 68 mg (31%) **7f** und 53 mg (23%) **8f**. Crystals of **7f** were obtained by crystallization from ethyl acetate/pentane. Due to decomposition **8f** could not be obtained in pure form.

(±)-(1S,3R,4aS,9S,9aR)-1-Methoxy-10-methyl-9-phenyl-3-phenylsulfanyl-1,2,3,4,4a,9,9a,10-octahydroacridine (**7f**)

M.p. 177 °C (ethyl acetate/pentane).– R_f 0.48 (diethyl ether/petroleum ether 1:5). – IR (KBr): ν = 3060 cm^{-1}, 3026 (C=CH), 2990, 2940, 2930 (CH), 1598, 1494 (C=C), 1454, 1438 (CH_2, CH_3), 1086 (C-O), 1054 (C-S-C), 750, 702 (CH). – UV (acetonitrile): λ_{max} (log ε) = 194 nm (4.915), 260 (4.187), 304 (3.447). – ^1H NMR (500 MHz, $CDCl_3$): δ = 1.14 (ddd, *J* = 2.5 Hz, *J* = 12.0 Hz, *J* = 14.0 Hz, 1H, 2-H_{ax}), 1.30 (dt, *J* = 11.0 Hz, *J* = 12.0 Hz, 1H, 4-H_{ax}), 1.80 (dt, *J* = 2.5 Hz, *J* = 11.0 Hz, 1H, 9a-H), 2.25 (ddt, *J* = 2.0 Hz, *J* = 14.0 Hz, *J* = 3.5 Hz, 1H, 2-H_{eq}), 2.64 (ddt, *J* = 2.0 Hz, *J* = 12.0 Hz, *J* = 3.5 Hz, 1H, 4-H_{eq}), 2.90 (s, 3H, NCH_3), 2.99 (m_c, 1H, 1-H), 3.03 (s, 3H, OCH_3), 3.33 (dt, *J* = 3.5 Hz, *J* = 11.0 Hz, 1H, 4a-H), 3.39 (tt, *J* = 3.5 Hz, *J* = 12.0 Hz, 1H, 3-H), 4.08 (d, *J* = 11.0 Hz, 1H, 9-H), 6.42 (ddd, *J* = 0.5 Hz, *J* = 1.5 Hz, *J* = 7.5 Hz, 1H, 5-H), 6.45 (dt, *J* = 1.5 Hz , *J* = 7.5 Hz, 1H, 7-H), 6.62 (dd, *J* = 0.5 Hz, *J* = 7.5 Hz, 1H, 8-H), 7.04 (m_c, 1H, 6-H), 7.16–7.42 (m, 10H, C_6H_5, SC_6H_5). – MS (70 eV); *m/z* (%): (415) [M^+], 306 (38) [M^+ – SPh], 222 (28) [$C_{16}H_{16}N^+$], 220 (25) [$C_{16}H_{14}N^+$], 144 (22) [$C_{10}H_{10}N^+$], 85 (98) [$SC_4H_5^+$]. – $C_{27}H_{29}NOS$ (415.6): calcd. 415.1969, found 415.1969 (MS).

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