Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 64 (2008) 1023–1028

Synthesis of 1,4-thiazino- and benzo-1,4-thiazinomorphinans: their acid-catalyzed rearrangement and study of the formation of unexpected oxidation products

Attila Sipos,[a,*] Levente Girán,[a] Harald Mittendorfer,[b] Helmut Schmidhammer[b] and Sándor Berényi[a]

[a]*Department of Organic Chemistry, University of Debrecen, PO Box 20, H-4010 Debrecen, Hungary*
[b]*Institute of Pharmacy, Department of Pharmaceutical Chemistry, University of Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria*

Received 23 May 2007; revised 19 August 2007; accepted 23 August 2007
Available online 26 August 2007

Dedicated to Professor Csaba Szántay on the occasion of his 80th birthday

Abstract—The formation of 1,4-thiazine and benzo-1,4-thiazine rings was performed at the 6,7-positions of the morphinan backbone in order to synthesize systems annulated with a new six-membered ring providing potential pharmacological activity and the opportunity of easy functionalization. An unexpected oxidation of cyclic sulfur was observed in both cases affording either sulfones or open-ringed bis-morphinan-type by-product. These phenomena are in conformity with the observations and mechanistic explanations made by several research groups in the past in connection with the photosensitized oxidation of cyclic sulfides.

1. Introduction

The synthesis of morphinans annulated with six-membered rings at the 6,7-positions of the C ring has been investigated by several research groups. In the last two decades cyclohexano-,[1a] decalino-,[1b] pyrido-,[1c] pyrimido-,[1c] benzpyrido-,[1d] and tetrahydrodiazolomorphinans[1e] were reported. With respect to their pharmacological properties the most interesting representatives of this group of compounds are the (benz)pyrido- and pyrimidomorphinans presented in Figure 1.

Ananthan and co-workers found that the annulation of a pyridine or pyrimidine ring on the C ring of naltrexone remarkably increases the binding affinity at the opioid receptors.[1c] They applied different substitution patterns on these templates, however, the most significant results were obtained for those having free rotating phenyl substituents formed at the new, six-membered moieties.

Contrary to this, Nagase et al. presented benzpyrido derivatives containing rigid phenyl moiety on the pyridonaltrexone backbone also having superior opioid binding affinity.[1d] It could be concluded from these examples that in accordance with the message–spacer–address theory of opioid receptor binding[2] the presence of free rotating or rigid phenyl segments on the novel heterorings is favorable for the insertion of these ligands on the surface of receptors.

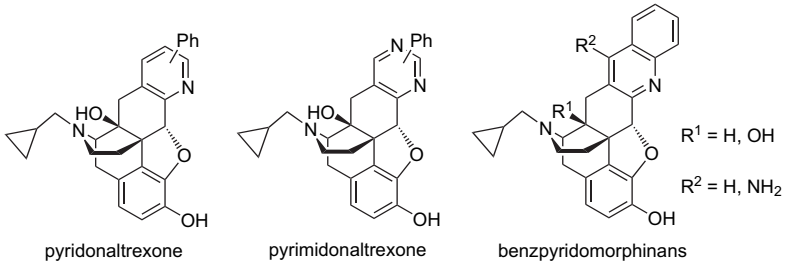


Figure 1. Remarkable examples of thiazinomorphinanes.

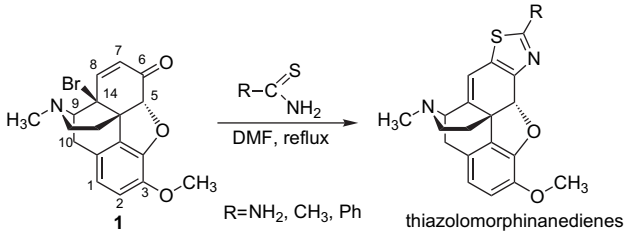
Keywords: 1,4-Thiazine; Benzo-1,4-thiazine; Morphinanedienes; Acid-catalyzed rearrangement; Oxidation.
* Corresponding author. Tel.: +36 52 512900/22473; fax: +36 52 512836; e-mail: asipos@puma.unideb.hu

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.08.075

2. Results and discussion

Our original intention was to explore the possibility of the synthesis of some 1,4-thiazino- and benzo-1,4-thiazinomorphinans with simple synthetic access and the opportunity for functionalization.

As a starting point of our work we considered our previous observations that, on the one hand, 14β-bromocodeinone[3] (**1**) is able to act as an α-haloketone in the presence of adequate nucleophilic partner, and, on the other hand, this ability was successfully applied in the synthesis of morphinanedienes fused with five-membered heteroring at the 6, 7-positions of the C ring[4] (Scheme 1).

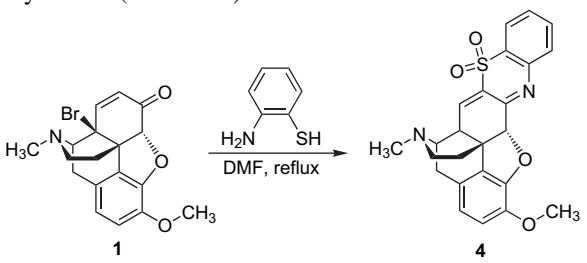


Scheme 1. Synthesis of thiazolomorphinanedienes.

With the application of cysteamine and 2-aminothiophenol as nucleophilic partners a possible six-membered ring closure was found to be practicable via the modified procedure of a Hantzsch-type thiazole-synthesis.[5] The formation of the desired compounds with a six-membered heteroring at the 6,7-positions was achieved with good yield in both cases, however, a detailed structural study of the products and the examination of the by-products of the reaction revealed some unexpected details.

In the case of the reaction with cysteamine the extensive structural study of the expected dihydrothiazinomorphinanediene (**2**) revealed that the cyclic sulfur was, in fact, in the highly oxidized form of the sulfone. The isolation and characterization of the by-product were also achieved, and the analytical data confirmed that this derivative is a bis-morphinan **3** attached via the segments of two opened 1,4-thiazine rings (Scheme 2). The IR spectrum of **3** contained the typical aldehyde stretching vibration peak at 1720 cm^{-1}, while MS data confirmed the dimeric molecular weight, and the ^1H NMR spectrum showed the presence of aldehyde-protons at 9.42 ppm.

Benzothiazinomorphinan **4** was synthesized in high yield via the reaction of 14β-bromocodeinone (**1**) and 2-aminothiophenol. The analytical data for product **4** showed that complete oxidation of the ring sulfur also occurred during the synthesis (Scheme 3).



Scheme 3. The reaction of 14β-bromocodeinone (**1**) with 2-aminothiophenol.

The structural elucidation of product **4** confirmed the presence of two tautomeric forms in solution (Fig. 2).

The 14-H tautomer was found to be more stable under all conditions examined than the diene-type tautomer. For instance, the ^1H NMR spectrum of **4** (measured in DMSO-d_6 at 22 °C) showed a 4:1 ratio in favor of the 14-H tautomer, however, the solid phase IR spectra of the compound did not contain N–H stretching vibrations. Computational conformation studies for the two tautomers revealed that in the case of energy minimized structures in 14-H tautomer all the contributing atoms of benzthiazino moiety are in the same plane, which is essential for the presence of maximum conjugational stabilization.[6] The application of the same

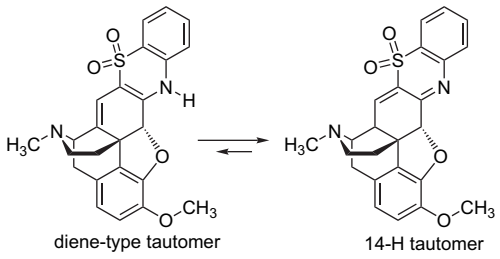
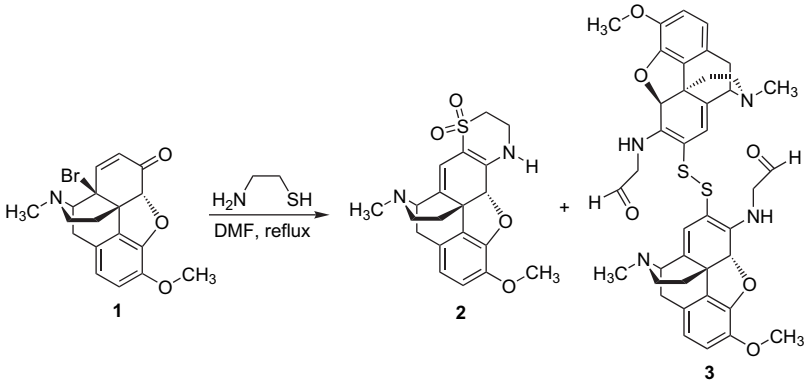


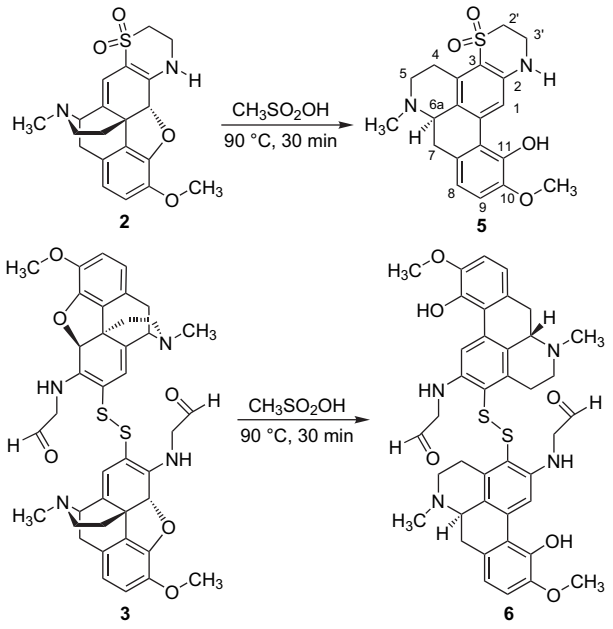
Figure 2. Benzothiazinomorphinan (**4**) tautomeric forms.



Scheme 2. The reaction of 14β-bromocodeinone (**1**) with cysteamine.

calculation procedure for the diene-type tautomer showed that this requirement is not realized for the benzothiazino part of the molecule.

The chemical properties of compound **4** also confirmed the domination of 14-H tautomer form in solution. The acid-catalyzed rearrangement of morphinanedienes is a widely studied research area in our laboratory since the late 1980s.[7] It is a well-established observation that the reaction of a morphinanediene in refluxing methanesulfonic acid yields apocodeine almost quantitatively in 30 min. In the acid-catalyzed rearrangement of benzothiazinomorphinan **4** we found that the starting compound **4** stayed unchanged even under more aggressive conditions. In contrast with this, the acid-catalyzed rearrangement of dihydrothiazinomorphinan **2** and bis-morphinan **3** confirmed the diene structure of these products yielding dihydrothiazinoapocodeine **5** and bis-apocodeine **6**, respectively (Scheme 4).

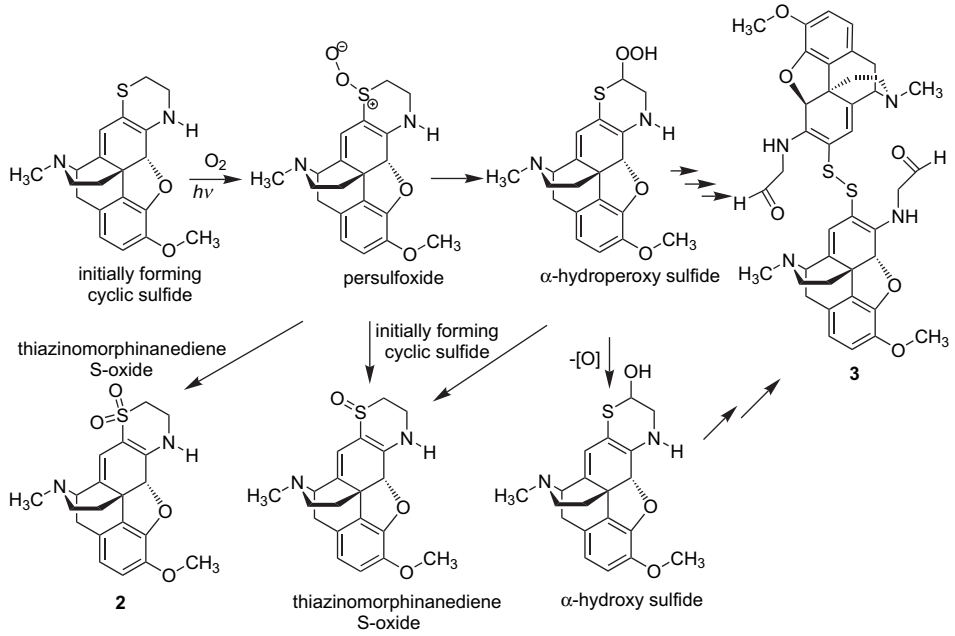


Scheme 4. Acid-catalyzed rearrangement of dienes.

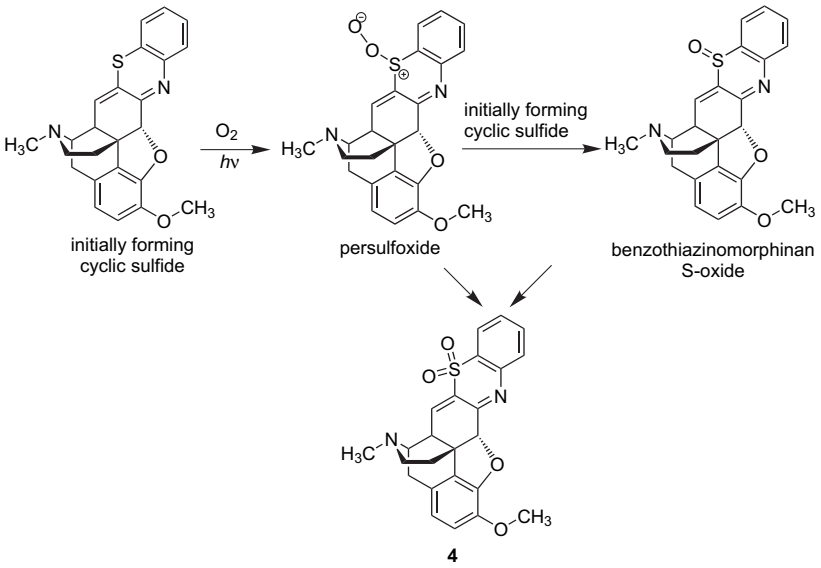
The oxidation of the ring-sulfide to sulfone during the hetero-ring formation is in accord with the observation presented by several research groups regarding the photosensitized oxidation of cyclic sulfides,[8] even if we did not use irradiation and an oxygen atmosphere to allow the formation of singlet oxygen molecules.[9] It was found in the corresponding literature that the oxidation of ring-sulfides in dihydro-1,4-thiazines and its benzologs required much milder conditions than those mostly saturated, standard, monocyclic systems studied by the referred photochemistry studies. Examples were found for open-air oxidation of ring-sulfides into sulfoxides[10] or even into sulfones.[11] Takata and co-workers described some fundamental rules in the atmospheric oxygen-induced oxidations of cyclic sulfides.[8a] They observed that the presence and number of hydrogens in α-position to the ring-sulfide had a decisive impact on the quality and the ratio of the products.

In the case of the reaction of 14β-bromocodeinone (**1**) with cysteamine the initially forming persulfoxide intermediate has two highly acidic α-protons offering the chance of the conversion into α-hydroperoxysulfide, which opens the route to the occurrence of the ring-opened bis-morphinan **3** (Scheme 5). The mechanistic observations of Takata et al. emphasized the importance of the C-acidity of α-protons in the α-hydroperoxysulfide formation step. The explanation for the high acidity of α-hydrogens in the persulfoxide intermediate is the presence of nitrogen in the oxidation-affected ring, which was also confirmed by computer-aided calculations of C–H bond orders.[12]

The lack of the formation of ring-opened by-products in the reaction of 14β-bromocodeinone (**1**) and 2-aminothiophenol could evidently be explained by the absence of hydrogens in



Scheme 5. Mechanistic explanation of the formation of unexpected sulfones.



Scheme 6. Interpretation of the formation of sulfone-type benzothiazinomorphinan (**4**).

the α-position to the ring-sulfides, which makes the conversion of persulfoxide intermediate into α-hydroperoxysulfide impossible (Scheme 6).

3. Conclusion

We have achieved the synthesis of morphinans annulated with 1,4-thiazine rings at ring C further extending the group of morphinans fused with six-membered ring at 6,7-positions. Our procedure was exactly the same as the one for the synthesis of 1,3-thiazolomorphinans. However, applying cysteamine and 2-aminothiophenol we found either the formation of 1,1-dioxides of the aimed compounds **2** and **4** or the occurrence of a side-product **3** significantly differing from the aimed thiazinomorphinans with respect to their structures. These phenomena were greatly in accordance with the results described on the photooxidation of cyclic sulfides.

Our further object, in connection with the presented chemical results, is to perform these heteroring formations with the complete exclusion of the effect of atmospheric oxygen and outer light to obtain the original unoxidized target compounds. From a pharmacological point of view we plan to synthesize *O*-demethylated congeners of the novel morphinans in order to test their binding affinity to opioid receptors and the *O*-demethylated aporphines from the two presented apocodeines to study the dopamine receptor binding features of these new apomorphine derivatives.

4. Experimental protocols

4.1. General

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Thin layer chromatography was performed on precoated Merck 5554 Kieselgel 60 F_{254} foils using chloroform/methanol=8:2 mobile phase; the spots were visualized with Dragendorff's reagent. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 360 (360 MHz and 90.6 MHz, respectively) or a Varian Gemini 200 spectrometer (200 MHz and 50.3 MHz, respectively), chemical shifts are reported in parts per million (δ) from internal TMS and coupling constants (J) are measured in hertz. High resolution mass spectral measurements were performed on a Bruker micrOTOF-Q instrument in the EI mode. Optical rotation was determined with a Perkin–Elmer Model 241 polarimeter. IR spectra were recorded on Perkin–Elmer 283 B spectrometer.

4.2. Chemistry

4.2.1. General procedure for the formation of 1,4-thiazine or benzo-1,4-thiazine rings on morphinan skeleton. A mixture of **2** (1.00 g, 2.46 mmol) and β-aminothiol (2.46 mmol) was dissolved and heated to reflux in anhydrous DMF (10 mL) for 30 min. The mixture was diluted with water (10 mL), and the pH was adjusted to 8 by the dropwise addition of concentrated ammonium hydroxide solution. The emulsion was extracted with ethyl acetate (3×20 mL). The organic phases were combined; the solvent was removed in vacuo. A crystalline product was precipitated by the addition of abs methanol.

4.2.1.1. 6,7:5′,6′-(2′,3′-Dihydro-1,4-thiazine-1′,1′-dioxide)-6,7-didehydro-8,14-didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan (2). Compounds **2** and **3** were separated by means of column chromatography (dichloromethane/methanol/concentrated ammonium hydroxide= 90:9:1). Compound **2** was the first eluted component. Yellow cubic crystals; mp: 211–213 °C; yield: 513 mg (54%); $[\alpha]_D^{25}$ −376 (*c* 0.1, methanol); R_f (90% CH_2Cl_2/9% CH_3OH/1% concentrated ammonium hydroxide) 0.74; ν_{max} (KBr disc) 3350, 2980, 1360, 1230, 1160; HRMS (EI) *m/z* (%) found: 387.4709 (M^++H, 100), calculated for $C_{20}H_{23}N_2O_4S^+$: 387.4721 (M^++H); δ_H (200 MHz, $CDCl_3$) 6.63 (2H, 2d, H1, H2, J_{1-2} 8.2), 5.94 (1H, s, H8), 4.09 (1H, s, H5), 3.84 (4H, m, H9, OCH_3), 3.61 (1H, br s, NH), 3.43 (2H, m, $H2'_a$, $H2'_b$), 3.35–2.11 (9H, m, $H10_a$, $H10_b$, $H16_a$, $H16_b$, NCH_3, $H3'_a$, $H3'_b$), 1.97–1.73 (2H, m, $H15_a$, $H15_b$);

δ_C (50.3 MHz, $CDCl_3$) 159.21 (C6), 146.62 (C3), 141.97 (C4), 108.30 (C7), 80.11 (C5), 58.71 (C9), 56.17 (OCH_3), 50.70 (C2′), 47.89 (C16), 47.21 (C13), 42.33 (NCH_3), 40.67 (C3′), 38.32 (C14), 35.25 (C15), 31.14 (C10).

4.2.1.2. Di-[6-(1′-amino-ethan-2′-al)-6,7-didehydro-8,14-didehydro-4,5α-epoxy-3-methoxy-17-methyl-morphinan-7-yl]disulfide (3). Compounds **2** and **3** were separated by means of column chromatography (dichloromethane/methanol/concentrated ammonium hydroxide= 90:9:1). Compound **3** was the second eluted component. Pale gray, plate shape crystals; mp: 170–173 °C; yield: 619 mg (34%); $[\alpha]_D^{25}$ −6.4 (*c* 0.1, methanol); R_f (90% CH_2Cl_2/9% CH_3OH/1% concentrated ammonium hydroxide) 0.61; ν_{max} (KBr disc) 3340, 2990, 2810, 1720, 1240, 1170; HRMS (EI) *m/z* (%) found: 739.9227 (M^++H, 22), 370.4638 [(M/2+H)$^+$, 100], calculated for $C_{40}H_{43}N_4O_6S_2^+$: 739.9221 (M^++H) and for $C_{20}H_{22}N_2O_3S^+$: 370.4653 [(M/2+H)$^+$]; δ_H (200 MHz, $CDCl_3$) 9.42 (2H, s, 2CHO), 6.49 (4H, 2d, H1, H2, H1′, H2′, J_{1-2} 8.0, $J_{1'-2'}$ 8.0), 6.28 (2H, br s, 2NH), 5.48 (2H, s, H8, H8′), 4.14 (2H, s, H5, H5′), 3.81–3.63 (12H, m, H9, H9′, $2OCH_3$, 2NH–C*H*$_2$–CHO), 3.24–2.17 (16H, m, $H10_a$, $H10_b$, $H15_b$, $H16_a$, $H16_b$, $H10'_a$, $H10'_b$, $H15'_b$, $H16'_a$, $H16'_b$, $2NCH_3$), 1.97 (2H, td, $H15_a$, $H15'_a$, $J_{15a,15b;16a,16b}$ 12.7, $J_{15a,15b}$ 5.1, $J_{15'a,15'b;16'a,16'b}$ 12.7, $J_{15'a,15'b}$ 5.1); δ_C (50.3 MHz, $CDCl_3$) 199.72 (2CHO), 151.42 (C6, C6′), 147.61 (C3, C3′), 145.11 (C4, C4′), 81.51 (C5, C5′), 61.44 (2NH–*C*H$_2$–CHO), 59.31 (C9, C9′), 56.72 ($2OCH_3$), 47.08 (C13, C13′), 46.86 (C16, C16′), 42.89 ($2NCH_3$), 36.26 (C15, C15′), 33.43 (C10, C10′).

4.2.1.3. 6,7:5′,6′-(2′,3′-Benzo-1,4-thiazine-1′,1′-dioxide)-7,8-didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan (4). Bright yellow, needle shape crystals; mp: 233–236 °C; yield: 931 mg (87%); $[\alpha]_D^{25}$ −298 (*c* 0.1, methanol); ν_{max} (KBr disc) 2970, 1380, 1220, 1170; HRMS (EI) *m/z* (%) found: 435.5157 (M^++H, 100), calculated for $C_{24}H_{23}N_2O_4S^+$: 435.5149 (M^++H); δ_H (360 MHz, $CDCl_3$) 7.24–6.93 (4H, m, Ar), 6.72 (2H, 2d, H1, H2, J_{1-2} 8.1), 5.61 (1H, d, H8, J_{8-14} 5.9), 4.14 (1H, s, H5), 3.81 (3H, s, OCH_3), 3.32–2.47 (4H, m, H9, $H10_a$, $H10_b$, H14), 2.79–2.19 (6H, m, $H15_b$, $H16_a$, $H16_b$, NCH_3), 1.73 (1H, td, $H15_a$, $J_{15a,15b;16a,16b}$ 11.6, $J_{15a,15b}$ 4.7); δ_C (90.6 MHz, $CDCl_3$) 162.11 (C6), 147.12 (C3′), 145.34 (C3), 142.57 (C4), 129.12 (C8), 118.43 (C7), 79.56 (C5), 60.33 (C9), 57.11 (OCH_3), 50.67 (C16), 49.21 (C13), 41.77 (NCH_3), 38.87 (C14), 33.54 (C15), 32.76 (C10).

4.2.2. General procedure for acid-catalyzed rearrangement of dienes. A mixture of the diene (1.00 g) and methanesulfonic acid (5 mL) was stirred for 20 min at 0 °C. Then the reaction mixture was added dropwise, with stirring and external ice-cooling, to a solution of potassium hydrogen carbonate (10 g) in water (50 mL). After extraction with chloroform (3×15 mL), the combined extracts were washed with saturated brine, dried ($MgSO_4$), and concentrated under vacuum to yield apocodeine.

4.2.2.1. (−)-*R*-2,3:5′,6′-(2′,3′-Dihydro-1,4-thiazine-1′,1′-dioxide)-11-hydroxy-10-methoxy-aporphine (5). Pale yellow cubic crystals; mp: 227–229 °C; yield: 812 mg (81%); $[\alpha]_D^{25}$ −172 (*c* 0.1, methanol); ν_{max} (KBr disc) 3420, 3370, 2960, 1350, 1240, 1160; HRMS (EI) *m/z* (%) found: 387.4709 (M^++H, 100), calculated for $C_{20}H_{23}N_2O_4S^+$: 387.4721 (M^++H); δ_H (360 MHz, DMSO-d_6) 7.12 (1H, s, H1), 6.85–6.72 (2H, 2d, H8, H9, J_{8-9} 7.8), 6.52 (1H, br s, OH), 5.78 (1H, br s, NH), 4.12 (1H, td, $H6_a$, J_{6a-7a} 10.8, J_{6a-7b} 2.4), 3.92 (3H, s, OCH_3), 3.71–3.41 (4H, m, $H2'_a$, $H2'_b$, $H3'_a$, $H3'_b$), 3.22–2.48 (9H, m, $H4_a$, $H4_b$, $H5_a$, $H5_b$, $H7_a$, $H7_b$, NCH_3); δ_C (90.6 MHz, DMSO-d_6) 149.76 (C10), 144.79 (C11), 60.56 (C6), 56.99 (OCH_3), 55.42 (C2′), 53.10 (C5), 48.11 (C3′), 40.65 (NCH_3), 36.25 (C7), 29.67 (C4).

4.2.2.2. Di-[(−)-*R*-2-(1′-amino-ethan-2′-al)-11-hydroxy-10-methoxy-aporphine-3-yl]disulfide (6). Green needle shape crystals; mp: 194–196 °C; yield: 731 mg (73%); $[\alpha]_D^{25}$ +23 (*c* 0.1, DMSO); ν_{max} (KBr disc) 3450, 3360, 2970, 2800, 1730, 1220; HRMS (EI) *m/z* (%) found: 739.9211 (M^++H, 33), 370.4648 [(M/2+H)$^+$, 100], calculated for $C_{40}H_{43}N_4O_6S_2^+$: 739.9221 (M^++H) and for $C_{20}H_{22}N_2O_3S^+$: 370.4653 [(M/2+H)$^+$]; δ_H (360 MHz, DMSO-d_6) 9.74 (2H, s, 2CHO), 6.78–6.61 (6H, m, H1, H8, H9, H1′, H8′, H9′), 6.41 (2H, s, 2OH), 6.11 (2H, s, 2NH), 4.23–4.08 (6H, m, $H6_a$, $H6'_a$, 2NH–*CH*$_2$–CHO), 3.87 (6H, s, $2OCH_3$), 3.27–2.41 (18H, m, $H4_a$, $H4_b$, $H5_a$, $H5_b$, $H7_a$, $H7_b$, $H4'_a$, $H4'_b$, $H5'_a$, $H5'_b$, $H7'_a$, $H7'_b$, $2NCH_3$); δ_C (90.6 MHz, DMSO-d_6) 200.12 (2CHO), 147.51 (C10, C10′), 145.78 (C2, C2′), 144.43 (C11, C11′), 66.64 (2NH–*C*H$_2$–CHO), 60.23 (C6, C6′), 56.49 ($2OCH_3$), 51.10 (C5, C5′), 40.95 ($2NCH_3$), 34.25 (C7, C7′), 29.87 (C4, C4′).

Acknowledgements

The authors are grateful for substantial discussions with Prof. Sándor Antus and for the financial support from the National Science Foundation (Grant OTKA reg. No. T049436 and NI61336). A.S. is indebted to the Eötvös Scholarship of the Hungarian State.

References and notes

1. (a) Nagase, H.; Abe, A.; Portoghese, P. S. *J. Org. Chem.* **1989**, *54*, 4120; (b) Kshirsagar, T. A.; Portoghese, P. S. *J. Org. Chem.* **1998**, *62*, 1706; (c) Ananthan, S.; Kezar, H. S.; Carter, R. L.; Saini, S. K.; Rice, K. C.; Wells, J. L.; Davis, P.; Xu, H.; Dersch, C. M.; Bilsky, E. J.; Porreca, F.; Rothman, R. B. *J. Med. Chem.* **1999**, *42*, 3527; Ananthan, S. PCT Int. Appl., WO 01,12,196, 2000; *Chem. Abstr.* **2001**, *134*, 178713; (d) Nagase, H.; Imamura, I.; Ohno, H.; Kameda, M.; Matsuda, S.; Migauchi, Y. PCT Int. Appl., WO 43977/98, 1998; *Chem. Abstr.* **1998**, *129*, 276082; (e) Liu, M.; Sainsbury, M.; Carter, N. *J. Chem. Soc., Perkin Trans. 1* **1999**, 241.
2. Portoghese, P. S. *J. Med. Chem.* **1992**, *35*, 1927.
3. Conroy, H. *J. Am. Chem. Soc.* **1955**, *77*, 5960.
4. Tóth, M.; Gyulai, Zs.; Berényi, S.; Sipos, A. *Lett. Org. Chem.* **2007**, *4*, 945.
5. Hantzsch, A.; Weber, J. H. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 3118.
6. *PC SPARTAN Pro, Version 1.0.1*; Wavefunction: Irvine, CA, 1999.
7. Berényi, S.; Hosztafi, S.; Makleit, S.; Szeifert, I. *Acta Chim. Acad. Sci. Hung.* **1982**, *110*, 363; Berényi, S.; Makleit, S.;

Rantal, F. *Acta Chim. Acad. Sci. Hung.* **1985**, *120*, 201; Csutorás, Cs.; Berényi, S.; Makleit, S. *Synth. Commun.* **1996**, *26*, 2251.
8. (a) Takata, T.; Ishibashi, K.; Ando, W. *Tetrahedron Lett.* **1985**, *26*, 4609; (b) Liang, J.-J.; Gu, C.-L.; Kacher, M. L.; Foote, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 4717; (c) Corey, E. J.; Ouannes, C. *Tetrahedron Lett.* **1976**, *19*, 4263.
9. The expression 'singlet oxygen' is used for the $O_2(a^1\Delta_g)$-state. The energy difference between ground state and singlet oxygen is 94.2 kJ/mol.
10. Pawełczyk, E.; Marciniec, B. *Pharmazie* **1974**, *29*, 585; Felsmeister, A.; Schaubman, R. *J. Pharm. Sci.* **1969**, *58*, 1232.
11. Asinger, F.; Schmitz, F. J.; Reichel, S. *Justus Liebigs Ann. Chem.* **1962**, *652*, 50; Warren, R. J.; Eisdorfer, I. B.; Thompson, W. E.; Zarembo, J. E. *J. Pharm. Sci.* **1966**, *55*, 144.
12. C–H bond order was calculated in the form of Mayer bond order on the basis of Mayer, I. *Int. J. Quantum Chem.* **1984**, *26*, 151; Bridgeman, A. J.; Cavigliasso, G.; Ireland, L. R.; Rothery, J. *J. Chem. Soc., Dalton Trans.* **2001**, 3556. We used the same computational packages referred in the mentioned papers.