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DIENE SYNTHESIS ASSISTED BY THEBAINE AND 2-THIOLEN-4-ON-1,1-DIOXIDES AS A ROUTE TO SULPHUR CONTAINING ALKALOIDS OF THE MORPHINANE SERIES

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Abstract - The reaction of 2-thiolen-4-on-1,1-dioxide 1a with thebaine in benzene was demonstrated to proceed regio- and stereoselectively and to produce 6,14-endo-etheno-7,8α (2',3'-thiolane-4'-on-1',1'-dioxido)-tetrahydrothebaine 3, the conversion of the latter into epimeric compound 9 being aided by sodium methylate. The cleavage of the thiolane ring in 3 resulted in 5,14-endo-ethane thebaine derivative; thermolysis was carried out to lead to tetrahydro-5H-furobenzazocine derivative. The formations of the ion complexes of thebaine and ketone 1a were observed in the solutions of methanol and acetonitrile.

Thebaine is of peculiar interest among alkaloids of the morphine series to represent one of the main companions of morphine. Large quantities of thebaine are available in the process of morphine production from the plant extracts[1]. In search for new analgetics, methods for modifying the structure of thebaine are needed since the alkaloid itself is highly toxic.

The researches by Bentley and coworkers[1-5] concerning diene syntheses stand out against a background of other reports on the codeine synthetic transformations. Those were the reactions of thebaine with dienophiles, which afforded the highly effective analgetics. It should be noted that recent published papers[6-9] are indicative of ever growing interest in thebaine transformations described.

The given paper reports the diene synthesis of thebaine and 2-thiolen-4-on-1,1-dioxides 1a,b , the process being considered a convenient method for the production of sulphur containing derivatives of the morphinane series.

Divinyl and methylvinyl sulphones were the samples for investigating the addition of sulphone dienophiles to thebaine. The reaction needed prolonged heating in toluene.

Our experiments proved the reaction of ketone 1a and thebaine 2 to proceed very rapidly (2 hs) in boiling benzene and to yield 85% of mixture of two products 3 and 4 in a 3:2 ratio.

The former was [4π + 2π]-adduct 3, the PMR spectrum of which exhibited three singlets at δ 2.34(NCH_3), and 3.52 and 3.72(OCH_3).

The two doublet at δ 3.35 and 4.04 p.p.m. corresponded to protons at C^7 and C^8, respectively. The C^5 proton revealed resonance as a singlet in the region of 4.50 p.p.m., and that of 3.42 p.p.m. showed a singlet of $C^{5'}$ protons. The bridging protons ($C^{17,18}$) were presented by the doublet of doublets with the chemical shifts of 5.62 and 5.78 p.p.m. (J 8.75 Hz). C^{13}NMR spectrun of the compound in the region of sp^2-atoms possessed 5 singlets, 4 doublets; and the region of sp^3-atoms

showed 3 singlets, 4 doublets, 3 quartets, and 4 triplets. The C^7 doublet at δ 57.08 p.p.m. and C^5 triplet at δ 57.58 p.p.m. were regarded the characteristic signals confirming the existence of thiolan-1,1-dioxide ring.

However, the regioselectivity of the diene synthesis was still doubted, though the signal correlations in H^1 and C^{13} NMR spectra were quite reliable. According to the reports[2,5,8], the reaction of thebaine with methylvinyl ketone and acetylenic dienophiles was realized in such a way, that the dienophile ketogroup was positioned at C^{17}.

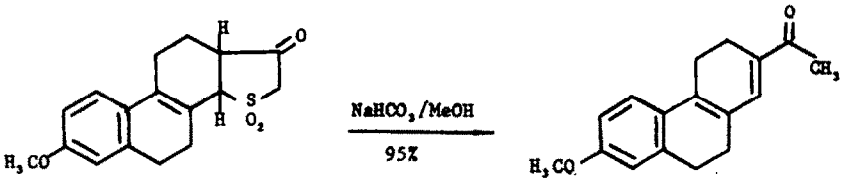
We reported the possibility of easy elimination of SO_2 from diene adducts of 2-thiolen-1,1-dioxide assisted by alkali and acidic reagents[10]. Thus, the cleavage of 5 followed Scheme 1.

The employment of this reaction for the subject discussed would have led to the derivative, the structural assignment of which could contribute to an interpretation of the diene synthesis regioselectively of thebaine and thiolenone 1a. Indeed, the treatment of adduct 3 by boiling methanol solution of $NaHCO_3$ resulted in desulphonation to yield 58% of novel compound 6. The spectral data assertained unequivocally that compound structure. H^1 NMR spectrum (Fig.1) contained 5 singlet signals at δ 3.81, 3.62, 3.30(OCH_3), 2.41(CH_3), 2.37(CH_3) p.p.m.; the C^7 proton was presented by a doublet of doublets at δ 6.15(J 8.75 and 1.8 Hz); the C^8 proton gave resonance as a doublet of doublets at δ 5.42 p.p.m. (J 8.75 and 1.2 Hz). The C^{17} and C^{18} protons were positioned at δ 4.75 p.p.m. and represented a multiplet with a number of coupling constants (1.2, 1.8, and 3.5 Hz). All the assignments were further confirmed by double-resonance experiments. Thus, the suppression of C^{17}-C^{18} multiplet signal caused the disappearance of constants, and the signal at δ 6.15 p.p.m. became a doublet (J 8.75 Hz), the constant of 1.2 Hz disappeared in the signal at δ 5.42 p.p.m. The signal at δ 2.82 p.p.m. became a singlet and thus was related to the C^5 proton (δ 2.82 p.p.m., $J^{5,18}$ 3.5 Hz).

UV spectrum of 6 contained maxima at 245(19200), 287(2048), and 305(58) to confirm the presence of chromophore corresponding to the phenol section in skeleton.

C^{13} NMR spectrum was in agreement with the structure suggested. The spectrum of 6 in the region of sp^2-atoms contained 5 singlets (one of them being C=O group at 210 p.p.m), 4 doublets; on the region of sp^3-atoms - 5 quartets, 3 triplets, 4 doublets, and 3 singlets.

Scheme II might be supposed for the formation of 6. The reaction started from eliminating the SO_2-grouping and the formation of cyclohexadiene ring of C with further addition of methanol by the activated double bond into the C^8 position. The following transformations were most probably produced in accordance with the transformation of thebaine adduct with methylvinyl ketone in alkali medium as described by Bentley and coworkers[11]. That transformation included the formation of enolat-ion 7, break of the ether bond resulting in cyclopropane intermediate 8, further plausible step being the opening of cyclopropane ring with the subsequent rearrangement into the more stable ketone 6.



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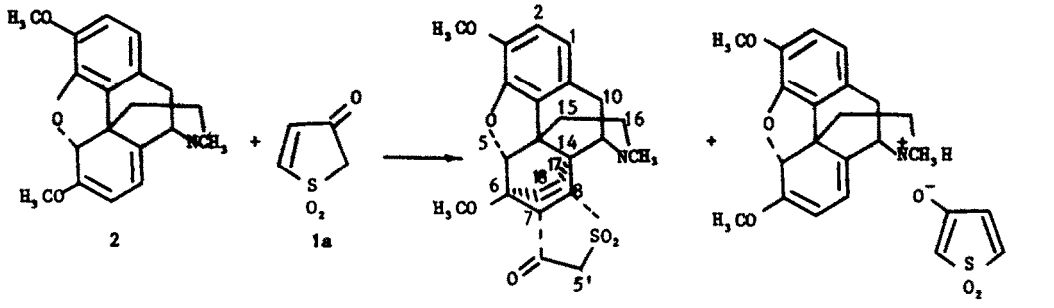
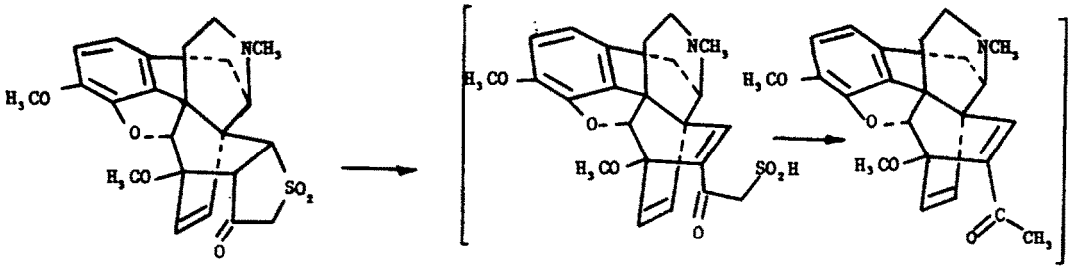


2 1a 3 4



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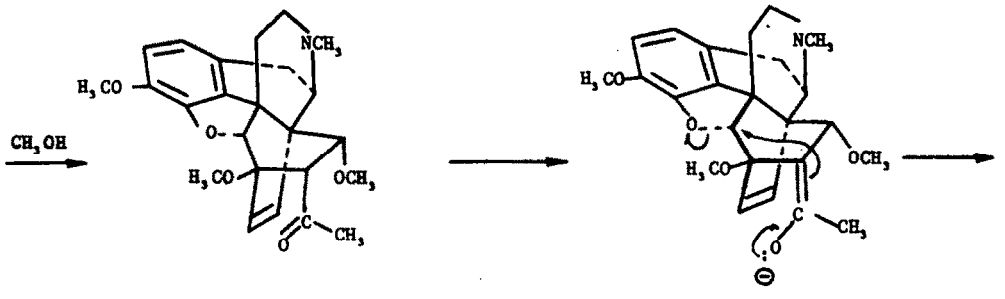

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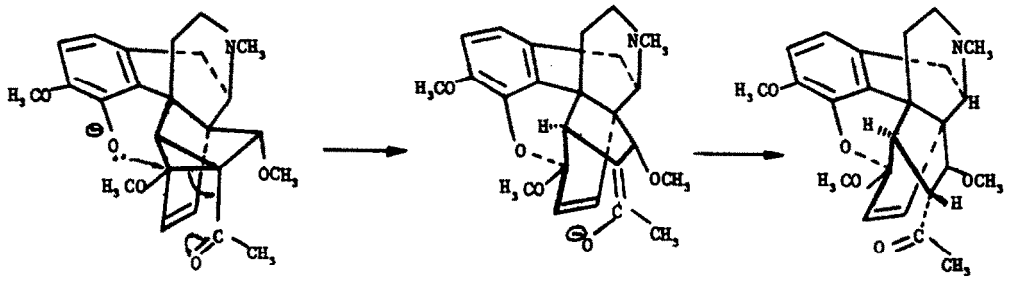


8 6

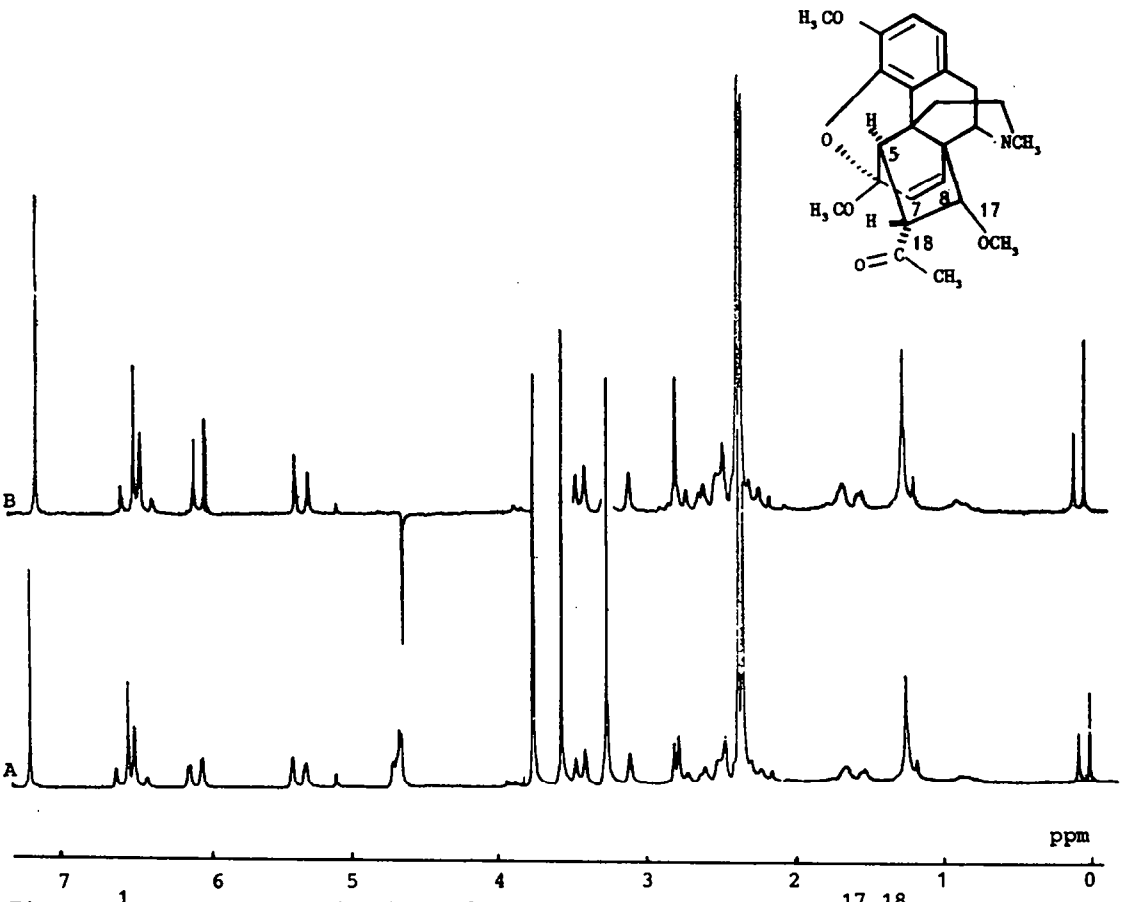


Figure: ^{1}H NMR spectrum ($CDCl_3$, 25°C, TMS, [β]-coupled protons[17,18], [α]-non-coupled protons) of 18-acetyl-17-methoxy-4-(0)-6-dihydro-5,14-ethano-6(0)-methyl thebainol 6.

Thus, the reaction of thebaine with 2-thiolen-4-on-1,1-dioxide represented a regiospecific procedure yielding adduct 3, the ketogroup of which was positioned at C^7.

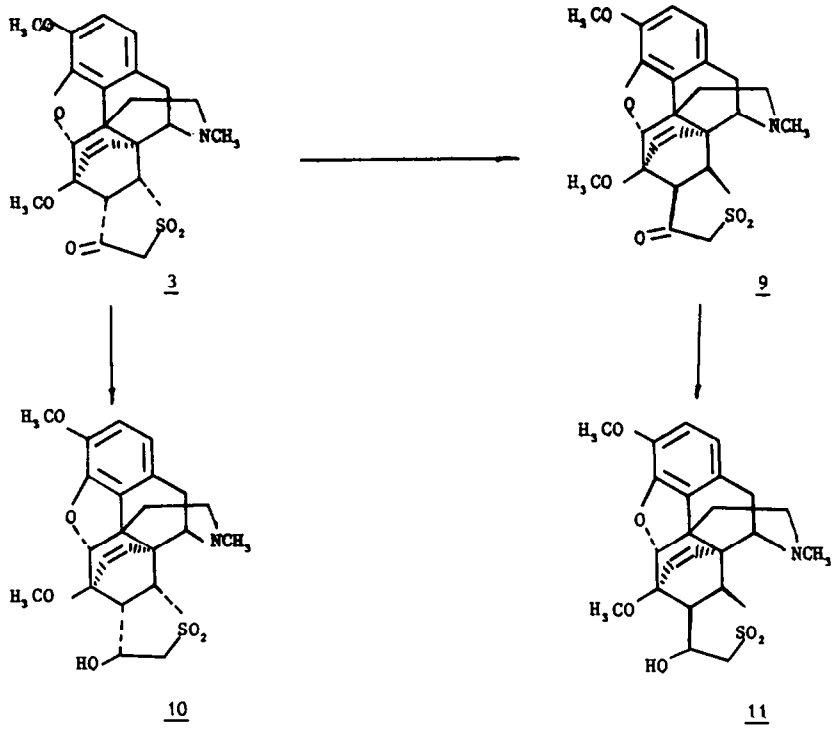
The discussion of stereoselectivity of the addition should take into account the experiment results on transformating tetrahydrothebaine sulphone 3 in ethanol solution assisted by sodium methylate.

The treatment of adduct 3 by the cold ethanol solution of NaOMe provided epimerization and the formation of ketone 9.

The main difference in ^{1}H NMR spectra of 3 and 9 epimers constituted the following: the singlet of CH_3 group protons and of C^5 proton of β-epimer 9 were shifted into the region of low field and positioned at δ 2.58 and 4.83 p.p.m., respectively. Bridging protons of the double bond gave a response in a lower field as well, and revealed as doublets with the chemical shifts at δ 5.40 and 6.12 p.p.m. The reduction of ketones 3 and 9 by $NaBH_4$ led in each case to individual alcohols 10, 11. The main difference in ^{1}H NMR spectra of epimeric alcohols 10 and 11 exhibited a still greater change in the chemical shift of C^5 proton, i.e. δ 4.6 p.p.m. for 10 and δ 5.20 p.p.m. for 11. Therefore, the epimerization of ketone 10 gave rise to a 5β -proton resonance as it had been previously reported for the involvement of 7β -electron attracting groups into thebaine molecule[3,12].

The $C^{4'}$ proton in PMR spectra for alcohols 10, 11 appeared as a twisted quartet centered at δ 4.75 and 4.56 p.p.m., respectively, i.e. it possessed highly approximated values of the constants with the both CH_2 croup ptotons and C^7 proton to constitute 5.5-6.5 and 4.0-5.0 Hz for 10 and 11, respectively. That constant value postulated the absence of axial-axial interacting, i.e. the given proton occupied

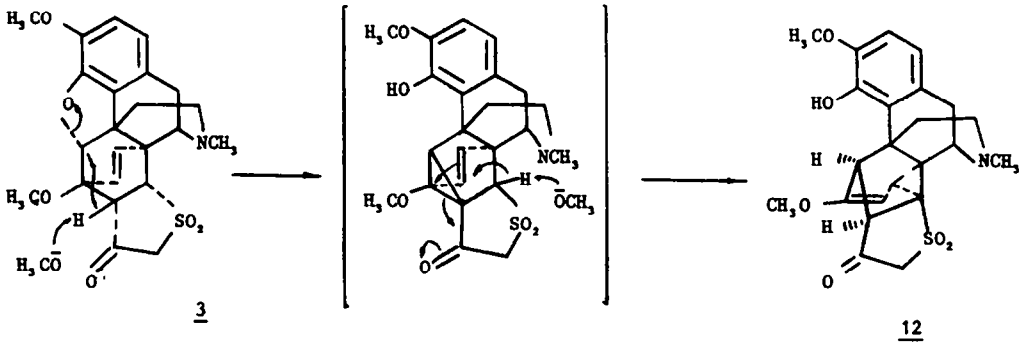
preferably the pseudo-equatorial site. Proceeding from the above said, the hydroxile group in both cases was oriented preferably pseudo-axially.



3 9 10 11

The treatment of 3 by sodium methylate in boiling ethanol solution provoked a deeper skeleton rearrangement. We believe this transformation to be analogous to that of dihydrothebaine quinone described in literature[13]. The presence of a sulphonic group favoured the higher mobility of the angular α-proton.

The effect of sodium methylate at 20°C resulted in the epimerization of tetrahydrothebaine sulphone 3 into 9, while the boiling medium of ethanol promoted rearrangements with the ether bond cleavage and the emergence of a cyclopropane fragment. The end compound possessed the structure of 12. Spectral analyses furnished certain structural proof for 12. IR spectrum showed bands at 1750(C=O), 1635, 1550(MeOC=C), 1200, 3380(OH). PMR spectrum presented a signal of C^7 vinyl proton as a doublet of doublets at δ 5.72 p.p.m. (J_{vic} 8 Hz for C^8) characterized by the remoted coupling constant (J 1.85 Hz) with a proton at C^5. The chemical shift of

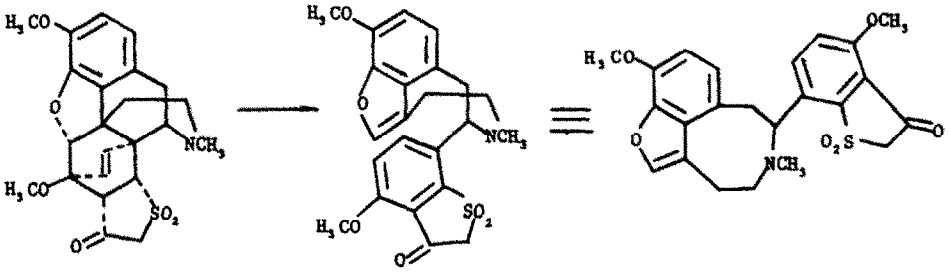


3 12

the latter was δ 3.97 p.p.m. to reveal a doublet of doublets with the coupling constants 1.85 Hz (C^7 proton) and 4.0 Hz (C^{18} proton) in confirmation of cis-position for C^5 and C^{18} protons. Proton at C^{18} gave a doublet of doublets centered at 4.76 p.p.m. (J 4.0 Hz); methoxyl group singlets - at 3.78 and 3.48 p.p.m.; NCH_3 groups - at 2.34 p.p.m.

Literature[6,8,14] furnished the observations of some surprising rearrangements of thebaine adducts with acetylenic dienophiles. We found the similar procedure of thebaine sulphone 3 transformation under boiling in xylene to produce a novel derivative of tetrahydro-5H-furobenzazacine 13, the structural assignments of which was based on spectral analysis data. IR spectrum contained a band of α,β-unsaturated ketone (ν1680 cm^{-1}), thus corroborating the formation of benzothiolene system. ^1H NMR spectrum provided a singlet of the furane C^2-proton at δ 7.40 p.p.m The sulphone ring protons gave a resonance singlet signal at δ 3.75 p.p.m., two singlets of methoxyle protons were positioned at 3.84 and 3.86 p.p.m., the singlet of NCH_3 group protons was shifted towards the higher field region, i.e. 2.04 p.p.m. UV spectrum showed the absorption maxima at 247(12000), 255(8980), 282(5200), 290 (2900), 415(110)nm.

Thermal cleavage of 3 was supposed to proceed through the break of C^{5-6} and C^{13-14} double bonds to yield product 13, this assumption was based on our earlier observations of easy thermal cleavage of 2-thiolen-4-on-1,1-dioxide adduct with cyclohexadiene resulting in 3-oxo-benzothiophen-1,1-dioxide[15].

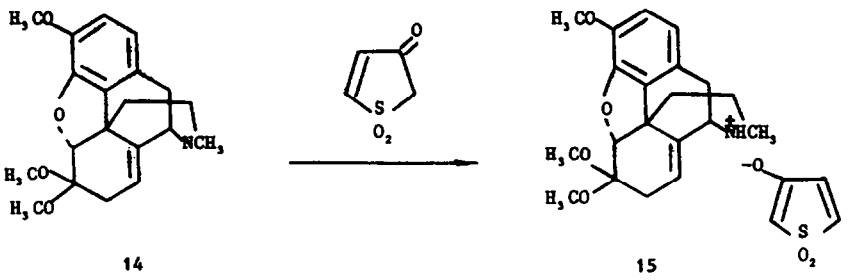


3 13

Another product obtained in interactions of 1a and 2 was represented by complex 4 in a 1:1 ratio. UV spectrum assertained the retention of the diene structure as well as the formation of enole shaping of ketone 1a by its maxima at 230(15200), 287(4280), 364(2620). No change in the product structure was promoted by heating 4 in xylene (140°C, 3 hs). We investigated the reactions of 1a with 2 in various solvents with respect to high influence of a solvent on the interaction of thebaine and different dienophiles[8,9]. It was observed that the reaction in methanol or acetonitrile at room temperature for 30 min. yielded 4 only; the medium of THP or CH_2Cl_2 gave 3 and 4 in a 1:1 ratio. PMR spectrum analysis of the mixture proved the ratio; C^7 and C^8 protons furnished doublets at 5.25 and 5.95 p.p.m., NCH_3 proton signal was shifted to the low field region at 2.34-2.95 p.p.m.

To provide another evidence for easy production of 4 in reaction of thebaine with sulphone 1a, we carried out the reaction of 2-thiolen-4-on-1,1-dioxide and neopinone dimethyl ketal 14[15] of the non-diene structure; the subsequent stirring for two hours resulted in yellow complex 15. UV spectrum of the latter contained maxima at 211(19200), 236(12000), 255(4980), 298(5000), 365(3900), 411(80); PMR spectrum gave four singlets at 2.72(NCH_3), 2.98, 3.50, 3,89(OCH_3), 4.75(C^5) p.p.m., C^8 proton appeared at 5.95 p.p.m.

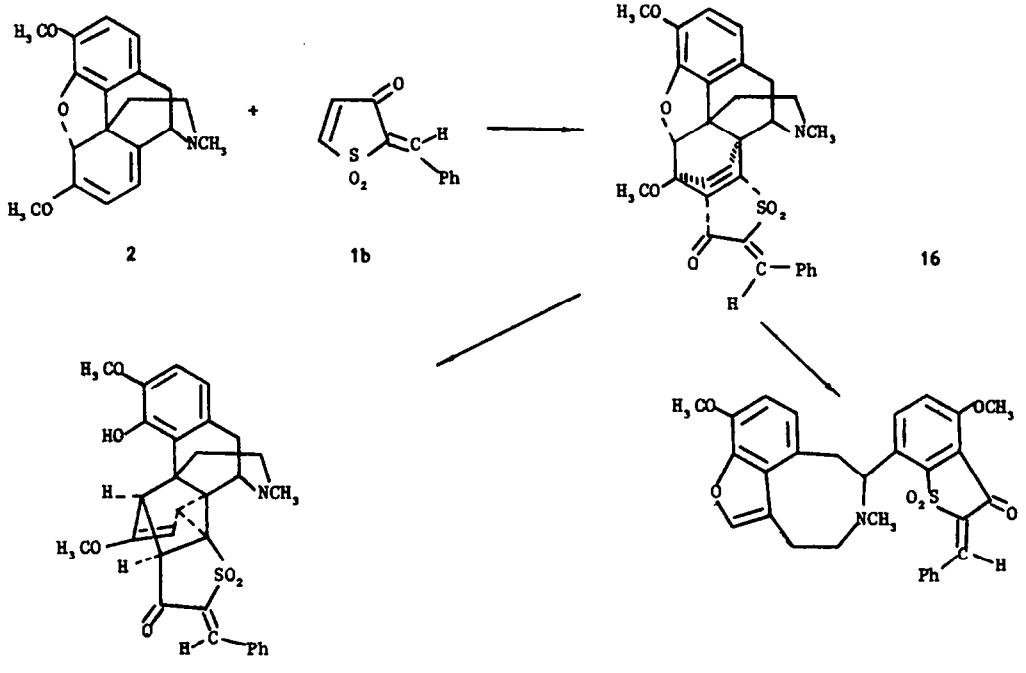
5-Benzilyden-2-thiolen-1,1-dioxide 1b reacted with thebaine at room temperature to produce adduct 16 in a 72% yield. PMR spectrum showed three singlets at 2.50, 3.72, and 3.85 p.p.m.; C^5 proton signal was observed at 4.85 p.p.m.; protons of



14 15

the endo-methylene bridge gave resonance as two doublets centered at 5.82 and 5.92 p.p.m. (J 9 Hz).

UV spectrum of 16 contained absorption maxima at 292(7800), 333(11200) nm. IR spectrum was characterized by a number of double bond bands at 1500, 1575, 1585, 1600, the absorption maximum of the carbonyl group was observed at 1695 cm^{-1}. Adduct 16 was readily involved into thermal cleavage (xylene, 3 hs) resulting in 17 in a quantitative yield. The rearrangement of adduct 16 (NaOMe, 80°C, 4 hs) in enolmethyl ester 18 proceeded with high yields. NMDR method proved C^{18} proton shift to the low field region to be 4.78 p.p.m., C^{5} proton signal showed a doublet of doublets at 4.10 p.p.m.



2 1b 16

18 17

In conclusion, the interactions of 2-thiolen-1,1-dioxides 1a,b and thebaine proceeded with high regio- and stereoselectivities to produce novel sulphur containing alkaloids of the morphinane series.

EXPERIMENTAL

^{1}H NMR spectra were determined on a "Tesla-BS-567B" device in $CDCl_3$ with TMS as an internal standard; chemical shifts were δ scaled. ^{13}C NMR were recorded on a "JEOL FX-90Q-22.5MHz" device; IR spectra were made on a "UR-20" device; UN spectra were recorded by a "Specord UV Vis" spectrometer. The reactions were controlled by the TLC method on "Silufol UV-254" plates, mixtures of benzene-ethyl acetate (20:3) and chlorophorm-methanol (9:1) being employed as eluents.

6,14-Endoetheno-7,8 α (2',3'-thiolan-4'-on-1',1'-dioxido)-tetrahydrothebaine 3.
The mixture of ketone 1a (1.32g) and thebaine 2 (3.11g) was heated in benzene under stirring for two hours. The reaction mass was then cooled and 4 was filtered off (0.55g). The mother solution was evaporated, the residue was solved in ethyl acetate, and 3 was filtered off (1.25g). Fractional crystallization was employed to isolate an additional gram of 3 and 4 (0.95g). Adduct 3, m.p. 205-206°C(ethyl acetate); IR(cm^{-1}): 1060, 1120, 1190, 1325, 1500, 1600, 1630, 1750; PMR(δ): 2.04 (d, 1H, H^{15}, J=7Hz), 2.34(s, NCH_3), 2.55(d, H^{16}, J=7Hz), 3.08(unsolved signal, 1H, H^{10}), 3.30(d, H^8, J=8Hz), 3.42(s, 2H, H^5), 3.50(d, 1H, H^{10}), 3.52(s, OCH_3), 3.72(s, OCH_3), 4.04(d, 1H, H^7, J=8Hz), 4.51(s, 1H, H^5), 5.06(d, 1H, H^9, J=9,<0.5Hz), 5.62(d), 5.78(d, 2H, $H^{17,18}$, J=8.75Hz), 6.66(dd, $H^{1,2}$, J=8Hz); ^{13}C NMR (δ): 212s(C=O), 147.76s, 141.97s, 132.22s, 127.54s($C^{11,12,3,4}$), 133.56d, 126.61d, 120.06d, 114.10d($C^{1,2,17,18}$), 94.21d(C^5), 81.84s(C^6), 63.56d(C^8), 57.58t(C^5), 57.08d(C^7), 56.60q, 53.92q(OCH_3), 48.50s, 44.83s($C^{13,14}$) 45.66d(C^9), 43.22q(NCH_3), 33.94t, 44.84t, 22.43t($C^{15,16,10}$); UV(λ_{max} ε)(ethanol): 205(26900), 287(2017).
Found(%): C 62.1; H 5.8; N 3.0; S 7.3, Calc (%): C 62.1; H 5.9; N 3.1; S 7.2 for: $C_{23}H_{26}NO_6S$.

Thebainiumthienyl-3-oxy-1,1-dioxide 4.
M.p. 192-193°C(benzene); IR(cm^{-1}):1050, 1110, 1130, 1150, 1220, 1260, 1285, 1320, 1500, 1595, 1610, 1730sh, 3400; PMR(δ):2.05(d, 1H, H^{15}), 2.23(d, 1H, H^{16}), 2.95(s, NCH_3), 3.16-3.57(m, 2H, H^{10}), 3.64(s, OCH_3), 3.85(s, OCH_3), 4.25-4.50(m, H^9), 5.12(d, 1H, H^8), 5.34(s, 1H, H^5), 5.95(d, 1H, H^7), 6.69(s, 2H, $H^{1,2}$), 7.15(m, 3H, $H^{2',3',5'}$); UV(λ_{max} ε)(ethanol): 230(15200), 287(4280), 364(2620), 410(50).
Found: C 62.4; H 6.0; N 2.9; S 7.0 , Calc : C 62.1; H 5.8; N 3.0; S 7.3 for: $C_{23}H_{26}NO_6S$.
The mixture of ketone 1a (0.42g) and thebaine (1.5g) was stirred in methanol for 12h at room temperature (stable red colour of the mixture appeared under stirring). After methanol was evaporated and the residue was recrystallized from ethyl acetate, compound 4 was obtained (1.25g) in a 86% yield.

18-Acetyl-17-methoxy-4-(0)-6-dihydro-5,14-ethano-6(0)-methyl thebainol 6.
The suspension of adduct 3 (0.5g) and $NaHCO_3$ (16g) in dry methanol (50ml) was boiled for 2h. Methanol was evaporated to reach a half of the volume and water (25ml) was added to the residue. The isolated precipitate was filtered off, washed with water, with ester, the residue was crystallized from methanol to obtain 6 (0.22g) in a 58% yield; m.p. 193-195°C; IR (cm^{-1}): 1040, 1080, 1090, 1100, 1200, 1500, 1600, 1700; PMR(δ): 1.52, 1.62(d,d, 2H, $H^{15,16}$), 2.37(s, NCH_3), 2.41(s, OC-CH_3), 2.70(d, 1H, H^{10}), 2.82(d, 1H, H^5, J=3.5Hz), 3.10(unsolved signal, 1H, H^{10}), 3.50(d, 1H, H^9), 3.30, 3.62, 3.81(s,s,s, OCH_3), 4.75(m, 2H, $H^{17,18}$, J=1.2, 1.8, 3.5Hz), 5.42(dd, 1H, H^{17}, J=8.75, 1.2Hz), 6.15(dd, 1H, H^{18}, J=8.75, 1.8Hz), 6.48, 6.62(d,d, 2H, $H^{1,2}$); ^{13}C NMR(δ): 210.06s(C=O), 147.59(C^4), 142.01s(C^3), 134.53s, 128.10s($C^{11,12}$), 134.76d, 127.29d, 119.29d, 113.74d($C^{1,2,7,8}$), 57.83q, 56.79q, 56.66q(OCH_3), 43.37q(NCH_3), 33.62q(CH_3), 45.11t, 30.22t, 22.06t($C^{10,15,16}$), 82.21s(C^6), 92.66d, 79.29d, 63.22d, 54.05d($C^{5,9,17,18}$), 48.30s, 46.22s($C^{13,14}$); UV(λ_{max} nm ε)(ethanol): 245(19200), 287(2048), 305(58).
Found: C 68.3; H 7.8; N 3.0, Calc : C 68.1; H 7.1; N 3.4 for: $C_{24}H_{29}NO_5$.

6,14-Endo-etheno-7,8 β (2',3'-thiolan-4'-on-1',1'-dioxido)-tetrahydrothebaine 9.
NaOMe, prepared from 0.7g of sodium and 0.9g of the absolute methanol, was added by two drops to the solution of adduct 3 (0.2g) in ethanol (10ml). The mixture was stirred for 3h. Ethanol was evaporated to a third part of the volume and water (20ml) was added. The precipitate formed was washed by ester and crystallized from methanol to obtain 9 (0.16g) in a 80% yield.
M.p. 205°C; IR(cm^{-1}): 1040, 1070, 1115, 1130, 1200, 1220, 1250, 1315, 1330, 1510, 1600, 1620, 1740; PMR(δ): 1.53, 1.66(d,d, 2H, $H^{15,16}$), 2.58(s, NCH_3), 3.00(s, 1H, H^{10}), 3.36-3.65(m, 5H, $H^{7,8,5',10}$), 3.62, 3.80(s, OCH_3), 4.83(s, H^5), 5.40, 6.12(d,d, 2H, $H^{17,18}$), 6.59(s, $H^{1,2}$).
Calc : C 62.1; H 5.9; N 3.1; S 7.2 Found: C 62.5; H 6.0; N 2.9; S 7.5, for: $C_{23}H_{26}NO_6S$.

6,14-Endo-etheno-7,8 α (2',3'-thiolan-4'-hydroxy-1',1'-dioxido)-tetrahydrothebaine 10.
$NaBH_4$ (0.15g) was added to the solution of adduct 3 (0.5g) in methanol (75ml). The mixture was stirred for 1h at room temperature and stored for 12h. Methanol was evaporated and water (100ml) was added to the residue, which was further neutralized with CH_3CO_2H to isolate the product by chloroform. After usual treatment, alcohol 10 (0.38g) was produced; m.p. 194-196°C(ether);

IR(cm^{-1}): 1040, 1110, 1120, 1310, 1500, 1600, 3340; PMR(δ): 1.90(d, 1H, H^{15}), 2.41(s, NCH_3), 2.55(d, 1H, H^{16}), 3.16(m, 1H, H^{10}), 3.35(m, 1H, H^8), 2.90(m, OH), 3.62(dd, 2H, H^5), 3.52(d, 1H, H^{10}), 3.80(dd, 1H, H^7), 4.58(s, 1H, H^5), 4.75(q, 1H, $H^{4'}$, J=5.5, 6.5Hz), 5.64, 6.20(d,d, 2H, $H^{17,18}$, J=9.5Hz), 6.70(s, 2H, $H^{1,2}$).

Found: C 62.1; H 5.8; N 3.0; S 7.1, Calc : C 62.1; H 6.0; N 3.1; S 7.2 for: $C_{23}H_{26}NO_6S$.

According to the technique described above, 7,8 β-alcohol 11 was produced; m.p. 210-212°C (ethyl acetate); IR(cm^{-1}): 1050, 1110, 1120, 1150, 1300, 1320, 1500, 1600, 1620, 3320; PMR(δ): 2.64(s, NCH_3), 3.45(m, 1H, H^8), 3.64, 3.86(s, OCH_3), 4.08(m, 2H, $H^{5'}$ and 1H, H^7), 4.86(q, 1H, $H^{4'}$, J=4.6, 5.0Hz), 5.20(s, 1H, H^5), 5.60, 6.12(d,d, 2H, $H^{17,18}$), 6.69(s, $H^{1,2}$).

Found; C 62.5; H 6.0; N 2.8; S 7.0; Calc : C 62.1; H 6.0; N 3.1; S 7.2 for: $C_{23}H_{28}NO_6S$

2', 8-Dehydro-7,8-dihydro-5,14(2',3'-thiolan-4'-on-1',1'-dioxido)thebainon- Δ^6-enol methyl ether 12.

NaOMe, the concentration of which has been described above, was added to the solution of adduct 3 (0.5g) in aqueous ethanol (30ml). The mixture was boiled for 4h under stirring. The solution was evaporated to 5ml and concentrated solution of NH_4Cl (25ml) was added to the residue. The reaction mass was extracted with CH_2Cl_2, washed with water, and dried by $MgSO_4$. The solvent was evaporated and the residue was crystallized from methanol to produce 12 (0.42g) in a 84% yield; m.p.216-218°C; IR (cm^{-1}): 940, 950, 1080, 1090, 1120, 1180, 1210, 1225, 1290, 1330, 1500, 1570, 1635, 1750, 3380; PMR(δ) $(CD_3)_2SOD_6$: 1.80(d, 1H, H^{15}), 2.25(d, 1H, H^{16}), 2.30(s, NCH_3), 3.04(m, H^{10}, H^4), 3.97(dd, 1H, H^5, J=1.85, 4Hz), 3.48, 3.78(s, OCH_3), 4.62(d, H^9), 3.88(d, 1H, H^8, J=8Hz), 4.76(d, 1H, H^{18}, J=4Hz), 5.40(s, OH), 5.72(dd, 1H, H^7, J=8, 1.85Hz), 6.65, 6.75(d, 2H, $H^{1,2}$). UV(λ_{max}, nm ε)(ethanol): 215(20160), 238(9200), 288(1313), 366(125), 420(71).

Found: C 61.8; H 6.7; S 7.5, Calc : C 61.8; H 6.7; S 7.5 for: $C_{23}H_{27}NO_6S$

10-Methoxy-6(4'-methoxy-benzo-2'-hydrothiophen-3'-on-S,S-dioxido)-5-methyl-3,4,6,7-tetrahydro-5H-furo[4.3.2-fg]-[3]-benzazacine 13.

The solution of 3(0.5g) was boiled in xylene (50ml) for 3h. Xylene was evaporated and the residue was solved in ethyl acetate to crystallize 13 (0.44g) from the ether-ethyl acetate mixture; m.p. 182-184°C; IR(cm^{-1}): 1050, 1100, 1140, 1300, 1500, 1600, 1690; PMR(δ): 2.04(s, NCH_3), 2.92-3.67(m, 7H, $H^{1,4,5}$), 3.75(s, 2H, H^2), 3.84, 3.86(s, OCH_3), 7.33(d, 2H, Ph), 7.40(s, 1H, H^2), 7.85(m, 2H, Ph); UV(λ_{max}, nm ε) (ethanol): 247(12000), 255(8970), 282(5200), 290(5000), 415(110).

Found: C 62.2; H 5.4; N 3.2,

Calc : C 62.6; H 5.2; N 3.2

for: $C_{23}H_{23}NO_6S$

Neopinoniumdimethylketal-thienyl-3-oxy-1,1-dioxide 15

The mixture of neopin-dimethyl-ketal (0.4g) and 2-thiolen-4-on-1,1-dioxide 1a (0.2g) was stirred on a magnetic stirrer in methanol (30ml) for 10h at room temperature. After methanol was evaporated, the residue was treated by ester and recrystallized from ethyl acetate to produce 15 (0.58g); m.p. 168-169°C; IR(cm^{-1}): 1050, 1100, 1120, 1130, 1150, 1270, 1300, 1335, 1500, 1610, 1660; PMR(δ): 2.00-2.50(m, 4H), 2.72(s, NCH_3), 2.98, 3.50, 3.93(s, OCH_3), 4.75(s, 1H, H^5), 5.70(t, 1H, H^8), 6.55-6.95(m, 4H); UV(λ_{max}, nm ε)(ethanol): 211(19200), 236(12000), 255(4980), 298(5000), 365(3900), 411(100).

Found: C 63.0; H 5.6; N 2.7; S 7.2, Calc : C 92.9; H 6.1; N 3.1; S 7.0, for: $C_{24}H_{28}NO_6S$.

6,14-Endo-etheno-7,8 α(2',3'-thiolan-5'-benzilyden-4'-on-1',1'-dioxido)-tetrahydrothebaine 16.

The solution of ketone 1b (1.1g) and thebaine (1.55g) in benzene (150ml) was stirred for 3h at room temperature. After the solvent was evaporated, the residue was solved in ethyl acetate to produce adduct 16 (1.91g) in a 72% yield; m.p. 184-186°C; IR(cm^{-1}): 1060, 1130, 1160, 1180, 1210, 1280, 1290, 1310, 1510, 1585, 1575, 1695; PMR(δ): 2.02(d, 1H, H^{15}), 2.50(s, NCH_3), 2.58(d, 1H, H^{16}) 2.92(m, 1H, H^{10}), 3.25(d, 1H, H^{10}), 3.78(d, 1H, H^8, J=8Hz), 3.72, 3.82(s, OCH_3), 4.25(d, 1H, H^7, J=8Hz), 4.85(d, 1H, H^5), 5.02(d, 1H, H^9), 5.82, 5.92(d,d, $H^{17,18}$, J=9Hz), 6.63(s, 2H, $H^{1,2}$), 7.95 (s, 1H, =CH), 7.82(d, 2H, Ph), 8.20(m, 3H, Ph); UV(λ_{max}, nm ε) (ethanol): 210(20900), 292(7800), 333(11200).

Found: C 68.2; H 5.8; N 2.8; S 6.3, Calc : C 68.0; H 5.5; N 2.6; S 6.05 for: $C_{30}H_{29}NO_6S$.

10-Methoxy-6(4'-methoxy-2'-benzylidene-benzothiophen-3'-on-S,S-dioxido)-5-methyl-3,4,6,7-tetrahydro-5H-furo[4.3.2-fd][3]-benzazocine 17.

17 was obtained according to the technique described for 12; IR(cm^{-1}): 1050, 1120, 1150, 1290, 1310, 1500, 1580, 1590, 1610, 1685, 1695; PMR(δ): 2.39(s, NCH_3), 2.99-3.80(m, $H^{3,4,6,7}$), 3.83(s, 6H, OCH_3), 6.66(s, 2H, $H^{1,2}$), 7.67-7.00(m, 7H, Ph, and 1H, H^2), 7.92(s, 1H, =CH); UV(λ_{max},nm) (ethanol); 246(15200), 258(10600), 288(6500), 310(6200).

Found: C 68.0; H 6.7; N 2.6; S 5.5,

Calc : C 68.0; H 5.6; N 2.6; S 6.1

for: $C_{30}H_{26}NO_6S$.

2', 8-Dehydro-7,8-dihydro-5,14(5'-benzylidene-2',3'-thiolan-4-on-1', 1'-dioxido)thebainon- Δ^6-enolmethyl ester 18

NaOMe (0.1ml) was added to the solution of adduct 15(0.3g) in aqueous ethanol (30ml) and the mixture was boiled for 4h. After the solution was evaporated to 5ml, the isolated crystals were filtered off, washed with alcohol (10ml), with water (25ml), with ester (50ml) and the residue solved in methanol, recrystallized to produce ester 18 (0.25g); m.p. 210-212°C; IR(cm^{-1}); 1060, 1085, 1095, 1105, 1135, 1150, 1200, 1220, 1310, 1550, 1600, 1655, 1680, 3550; PMR(δ) ($CD_3)_2CO$; 1.75, 2.05(d,d, 2H, $H^{15,16}$), 2.20(s, NCH_3), 3.12(d, 1H, H^{10}), 3.40(m, 1H, H^{10}), 4.10(dd, H^5, J=2, 4Hz), 3.56, 3.78(s, OCH_3), 4.58(d, 1H, H^9), 4.78(d, 1H, H^{18}, J=4Hz), 5.50(s, OH), 5.45(dd, 1H, H^7, J=2, 8Hz), 6.66(s, 2H, $H^{1,2}$), 7.25(m, 3H, Ph), 7.80(s, 1H, =CH), 8.05(m, 2H, Ph); UV(λ_{max}, nm ε)(ethanol); 215(19520), 237(6540), 289(1265), 295(680), 340(170), 350(140).

Found: C 67.5; H 5.0; N 2.6; S 6.7,

Calc : C 68.0; H 5.5; N 2.6; S 6.0

for: $C_{30}H_{29}NO_6S$

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