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SYNTHESIS AND REACTIONS OF THE DIELS-ALDER ADDUCT OF THEBAINE WITH 4-PHENYL-1,2,4-TRIAZOLINE-3,5-DIONE

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Abstract—The title compound was prepared. Upon treatment with HCl a rearrangement occurred and the "open" compound **5** was obtained as its colorless hydrochloride. This salt readily lost HCl and gave the betaine **5**. The rearranged "closed" compound **6** was obtained from **5**.

Quaternary salts **13** and **14** may be formed in methanolic solution from thebaine and codeine and tetracyanoethylene. The salt **13** reacts with the title dienophile and affords the "open" adduct **15**.

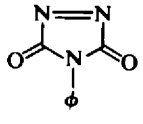
Although thebaine has been known for a long time as a dienic participant in the Diels-Alder reaction,[1] the list of dienophilic components with which it reacts has been increased many fold by Bentley *et al.*[2] They have reported that the reaction of thebaine with dimethyl azodicarboxylate does not lead to a Diels-Alder adduct but rather a hydrazo-ester which may be hydrolyzed to give a secondary amine.[3] However, diethyl azodicarboxylate gives a normal adduct with N-trifluoroacetyl-*nor*-thebaine.[4]

Since azodicarboxylates exist mainly in the *trans*-configuration and in certain cases this may hinder or obviate the formation of a Diels-Alder adduct irradiation may be used to convert it into the *cis*-isomer. Better still, the azo-system may be built into a ring thus forcing it into a cisoid configuration. Thus it was found that 4-phenyl-1,2,4-triazoline-3,5-dione **1** is an excellent dienophile.[5] In fact it has already been employed in a Diels-Alder reaction with thebaine, **2**, as have been other cyclic azo-oxo dienophiles.[6] We have also reacted thebaine and certain other morphine derivatives with **1** and report herein some of the reactions of their products.

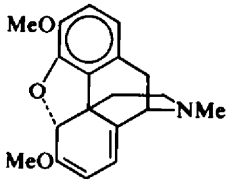
Addition of the deep red acetone solution of **1** to an acetone solution of thebaine leads with rapid concurrent discharge of the color to the formation of **3** in high yield. The IR spectrum of **3** exhibits the absorption bands at 1774 and 1718 cm^{-1} characteristic for Diels-Alder adducts of **1**. Its NMR spectrum exhibits coupling of H-5 with H-7 (coupling constant 1·3 Hz) due to a W-system in which these two protons take part. Its mass spectrum exhibits the molecular ion, m/e 486, as well as the base peak, *m/e* 311 which shows the occurrence of a retro-Diels-Alder reaction in the mass spectrometer.

Attempted preparation of the hydrochloride of **3** led not to this simple salt but to a different salt. In its IR spectrum it exhibited in addition to two bands analogous to those mentioned above at 1772 and 1723 cm^{-1}, a band at 1693 cm^{-1} corresponding to an α,β-unsaturated CO group. The NMR spectrum pointed to the disappearance of one OMe group. The mass spectrum showed this as well. The hydrochloride **4** is obtained also upon direct acidification of the reaction mixture of **1** + **2** without isolation of **3**. It loses HCl merely on warming in water but the free base **5** reverts to the hydrochloride **4** when hydrochloric acid is added to its solution in acetone.

The IR spectrum of **5** in chloroform is normal insofar as the CO absorption of the triazolinedione ring is concerned but its IR spectrum in KBr is abnormal and doesn't exhibit any CO absorption above 1700 cm^{-1} (Experimental). Its yellow color both in the solid state and as it loses hydrochloric acid from the aqueous solution of the salt as well as its above spectrum in the solid state in KBr may be explained by its betaine structure. Thus the



1



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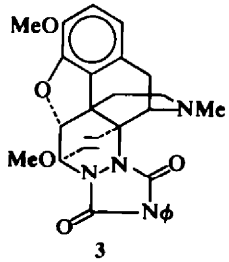

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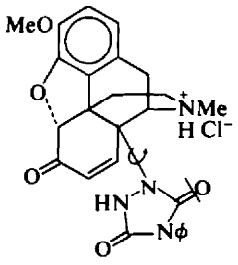

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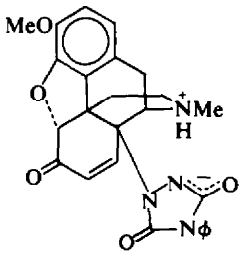

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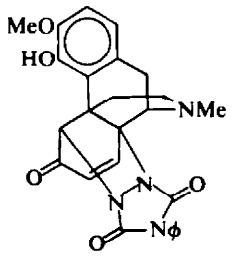

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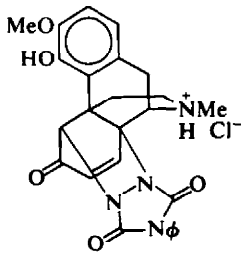

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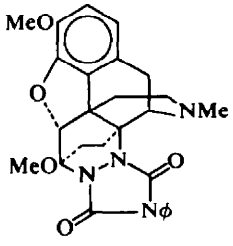
ureide absorption remaining in the carbonyl region is normal at 1690 and 1670 cm^{-1}. In chloroform solution there is probably enough free HCl to destroy the intramolecular betaine structure. From this follows that if one were to treat **15** with base we should also obtain the yellow color of a betaine (see below).

Attempted crystallization of **5** from ethanol afforded a new compound **6** which could also be obtained after heating a methanolic solution of **5** under reflux or after heating a solution of **5** in dry DMSO. The most efficient way of obtaining **6** is by dissolving **5** in warm pyridine and diluting the solution with water. The IR spectrum of **6** (KBr) exhibits carbonyl bands at 1775, 1720 and 1680 cm^{-1}. The hydroxylic absorption appears at 3520 cm^{-1} ($CHCl_3$). Here also the molecular peak appears at m/e 472 pointing to the occurrence of a rearrangement and the formation of an isomer of **5**. Splitting occurs in the resonance of H-5. This occurs also in the quartet of H-7 which here appears at higher field than that for H-8, in contradistinction to the situation in **3** where the triazoline is attached to C-6 and its H-18 is at lower field than its H-17. The hydroxylic proton appears at 6·07 ppm and disappears upon addition of D_2O. The rearranged compound **6** gives a normal hydrochloride **7** which does not lose HCl under the conditions of the conversion of **4** into **5**.

Bentley has reported on the addition of nitrosobenzene to thebaine.[7] Our sequence **3** → **5** → **6** is entirely analogous to their sequence **8** → **9** → **10**.

In both **3** and **8**, C-6 is a potential carbonyl-carbon and it is not surprising that under acidic conditions this potential is realized. Our compound **5** is yellow and its analog **9** has been reported[7] to be yellow.

Diimide reduction of **3** afforded **11**. Its molecular weight was 488 and there were no vinylic protons in its NMR spectrum. The ubiquitous lines in the IR spectrum were there, at 1760 and 1705 cm^{-1}.



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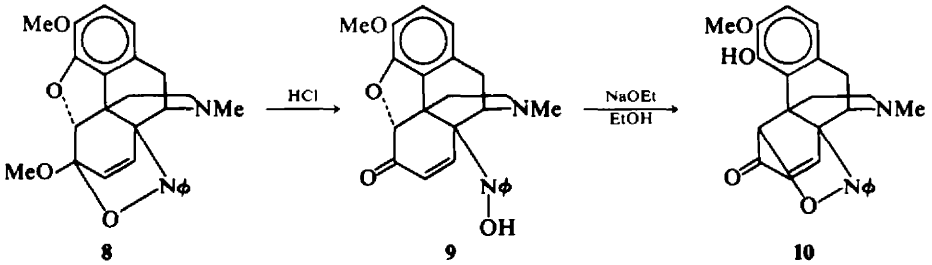
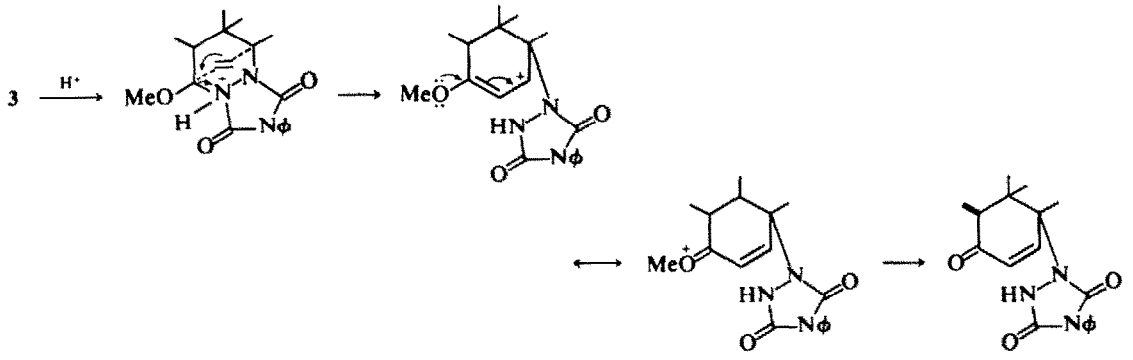
A normal hydrochloride **12** was obtained. No ring opening such as **3** → **4** occurred. Here also the lines at 1770 and 1710 cm^{-1} appeared in the IR spectrum. The C-6 methoxyl group did not disappear from the NMR spectrum. It appears that in **3** the double bond between C-7 and C-8 assists the opening of the C-6 to nitrogen bond through the formation of a resonance stabilized charged species (Scheme 1).

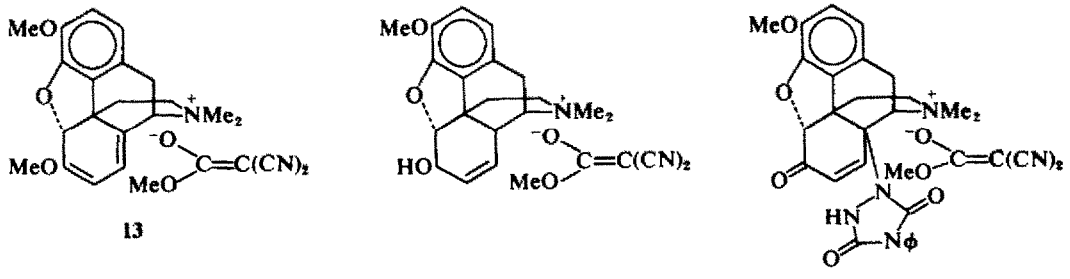
In connection with attempts to react thebaine with relatively highly substituted (and, therefore, more sterically -hindered) dienophiles we tried tetracyanoethylene despite the statements of Bentley *et al.* with respect to this question in general and this dienophile in particular.[2] Indeed we were unable to isolate a Diels-Alder adduct of thebaine with tetracyanoethylene when we used various aprotic solvents. Being blissfully ignorant at the time of the potentialities of this dienophile in the presence of alcohols[8] we used methanol as solvent and obtained a beautiful crystalline product



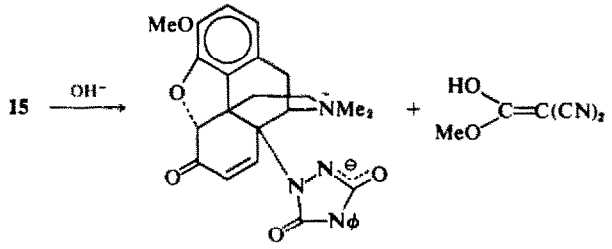
8 9 10



SCHEME 1



13 14 15



16

13 in high yield. Our self-satisfaction ended when codeine which is not a 1,3-diene also gave a similar product **14** with tetracyano-ethylene. The behavior and properties of the two products showed them to be salt-like in character and their structures are **13** and **14**, respectively. We describe these compounds herein because we then studied the reaction of **13** with **1**. We believe the structure of this Diels-Alder adduct does not correspond to the "closed" analog **3** but rather to the "open" one **5**. When base is added to **15** a yellow, then orange color develops. We believe this is due to formation of the betaine **16** with concurrent removal of the enolate gegenion into the alkaline solution.

EXPERIMENTAL

IR spectra were measured on a Perkin-Elmer model 237 grating spectrophotometer. 60 MHz NMR spectra were measured on the corresponding Varian instrument. Mass spectra were measured on an Atlas CH 4 instrument using the heated inlet system at 200°. The electron energy was maintained at 70 eV and the ionization current at 20 μA. All m.ps are uncorrected.

4-Phenyl-1,2,4-triazoline-3,5-dione, **1**. This was prepared according to Cookson's procedure[5] from 4-phenyl-1,2,4-triazolidine-3,5-dione and t-butyl hypochlorite in dioxan at room temp. The dioxan was removed in a vacuum at 40° and was replaced by acetone. The red acetone solution was used immediately.

Adduct **3** *of thebaine with* **1**. A red soln of **1** (2·0 mmol) in acetone (10 ml) was added dropwise at room temp to a soln of thebaine (0·623 g; 2·0 mmol) in acetone (40 ml). After stirring for 20 min more most of the solvent was removed in a vacuum below 40°. The residual solution (*ca* 5 ml) after overnight refrigeration afforded the colorless crystalline adduct. The product **3** (0·86 g; 89%) had m.p. 199–201° (dec). Recrystallization raised the m.p. to 200–204° (dec, acetone). Lit.[6] m.p. 210–212°. (Calc. for $C_{27}H_{26}N_4O_5$: C, 66·65; H, 5·39; N, 11·52; M.W. 486·51. Found: C, 66·76; H, 5·32; N, 11·57%; M.W. 486); IR ($CHCl_3$): 1774(m), 1718(m), (ureide CO); NMR ($CDCl_3$): τ 2·58 (s, 5 N-C_6H_5); 3·31 (ABq, $J_{1,2}$ = 8 Hz, H-1, H-2);

3·98 (dxd, $J_{7,8}$ = 9 Hz, $J_{7,5}$ = 1·3 Hz, H-7); 4·25 (d, $J_{8,7}$ = 9 Hz, H-8); 4·98 (d, J = 1·3 Hz, H-5); 5·42 (d, $J_{9\alpha,10\alpha}$ = 6·5 Hz, H-9α); 6·08 (s, 3 $OC\underline{H}_3$); 6·17 (s, 3 $OC\underline{H}_3$); 6·60 (d, $J_{10\beta,10\alpha} = -19$ Hz; H-10β); 7·48 (s, 3 $NC\underline{H}_3$); 7·42 (dxd, $J_{10\alpha,10\beta} = -19$ Hz, $J_{10\alpha,9\alpha}$ = 6·5 Hz, H-10α); 7·10–7·60 (m, 2H-16); 8·30–7·60 (m, 2H-15). Irradiation at 7·38 causes the doublet at 5·42 to collapse into a singlet. Mass spectrum (*m/e* > 6%): 486(0·75), 312(21), 311(100), 310(24), 296(21), 281(6), 280(8), 268(9), 256(9), 255(50), 254(8), 253(15), 240(7), 239(8), 237(8), 225(7), 177(14), 174(11), 152(8), 120(6), 119(24), 93(7), 70(6), 64(8), 63(6), 58(8).

Preparation of the hydrochloride **4**

(a) To a soln of **3** (487 mg) in acetone (250 ml) at 50° was added in one portion conc HCl. The salt **4** precipitated upon cooling. It was removed and dried. The colorless salt (459 mg; 88%) had m.p. 228° (darkening) – 250° (dec). (Found: C, 59·42; H, 5·19; N, 10·32; Cl, 6·52; M.W. 472. $C_{28}H_{25}N_4O_5Cl.1\ H_2O$ requires: C, 59·26; H, 4·75; N, 10·64; Cl, 6·74%; M.W. —HCl—H_2O, 472·48); IR(KBr): 1772, 1723 (ureide CO), 1693 cm^{-1} (α,β-unsatd CO); NMR (DMSO-d_6): τ 2·50 (s, 5 N-$C_6\underline{H}_5$); 3·05 (d, $J_{8,7}$ = 10 Hz, H-8); 3·10 (ABq, $J_{1,2}$ = 8 Hz, H-1, H-2); 3·53 (d, $J_{7,8}$ = 10 Hz, H-7); 4·60 (m, H-9α); 4·67 (s, H-5); 6·23 (3 $OC\underline{H}_3$); 7·00 (s, 3 $NC\underline{H}_3$); 7·38–5·33 (br m, 2H-10, 2H-16); 8·48–7·90 (m, 2H-15); M.S. (*m/e* > 3%): 472(0·4), 119(8), 94(5), 93(100), 92(9), 91(13).

(b) To the refluxing reaction mixture obtained from **1** (385 mg) in acetone (10 ml) and **2** (622 mg) in acetone (4 ml) was added conc HCl (2 ml). The salt **4** precipitated upon cooling (983 mg; 96%), m.p. 232 (darkening) – 251° (dec). The product was identical in all respects to that obtained by procedure (a).

Free base **5**. The salt **4** (523 mg) was dispersed in water (20 ml) and the whole was boiled for 2 min. A yellow product precipitated. After cooling the solid was removed and dried in a vacuum. The yellow amorphous **5** (416 mg; 86%) had m.p. 215 (darkening) – 225° (dec). It was insoluble in most common organic solvents. (Found: C, 63·00; H, 5·52; N, 11·12; M.W. 472. $C_{26}H_{24}N_4O_5.1H_2O$ requires: C, 63·67; H, 5·30; N, 11·43%; M.W. –H_2O, 472·48); IR(KBr): 3350, 1690, 1670, 1615 cm^{-1}; IR($CHCl_3$): 1771, 1712 cm^{-1}; NMR(DMSO-d_6): τ 2·55 (s, 5 N-$C_6\underline{H}_5$); 3·21 (ABq, $J_{1,2}$ = 8·5 Hz, H-1, H-2); 3·30 (d, $J_{8,7}$ = 10 Hz, H-8); 3·85 (d, $J_{7,8}$ = 10 Hz, H-7); 4·90 (s, H-5); 5·37 (m, H-9); 6·25 (s, 3 $OC\underline{H}_3$); 6·55 (d, $J_{10\beta,10\alpha} = -19$ Hz, H-10β); 7·35 (s, 3 $NC\underline{H}_3$); 7·60–6·84 (m, 2H – 16 + H – 10α); 8·60–7·60 (m, 2H–15). Upon addition of 1 drop D_2O the following changed lines were observed: N-CH_3, 7·16; H-9, 4·92; H – 1 + H – 2; 3·15; M.S. (*m/e* > 15%): 472 (100), 307(19), 297(38), 296(52), 295(17), 293(17), 292(39), 282(19), 281(29), 266(24), 242(21), 230(86), 229(17), 119(43), 93(82), 91(19), 66(26), 65(19), 58(38).

The yellow color of a solution of **5** (236 mg) in acetone (5 ml) was discharged after stirring with conc HCl (6 drops). A colorless ppt of **4** was obtained (255 mg; quant), identical to that described above.

Rearrangement of **5**

(a) Water (450 ml) was added slowly to a solution of **5** (2·36 g) in hot pyridine (25 ml). The soln was allowed to stand until the yellow color disappeared (4 days). Concurrently a colorless solid precipitated. Removal and drying of the solid in a high vacuum afforded the isomer **6** (2·15 g; 91%), m.p. 266–276° (dec). The analytical sample had m.p. 275–279° (dec; methylene chloride-hexane). (Found: C, 65·89; H, 5·07, N, 11·52, M.W. 472. $C_{26}H_{24}N_4O_5$ requires: C, 66·09; H, 5·12; N, 11·86%, M.W. 472·48); IR(KBr): 1775, 1720 (ureide CO), 1680 cm^{-1} (sh, α,β-unsatd CO); NMR($CDCl_3$): τ 2·58 (s, 5 N-$C_6\underline{H}_5$); 3·10 (d, $J_{8,7}$ = 9·8 Hz, H-8); 3·30 (s, H – 1 + H – 2); 3·88 (dxd, $J_{7,8}$ = 9·8 and $J_{7,5}$ = 1·6 Hz, H-7); 3·93 (br s, 1 $O\underline{H}$), 4·65 (d, $J_{5,7}$ = 1·6 Hz, H-5); 5·95 (d, $J_{9\alpha,10\alpha}$ = 6 Hz, H-9α), 6·19 (s, 3 $OC\underline{H}_3$), 6·62 (d, $J_{10\beta,10\alpha} = -18$ Hz, H-10β); 7·05 (d, J = 6 Hz, 0·67 H, lower part of H-10α); 7·44 (s, 3 $NC\underline{H}_3$); 8·40–7·15 (m, 4·33H, 0·33H – 10α + 2H – 16 + 2H – 15). Irradiation at 5·95 caused collapse of d at 7·05 into s; at 4·65 causes collapse of q at 3·88 into d, J = 9·8 Hz). Addition of D_2O caused disappearance of line at 3·93; M.S. (*m/e* > 12%): 473(30), 472(92), 297(47), 296(63), 295(12), 282(17), 243(12), 242(23), 240(12), 239(12), 231(17), 230(100), 229(29), 228(13), 119(12), 58(12).

(b) Crystallization of **5** from hot EtOH or hot MeOH after standing of solutions for 1-2 days also afforded **6** identical in its properties to that prepared by procedure (a). Heating in DMSO at 60° for 24 hr followed by replacement of the solvent by chloroform and crystallization from di-isopropyl ether also gave **6**.

The *hydrochloride* **7** was obtained by adding conc HCl to a refluxing soln of **6** (945 mg) in acetone (100 ml). After standing overnight at room temp the colorless solid was removed and dried (1·01 g; 99%), m.p. 240–250° (dec). The analytical sample formed needles, m.p. 250–258° (dec; water). (Found: C, 55·13; H, 5·58; N, 9·98; M.W. 472. $C_{26}H_{25}N_4O_5Cl.3H_2O$ requires: C, 55·47; H, 5·55; N, 9·95%; M.W.-$3H_2O$-HCl, 472·48); IR(KBr): 3450, 1780, 1730, 1695 cm^{-1}; NMR (DMSO-d_6); τ 2·50 (m, 5 N-C_6H_5); 2·65 (d, $J_{8,7}$ = 10 Hz, H-8); 3·15 (ABq, $J_{1,2}$ = 10 Hz, H-1, H-2); 3·69 (dxd, $J_{7,8}$ = 10 Hz, $J_{7,5}$ = 1·6 Hz, H-7); 4·73 (d, $J_{5,7}$ = 1·6 Hz, H-5); 5·00 (v. br. $N\underline{H}$, $O\underline{H}$); 5·36 (br m, H-9); 6·23 (s, 3 OCH_3); 6·91 (br s, 3 NCH_3); 6·32–7·30 (m, 2H-10, 2H-16); 7·65–8·35 (m, 2H–15). Addition of D_2O sharpened the $NC\underline{H}_3$ peak while the broad signal at 5·00 was found to be under the water peak at 5·60.

Reduction of **3**. The adduct **3** (487 mg) and dipotassium azodicarboxylate (4·08 g) were added to dry pyridine (25 ml). AcOH (1 ml) in pyridine (5 ml) was added with stirring during 1 hr. Stirring was continued for 24 hr whereupon an additional portion of AcOH in pyridine was added as before. The yellow color disappeared after 64 more hr. The whole was filtered through celite and the pyridine was removed. Since TLC showed the reaction still to be incomplete, the crude mixture was redissolved in pyridine (50 ml) and an excess of the above reducing agent (8·16 g) was added. AcOH-pyridine (1 ml : 5 ml) portions were added during 1 hr and after 24, 32, 48 and 92 hr. After 112 hr the mixture was filtered through celite and the pyridine was removed. The semi-solid residue was dissolved in benzene and chromatographed on basic alumina (50 g, grade V) using 5% chloroform in benzene for elution. A colorless solid, **11** was obtained (192 mg; 39%). When the weight of reducing agent was increased to 24·3 g and 32·4 g and the volume of pyridine to 120 ml, the yield increased to 46% and 58%, respectively. The analytical sample formed small needles, m.p. 211–212° (CH_2Cl_2-hexane). (Found: C, 64·63; H, 5·71; N, 10·80; M.W. 488). $C_{27}H_{28}N_4O_5.1H_2O$ requires: C, 63·56; H, 5·53; N, 11·06%; M.W. 488·50); IR($CHCl_3$): 1760, 1705 cm^{-1} (ureide CO); NMR($CDCl_3$): τ 2·50 (m, 5N-$C_6\underline{H}_5$); 3·22 (ABq, J = 8 Hz, H – 1 + H – 2); 5·03 (s, H-5); 5·93 (d, $J_{9\alpha,10\alpha}$ = 7 Hz, H-9); 6·10 (s, 3 $OC\underline{H}_3$); 6·11 (s, 3 $OC\underline{H}_3$); 6·64 (d, $J_{10\beta,10\alpha}$ =

– 18·5 Hz, H-10β); 7·85–7·15 (m, 2H – 16 + H – 10α); 7·54 (s, 3 NCH$_3$); 9·15–7·85 (complex m, 2H-7, 2H-8, 2H-15); M.S. (*m/e* > 10%): 488(100), 474(12), 473(33), 313(17); 312(67), 255(14), 254(10), 230(14), 119(10), 58(12).

The *hydrochloride*, **12**, was obtained by adding conc HCl (6 drops) to a soln of **11** (102 mg) in hot acetone (4 ml). The colorless ppt was collected after 30 min. It afforded colorless needles (80 mg; 73%), m.p. 253–257° (dec). It was recovered unchanged after boiling for 2 min in water. (Found: C, 61·04; H, 5·16; N, 10·70; Cl, 6·57%. M.W.-HCl, 488. $C_{27}H_{29}N_4O_5Cl$ requires: C, 61·77; H, 5·57; N, 10·67; Cl, 6·75%; M.W.-HCl, 488·51); IR(KBr): 1770, 1710 cm^{-1} (ureide CO). NMR (DMSO-d_6): τ 2·50 (br m, 5 N-C$_6$H$_5$); 3·10 (ABq, H-1, H-2); 4·75 (br s, H-5); 5·40 (m, H-9); 6·18 (s, 3 OCH$_3$); 6·23 (s, 3 OCH$_3$); 7·10 (s, 3 NCH$_3$); 8·50–5·80 (m, unassigned); M.S. (*m/e* > 10%): 488(100), 475(25), 474(81), 473(13), 361(12), 313(19), 312(71), 298(32), 282(14), 281(12), 256(29), 255(45), 254(36), 253(12), 243(13), 242(26), 241(23), 240(13), 239(10), 230(49), 229(25), 228(32), 227(10), 223(20), 214(14), 213(10), 176(17), 119(12), 91(10), 58(36), 55(10).

Reaction of **2** *with tetracyanoethylene.* A soln of thebaine (0·93 g) and tetracyanoethylene (0·4 g) in MeOH (16 ml) was allowed to stand under N_2 at room temp for 40 hr. The crystalline ppt **13** was removed and dried (0·96 g), m.p. 181°. Additional crops were isolated from the mother liquor (0·35 g; total yield 97%). The analytical sample had m.p. 184° (MeOH). (Found: C, 66·90; H, 6·09; N, 9·34; M.W.-anion, 326. $C_{35}H_{27}N_3O_5$ requires: C, 66·80; H, 6·05; N, 9·35%; M.W. 449·49); UV(MeOH); nm(ε): 283(1890); 233(23350); IR(KBr): 2195, 2165, 1645, 1600 cm^{-1}. NMR (DMSO-d_6): τ 3·29 (ABq, H-1, H-2); 4·10 (d, J = 6 Hz, H-7); 4·53 (s, H-5); 4·77 (d, J = 6 Hz, H-8); 5·52 (d, J = 6 Hz, H-9); 6·26 (s, 3 OCH$_3$); 6·42 (s, 3 OCH$_3$); 6·59 (s, 3 = C(O)—OCH$_3$); 6·72 (s, 3 $\overset{+}{N}$CH$_3$); 6·85 (s, 3 $\overset{+}{N}$CH$_3$); 8·25–5·90 (m, 2H-10, 2H-15, 2H-16); M.S. (*m/e* > 5%): 326(0·5), 325(1·6), 311(0·5), 280(5), 265(8), 255(13), 254(100), 253(7), 240(10), 239(60), 211(11), 196(6), 168(8), 152(7), 140(7), 139(12), 127(16), 72(9), 59(14), 58(47), 45(8), 44(17), 42(8).

Reaction of codeine with tetracyanoethylene. A soln of codeine (0·48 g) and tetracyanoethylene (0·19 g) in MeOH (6 ml) was allowed to stand under N_2 overnight. The crystalline ppt and additional crops gave the total product **14** (0·24 g; 34%), m.p. 223°. The analytical sample had m.p. 228·5° (MeOH). (Found: C, 66·10; H, 6·12; N, 9·42; OCH$_3$, 14·47; M.W.-anion, 314. $C_{24}H_{27}N_3O_5$ requires: C, 65·89; H, 6·22; N, 9·61; OCH$_3$, 14·19%; M.W. 437·48): UV(MeOH): 286(8520), 232(28400); IR(KBr): 2180, 2150, 1650, 1602 cm^{-1}; NMR(DMSO-d_6): τ = 3·33 (ABq, H-1, H-2); 4·31(m, H-7); 4·73(m, H-8); 5·18(q, $J_{5,6}$ = 6 Hz, H-5β); 6·17–5·60 (m, H-6β, H-9α); 6·25 (s, 3 OCH$_3$); 6·56, 6·58, 6·60 (3s, 6 $\overset{+}{N}$CH$_3$ + 3 = C(O)—OCH$_3$); 8·33–6·70 (m, 7H: 2H-10, H-14, 2H-15, 2H-16); M.S. (*m/e* > 10%): 314(6), 313(27), 300(20), 299(100), 298(13), 242(44), 240(13), 229(21), 215(16), 214(10), 211(10), 209(10), 198(10), 197(10), 181(10), 162(17), 124(17), 73(29), 72(10), 59(40), 58(57), 53(15), 45(85), 44(35), 42(21).

Reaction of **13** *with* **1**. To a soln of **13** (0·45 g) in acetone (35 ml) was added with stirring powdered **1** (0·18 g). After 30 min additional stirring and removal of the solvent the residue was triturated and stirred with water during 5 days. After removal of the ppt and drying in a high vacuum the adduct **15** was obtained (0·60 g; 96%), m.p. 167–170° (dec); IR(CHCl$_3$): 3570–3120, 2180, 2160, 1775, 1720, 1630 cm^{-1}; NMR (Acetone-d_6): τ 2·90–2·30 (m, 5 N-C$_6$H$_5$, H-8); 3·08 (ABq, H-1, H-2); 3·78 (dxd, $J_{7,8}$ = 10 Hz, $J_{7,5}$ = 2 Hz, H-7); 4·58 (d, $J_{5,7}$ = 2 Hz, H-5), 5·30–4·90 (m, H-9α, NH exchanged with D_2O); 6·00, 5·19, 5·30, 5·55 (4s, 6 $\overset{+}{N}$-CH$_3$, 3 OCH$_3$, 3 = C(O)—OCH$_3$); 6·70–6·20 (m, 2H-10); 8·00–6·70 (m, 2H – 16 + 2H – 15); M.S.: 487(0·6), 486(2), 485(5), 483(4), 473(37), 296(52), 281(100), 266(67).

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