[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE RADIATION LABORATORY, UNIVERSITY OF CALIFORNIA]

Δ^7- and Δ^8-Desoxycodeine

BY HENRY RAPOPORT AND ROBERT M. BONNER

Hydrogenolysis of *p*-toluenesulfonylcodeine with lithium aluminum hydride gave a single, non-phenolic desoxycodeine. Its structure was established as that of the true desoxycodeine, Δ^7-desoxycodeine, by its stability to acid hydrolysis, formation of an N-cyano compound with cyanogen bromide, degradation to an α-methine which could be isomerized to a β-methine, and hydrogenation to dihydrodesoxycodeine-D. In an analogous manner, Δ^8-desoxycodeine was prepared from neopine.

If the possibility of stereochemical differences at carbon-14 is disregarded, there are four conceivable non-phenolic desoxycodeines, differing only in the position of the double bond. Of these, two are known and their structures have been established as Δ^6-desoxycodeine (desoxycodeine-C)[1] and Δ^8-desoxycodeine (desoxycodeine-D).[2] The true desoxycodeine, Δ^7-desoxycodeine (II), differing from codeine only in that the hydroxyl group has been replaced by hydrogen, heretofore has remained unknown, and its preparation is the subject of the present report.

Recent work on the preparation of cholestene[3] has presented an attractive method for hydrogenolysis of the carbon–oxygen bond without concurrent hydrogenation of an olefinic double bond—namely, by lithium aluminum hydride reduction of the corresponding *p*-toluenesulfonate ester. In applying this reaction to codeine, the requisite *p*-toluenesulfonylcodeine (I) was first prepared in nearly quantitative yield by treating codeine with *p*-toluenesulfonyl chloride in pyridine at 0°. Attempted reduction with lithium aluminum hydride in ethereal solution resulted only in the recovery of unreacted tosyl derivative. However, in refluxing tetrahydrofuran, hydrogenolysis proceeded readily and excellent yields of Δ^7-desoxycodeine (II) were obtained.[3a]

Although the product melted sharply, we felt this to be insufficient proof of homogeneity since similar, supposed pure, sharply melting desoxycodeines had been subsequently shown to be mixtures.[4] The impurity suspect was Δ^6-desoxycodeine which might easily have arisen through an allylic rearrangement. To establish homogeneity, the desoxycodeine was subjected to several fractionation procedures, and the physical constants (m.p. and optical rotation) of the various fractions were compared. Fractional crystallization of the free base, fractional crystallization of the perchlorate and *d*-acid tartrate, and chromatographic adsorption on alumina using either ether (seventeen fractions) or benzene–hexane (thirty fractions) as eluting solvent were applied, and in every case all the fractions were identical.

Once the homogeneity of the product was demonstrated, there remained to be proved that its structure was as shown in formula II. The oxide bridge was intact, since the product failed to couple with diazotized sulfanilic acid. Also, it was recovered quantitatively after heating at 80° for 45 minutes in 1 *N* hydrochloric acid. If the double bond had been at position 5,6 the compound would be an enol ether and easily hydrolyzed by this treatment. Thus the product was the non-phenolic desoxycodeine with the double bond at position 7,8 since the other two possibilities (Δ^6 and Δ^8) are known and different from the present compound.

Confirmatory evidence for this structural assignment was obtained in the following way. With cyanogen bromide, N-cyanonordesoxycodeine (III) was obtained. This indicates that the double bond is not at position 8,14 since in the latter case the nitrogen–carbon bond to position 9 is broken with addition of the elements of cyanogen bromide.[2,5] Degradation of the desoxycodeine led to a methine (IV) which on heating in ethanolic potassium hydroxide isomerized to a new methine (V) with an accompanying large increase in rotation. This is parallel to several observations of the isomerization of α- to β-methines wherein the double bond shifts from the 7,8- to the 8,14-position.[6] The β-methine (V) thus obtained is identical with the methine resulting from degradation of Δ^8-desoxycodeine. The desoxy-α-methylmorphimethine (IV) originally formed has a surprisingly high positive rotation and it was thought that perhaps partial isomerization had occurred during the degradation. This possibility was eliminated, however, since the α-methine in butyl ether was found to be stable to alkali, and the same methine was formed when the degradation was carried out either in the presence or absence of butyl ether.

Finally, hydrogenation of the desoxycodeine in methanol gave the non-phenolic dihydrodesoxycodeine-D (VI) in nearly quantitative yield. If the double bond had been conjugate with the oxide ring (position 6,7), a large proportion of phenolic material would have resulted from this hydrogenation.[7] From these results it follows that lithium aluminum hydride reduction of *p*-toluenesulfonylcodeine yields Δ^7-desoxycodeine (II).

Our earlier attempts at the preparation of desoxycodeine had centered about Raney nickel desulfurization experiments on α-ethylthiocodide (VII). Nickels of various activities[8] were used, but in every case desulfurization was accompanied by oxide ring opening and/or partial hydrogenation

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[1] L. F. Small and F. L. Cohen, THIS JOURNAL, **53**, 2214 (1931).

[2] L. F. Small and J. E. Mallonee, *J. Org. Chem.*, **5**, 350 (1940).

[3] P. Karrer and H. Schmid, *Helv. Chim. Acta*, **32**, 1371 (1949).

[3a] NOTE ADDED IN PROOF.—After this report had been accepted for publication, the preparation of Δ^7-desoxycodeine by the same method was reported by P. Karrer and G. Widmark, *Helv. Chim. Acta*, **34**, 34 (1951).

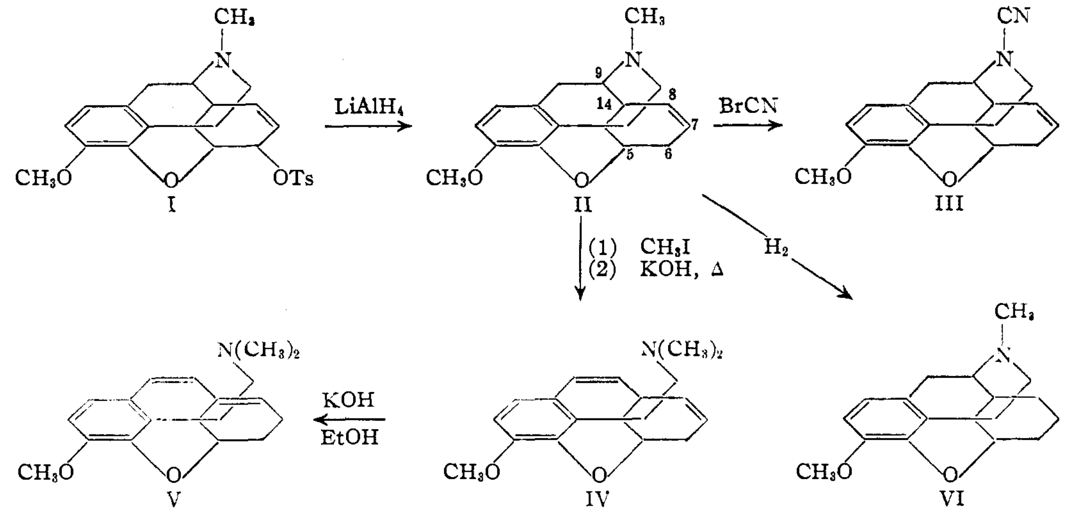
[4] (a) L. F. Small and F. L. Cohen, THIS JOURNAL, **53**, 2227 (1931); (b) L. F. Small and R. E. Lutz, *ibid.*, **56**, 1738 (1934).

[5] J. von Braun, *Ber.*, **47**, 2312 (1914).

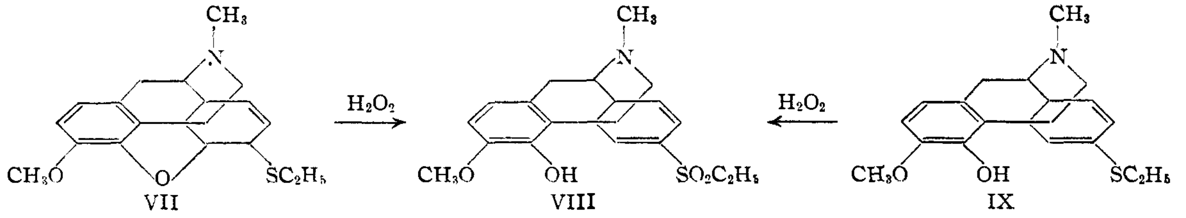
[6] S. P. Findlay and L. F. Small, THIS JOURNAL, **72**, 3249 (1950).

[7] R. E. Lutz and L. F. Small, *ibid.*, **54**, 4715 (1932).

[8] (a) R. Mozingo, *Org. Syntheses*, **21**, 15 (1941); (b) G. B. Spero, A. V. McIntosh, Jr., and R. H. Levin, THIS JOURNAL, **70**, 1907 (1948).

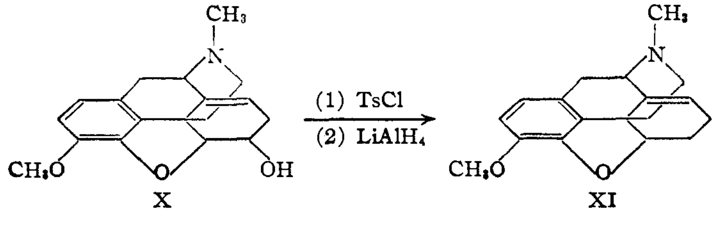


of the double bond. As a derivative, α-ethylthiocodide was oxidized to the sulfone. However, oxide ring opening had taken place, and the product was the phenolic sulfone (VIII), identical with the compound obtained from oxidation of β-ethylthiocodide (IX).



The ease with which lithium aluminum hydride was found to reduce *p*-toluenesulfonylcodeine to Δ^7-desoxycodeine led us to examine this reaction as a means of preparing Δ^8-desoxycodeine (XI) (desoxyneopine, desoxycodeine-D) directly from neopine (X) through its *p*-toluenesulfonyl derivative. Δ^8-Desoxycodeine has been prepared previously[2] by prolonged treatment of 8-chlorodihydrocodide with sodium in cyclohexanol. It was obtained as an oil and, although both Δ^7- and Δ^8-desoxycodeine may possibly result from the dehydrohalogenation, the product was conclusively demonstrated to have the Δ^8-structure.

In order to effect the hydrogenolysis of *p*-toluenesulfonylneopine, more vigorous conditions were necessary than was the case with the codeine derivative. Whereas lithium aluminum hydride in boiling tetrahydrofuran (65°) gave excellent yields with the latter compound, a temperature around 100° was required to reduce the neopine analog. This is not surprising in view of the fact that the allylic alcohol system of codeine is lacking in neopine.



The product gave a faintly positive test for phenolic material with diazotized sulfanilic acid. As is frequently the case when the phenol group is at position 4 in the morphine series, the contaminant exhibited crypto-phenolic properties and could not be extracted from organic solvents with aqueous alkali. However, it could be conveniently eliminated by using the diagnostic test on a large scale for separation purposes. A quantity of diazotized sulfanilic acid equivalent to one-third the product was added and phenolic material, now readily soluble in aqueous alkali by virtue of the sulfonic acid group in the coupled product, was completely removed by extraction. Although the phenolic material is not recoverable, this procedure may prove useful in other cases in the morphine series where it is necessary to remove small amounts of crypto-phenolic impurities.

The pure Δ^8-desoxycodeine (XI) was obtained as a crystalline solid, m.p. 61.5–62°, in contrast to the oil previously reported.[2] Also, the melting points of the various derivatives were found to be slightly higher, and the reported difficulty with carbon analyses[2] was not encountered. A possible explanation of the higher melting points obtained in the present work may be the presence of a small amount of Δ^7-desoxycodeine in the material prepared from 8-chlorodihydrocodide. The reactions used by Small and Mallonee[2] to establish the structure of Δ^8-desoxycodeine were confirmed. Hydrogenation under various conditions gave dihydrodesoxycodeine-D and degradation resulted directly in desoxy-β-methylmorphimethine (V).

Δ^8-Desoxymorphine, a by-product in the previous[2] preparation of Δ^8-desoxycodeine, was readily prepared in good yield by ether cleavage using pyridine hydrochloride.[9] Methylation with diazomethane regenerated Δ^8-desoxycodeine.

Experimental[10]

***p*-Toluenesulfonylcodeine (I).**—To a solution of 25.0 g. (0.084 mole) of codeine in 25 ml. of dry pyridine, cooled in an ice-bath, was added a solution of 17.5 g. (0.092 mole) of *p*-toluenesulfonyl chloride in 15 ml. of pyridine at such a rate that the temperature did not rise above 10°. The reaction mixture was allowed to stand at 0° for four hours and then poured into 900 ml. of ice-water with rapid stirring. Basification with concentrated aqueous ammonia caused a precipitate to form from which the supernatant liquid was decanted. On addition of another 900 ml. of water and rubbing with a stirring rod, the precipitate became crystalline. It was filtered and slurried two more times with 400-ml. portions of water, after which it was dried to constant weight in a vacuum desiccator. The crude *p*-toluenesulfonylcodeine thus obtained weighed 36.0 g. (95% yield) and melted at 120–121°. Crystallization from benzene–hexane or butanone gave material of m.p. 121–121.5°; $[\alpha]^{25}_D$ −209° (*c* 0.99, dioxane).

Anal. Calcd. for $C_{25}H_{27}NO_6S$: C, 66.2; H, 6.0; S, 7.1; equiv. wt., 453.5. Found: C, 66.4; H, 6.1; S, 7.0; equiv. wt., 456.

Δ^7-Desoxycodeine (II).—Twenty-five ml. of a 2.4 *M* solution of lithium aluminum hydride in tetrahydrofuran was added to a solution of 25.0 g. (0.055 mole) of *p*-toluenesulfonylcodeine (m.p. 120–121°) in 100 ml. of tetrahydrofuran. After the initial mild exothermic reaction (controlled by cooling in a water-bath) had subsided, the mixture was heated under reflux with stirring in a nitrogen atmosphere for three hours. To the reaction mixture, cooled in an ice-bath, was then added 100 ml. of ether followed by the dropwise addition of water to decompose excess lithium aluminum hydride. Filter-aid (5 g.) was thoroughly mixed with the precipitate, and the mixture was filtered. The insoluble material was digested with three 200-ml. portions of ether and the combined ether solutions were extracted with three 75-ml. portions of 3 *N* hydrochloric acid. After basification with sodium hydroxide, the aqueous portions were extracted with ether (four 100-ml. portions) and the ether extracts were dried and evaporated. The residue of desoxycodeine weighed 14.0 g. (90% yield) and melted at 81–83°. It gave a very faintly positive test for phenolic material (with diazotized sulfanilic acid) that could be completely eliminated by crystallization from aqueous acetone (70% recovery), by purification through the perchlorate (85% recovery), or by the diazotized sulfanilic acid method described below under Δ^8-desoxycodeine. The purified material had a m.p. of 82–83°; $[\alpha]^{25}_D$ −68.0° (*c* 1.78, ethanol).

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.3; H, 7.5; equiv. wt., 283. Found: C, 76.4; H, 7.6; equiv. wt., 283.

The perchlorate was prepared by adding 1 *N* ethanolic perchloric acid to an ethanolic solution of the base until the solution was acid to congo red. Crystallization from aqueous ethanol (1 g. of perchlorate per 25 ml. 95% ethanol plus 1 ml. water) gave material of m.p. 250° (dec.); $[\alpha]^{25}_D$ −41.3° (*c* 1.01, acetone).

Anal. Calcd. for $C_{18}H_{22}ClNO_6$: C, 56.3; H, 5.8. Found: C, 56.1; H, 5.8.

The hydrochloride was prepared by adding ethanolic hydrochloric acid to the base in ethanol. Addition of ether caused crystallization and the hydrochloride was recrystallized from butanone, m.p. 239–240°; $[\alpha]^{25}_D$ −40.3° (*c* 0.68, ethanol).

Anal. Calcd. for $C_{18}H_{22}ClNO_2$: Cl, 11.1. Found: Cl, 11.0.

The acid tartrate was prepared in concentrated aqueous solution by heating a suspension of the base with a 100 mole % excess of *d*-tartaric acid until solution was complete. After recrystallization from water it melted at 123–125°; $[\alpha]^{25}_D$ −41.1° (*c* 1.04, water).

Anal. Calcd. for $C_{22}H_{27}NO_8$: C, 61.0; H, 6.3. Found: C, 60.7; H, 6.5.

Addition of methyl iodide to a methanolic solution of the base gave the **methiodide**, m.p. 257–258° (dec.) after crystallization from methanol; $[\alpha]^{25}_D$ −25.9° (*c*, 0.97, methanol).

Anal. Calcd. for $C_{19}H_{24}INO_2$: C, 53.6; H, 5.7. Found: C, 53.4; H, 5.8.

N-Cyanonor-Δ^7-desoxycodeine (III).—Following the general procedure of von Braun,[5] a solution of 0.29 g. (2.7 millimoles) of cyanogen bromide in 5 ml. of chloroform was added to a solution of 0.57 g. (2.0 millimoles) of desoxycodeine in 3 ml. of chloroform, and the resulting solution was heated under reflux for two hours. To the residue after evaporating the chloroform was added 5 ml. of water and the mixture was heated to boiling. After cooling, filtration gave 0.46 g. of N-cyano compound. Extraction of the filtrate with ether gave an additional 0.05 g.; yield 0.51 g., 87%, m.p. 145–148°. Crystallization from aqueous ethanol resulted in material of m.p. 149–150°; $[\alpha]^{25}_D$ −133.8° (*c* 1.03, ethanol).

Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.4; H, 6.2; N, 9.5. Found: C, 73.4; H, 6.3; N, 9.5.

Desoxy-α-methylmorphimethine (IV).—After adding 20 ml. of 40% aqueous sodium hydroxide to a hot solution of 3.0 g. of Δ^7-desoxycodeine methiodide in 20 ml. of water, the mixture was heated under reflux for 10 minutes. Three 50-ml. portions of ether were used to extract the cooled mixture, and the combined ether extracts were washed with three 25-ml. portions of 3 *N* hydrochloric acid. These washes were basified and extracted with ether (three 50-ml. portions), and evaporation of the dried ether solution left 2.1 g., quantitative yield, of the oily methine; $[\alpha]^{25}_D$ +130° (*c* 1.30, dioxane). The methine was distilled readily at 115–120° (bath temperature) at 0.01 mm. but remained as an oil, $[\alpha]^{25}_D$ +133° (*c* 1.25, dioxane).

Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.7; H, 7.8. Found: C, 76.6; H, 7.8.

When the degradation was carried out as above but in the presence of di-*n*-butyl ether, the resulting methine had $[\alpha]^{25}_D$ +136° (*c* 1.26, dioxane). After a solution of the methine in di-*n*-butyl ether was heated under reflux with 20% aqueous sodium hydroxide for two hours, the recovered methine had $[\alpha]^{25}_D$ +128° (*c* 1.26, dioxane).

The perchlorate was prepared by adding 1 *N* ethanolic perchloric acid to the methine dissolved in ethanol and was crystallized from ethanol, m.p. 180–181°; $[\alpha]^{25}_D$ +86.3° (*c* 1.02, acetone).

Anal. Calcd. for $C_{19}H_{24}ClNO_6$: C, 57.4; H, 6.1. Found: C, 57.6; H, 6.1.

The picrate was prepared by adding saturated, ethanolic picric acid to an ethanolic solution of the methine and was crystallized from ethanol, m.p. 163–164°; $[\alpha]^{25}_D$ +54.7° (*c* 0.47, acetone).

Anal. Calcd. for $C_{25}H_{26}N_4O_9$: C, 57.0; H, 5.0; N, 10.6. Found: C, 56.9; H, 5.2; N, 10.9.

Desoxy-β-methylmorphimethine (V).—A solution containing 0.5 g. of desoxy-α-methylmorphimethine (IV) and 0.6 g. of potassium hydroxide in 4 ml. of ethanol and 3 ml. of water was heated under reflux for 24 hours in a nitrogen atmosphere, after which it was poured into 50 ml. of water. The alkaloidal material was isolated by extraction into ether, then into aqueous acid, and back again into ether after basifying. Evaporation of the final, dried ether extracts left 0.48 g. of residue which solidified on scratching and melted at 73–75°. Crystallization from aqueous ethanol gave material of m.p. 75–76° (reported[2] m.p. 76–77°); $[\alpha]^{25}_D$ +314° (*c* 0.99, dioxane).

The perchlorate was prepared as above and was crystallized from ethanol, m.p. 230–231°; $[\alpha]^{25}_D$ +182.5° (*c* 0.99, acetone).

Anal. Calcd. for $C_{19}H_{24}ClNO_6$: C, 57.4; H, 6.1. Found: C, 57.1; H, 6.1.

The picrate, prepared as above, was crystallized from ethanol, m.p. 173–175° (dec.); $[\alpha]^{25}_D$ +91.5° (*c* 0.54, acetone).

Anal. Calcd. for $C_{25}H_{26}N_4O_9$: C, 57.0; H, 5.0; N, 10.6. Found: C, 57.2; H, 5.2; N, 10.3.

The methiodide was prepared in and crystallized from methanol, m.p. 314° (dec.); $[\alpha]^{25}_D$ +157° (*c* 0.49, methanol).

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[9] V. Prey. *Ber.*, **74**, 1219 (1941).

[10] All melting points are corrected and those above 200° were taken in evacuated capillaries; microanalyses were performed by the Microchemical Laboratory, University of California.

Anal. Calcd. for $C_{20}H_{26}INO_2$: C, 54.7; H, 6.0; I, 28.9. Found: C, 54.6; H, 6.1; I, 28.6.

Dihydrodesoxycodeine-D (VI).—Hydrogenation of 1.0 g. (3.5 millimoles) of desoxycodeine in 20 ml. of methanol at room temperature and atmospheric pressure using 20 mg. of platinum oxide as catalyst ceased after one hour with the absorption of 1.02 molar equivalents of hydrogen. The solution was filtered and the residue after concentration of the filtrate was sublimed at 100° (0.1 mm.) to give a practically quantitative yield of dihydrodesoxycodeine-D of m.p. 102–105°. This material was converted to the *d*-acid tartrate salt, which after thorough drying melted at 155–156°; $[\alpha]^{25}_{\mathrm{D}}$ −39.1° (*c* 1.77, water). The reported values for this compound are m.p. 123–125°, $[\alpha]^{30}_{\mathrm{D}}$ −39.6° for the hydrate[4a] and m.p. 154–154.5°, $[\alpha]^{18}_{\mathrm{D}}$ −29.9°[11] for the anhydrous material. Liberation of the free base from this salt gave dihydrodesoxycodeine-D of m.p. 106–107°; $[\alpha]^{18}_{\mathrm{D}}$ −77.5° (*c* 0.87, ethanol). An authentic sample, prepared as described,[4a] had m.p. 106–107°, $[\alpha]^{22}_{\mathrm{D}}$ −78° (*c*, 0.87, ethanol), and gave no depression in a mixed-melting point determination with the material prepared above.

α-Ethylthiocodide (VII).—α-Ethylthiocodide was prepared by shaking a mixture of bromocodide, ethyl mercaptan, and 1 *N* sodium hydroxide for four hours at 100°.[12] The product was purified by crystallization of the **perchlorate** from ethanol, m.p. 191–192°; $[\alpha]^{20}_{\mathrm{D}}$ −249° (*c* 1.14, acetone).

Anal. Calcd. for $C_{20}H_{26}ClNO_6S$: C, 54.1; H, 5.9; S, 7.2. Found: C, 54.0; H, 6.0; S, 7.2.

The base liberated from the perchlorate was crystallized from aqueous ethanol (37% yield from bromocodide) and melted at 75–77° (dimorphic forms reported,[13] m.p. 77–79° and 86–87°).

β-Ethylsulfonylcodide (VIII).—To a solution of 3.0 g. (8.75 millimoles) of α-ethylthiocodide (VII) in 10 ml. of glacial acetic acid was added a solution of 1.8 g. of 35% aqueous hydrogen peroxide in 5 ml. of glacial acetic acid and the mixture was allowed to stand at room temperature for two days. After diluting with water and bubbling in sulfur dioxide, the solution was concentrated under reduced pressure to remove the acetic acid. Water was then added to the concentrate and it was carefully basified in the cold with sodium carbonate. The solid which precipitated was crystallized from aqueous ethanol to give 3.0 g., 92% yield, m.p. 193–193.5°; $[\alpha]^{25}_{\mathrm{D}}$ +50.5° (1.06, ethanol).

Anal. Calcd. for $C_{20}H_{25}NO_4S$: C, 64.0; H, 6.7; S, 8.5. Found: C, 64.4; H, 6.8; S, 8.6.

This compound gave a positive test with diazotized sulfanilic acid and was identical with the sulfone prepared in the same manner from β-ethylthiocodide (IX).[13]

Neopine (X).—Neopine was obtained from neopine hydrobromide[14] and crystallized from cyclohexane as described,[15] m.p. 127–128°.

The methiodide, prepared in the usual manner and crystallized from methanol, melted at 249–250° (dec.); $[\alpha]^{25}_{\mathrm{D}}$ +23.0° (*c* 0.98, methanol).

Anal. Calcd. for $C_{19}H_{24}INO_3$: C, 51.7; H, 5.5; I, 28.8. Found: C, 51.8; H, 5.5; I, 29.2.

***p*-Toluenesulfonylneopine.**—To a solution of 10 g. (0.033 mole) of neopine in 10 ml. of pyridine, cooled to 0°, was added a solution of 7.0 g. (0.037 mole) of *p*-toluenesulfonyl chloride in 7 ml. of pyridine, and the resulting solution was allowed to stand at 0° for 15 hours. The crude *p*-toluenesulfonylneopine, isolated as described for the codeine derivative, amounted to 12.2 g. (80%) and melted at 156–161°. Crystallization from a mixture of cyclohexane (400 ml.) and benzene (125 ml.) afforded 8.9 g. (59%) of material melting at 163–164°; $[\alpha]^{25}_{\mathrm{D}}$ −54.2 (*c* 1.00, dioxane).

Anal. Calcd. for $C_{25}H_{27}NO_5S$: C, 66.2; H, 6.0; S, 7.1. Found: C, 66.3; H, 6.0; S, 7.1.

Δ^8-Desoxycodeine (XI).—A suspension of 10 g. (0.022 mole) of *p*-toluenesulfonylneopine (crude or pure) in 300 ml. of di-*n*-butyl ether was stirred at 105° in a nitrogen atmosphere and to it was added 15 ml. of 1.8 *M* lithium aluminum hydride in tetrahydrofuran. Stirring and heating at 105° were continued for three hours after which the reaction mixture was cooled and 10 ml. of water was added to decompose excess lithium aluminum hydride. The Δ^8-desoxycodeine was isolated from the reaction mixture in the same manner as described for Δ^7-desoxycodeine and 3.8 g. (61%) of oily material was obtained. Since a coupling test with diazotized sulfanilic acid indicated the presence of phenolic material, the oily product was treated in the following manner in order to remove all phenolics. The oil (3.8 g., 0.013 mole) was dissolved in 50 ml. of methanol, a solution of 0.22 g. of sodium hydroxide and 1.7 g. of potassium carbonate ($\cdot 1.5H_2O$) in 20 ml. of water was added, and to the resulting solution, cooled to 0°, was added the suspension of diazotized sulfanilic acid prepared[16] from 0.76 g. (4.4 millimoles) of sulfanilic acid. The temperature was kept below 4° during the addition and, after standing at 0° for one hour, the reaction mixture was extracted with five 100-ml. portions of ether. Evaporation of the combined ether extracts after washing with dilute sodium hydroxide and water and drying left a residue which sublimed slowly at 50–60° (0.01 mm.). A total of 3.0 g. (48% yield) of pure Δ^8-desoxycodeine resulted as a crystalline sublimate, m.p. 61.5–62.0°; $[\alpha]^{25}_{\mathrm{D}}$ −21.1° (*c* 1.01, ethanol).

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.3; H, 7.5. Found: C, 76.3; H, 7.4.

The hydrochloride was prepared and purified as previously described,[2] m.p. 238–239°; $[\alpha]^{25}_{\mathrm{D}}$ +5.93° (*c* 1.01, methanol), $[\alpha]^{25}_{\mathrm{D}}$ −15.0° (*c* 0.21, water) [reported[2] m.p. 234–235°, $[\alpha]^{28}_{\mathrm{D}}$ −12.1° (*c* 0.21, water)].

Anal. Calcd. for $C_{18}H_{22}ClNO_2$: C, 67.6; H, 6.9. Found: C, 67.5; H, 6.8.

The acid oxalate was prepared with alcoholic oxalic acid and crystallized from ethanol, m.p. 225–226° (reported[2] m.p. 220–221°); $[\alpha]^{25}_{\mathrm{D}}$ −10.9° (*c* 0.93, water).

Anal. Calcd. for $C_{20}H_{23}NO_6$: C, 64.3; H, 6.2. Found: C, 64.6; H, 6.1.

Addition of methyl iodide gave the **methiodide** which was crystallized from methanol, m.p. 233–234° (reported[2] m.p. 204–206°); $[\alpha]^{25}_{\mathrm{D}}$ +16.1° (*c* 1.03, methanol).

Anal. Calcd. for $C_{19}H_{24}INO_2$: C, 53.6; H, 5.7; I, 29.8. Found: C, 53.6; H, 5.8; I, 29.6.

Hydrogenation of Δ^8-Desoxycodeine.—A solution of 0.3 g. of Δ^8-desoxycodeine in 10 ml. of methanol was hydrogenated at room temperature and atmospheric pressure using 20 mg. of platinum oxide as catalyst. After absorption of one molar equivalent of hydrogen in 15 hours, hydrogen uptake ceased. The solution was filtered, the methanol evaporated, and the residue sublimed to give a quantitative yield of dihydrodesoxycodeine-D, m.p. 101–105°, $[\alpha]^{25}_{\mathrm{D}}$ −79° (*c*, 0.86, ethanol), which gave no depression in a mixed melting point determination with authentic material. In the presence of perchloric acid, hydrogenation proceeded more slowly (48 hours) and the same product was obtained.

Desoxy-β-methylmorphimethine (V) from Δ^8-Desoxycodeine.—The oil formed by boiling 0.7 g. of Δ^8-desoxycodeine methiodide in 10 ml. of 6 *N* sodium hydroxide for three minutes was extracted into ether, the ether was extracted with 3 *N* hydrochloric acid, and the alkaloidal material was re-extracted into ether after basifying. Evaporation of the dried ether solution left 0.49 g. (100% yield) of solid methine which was crystallized from aqueous ethanol, m.p. 75–76°. A mixed melting point determination with desoxy-β-methylmorphimethine prepared by isomerization of desoxy-α-methylmorphimethine above showed no depression.

Δ^8-Desoxymorphine.—A mixture of 0.5 g. of Δ^8-desoxycodeine and 1.5 g. of pyridine hydrochloride was heated at 215° for 25 minutes in a nitrogen atmosphere after which it was cooled and diluted with 20 ml. of water. The resulting solution was basified (*p*H 11) with sodium hydroxide, washed with ether, and then adjusted to *p*H 7 by adding hydrochloric acid. The precipitate that formed was dried and sublimed at 140–150° (0.01 mm.) yielding 0.33 g. (70%) of Δ^8-desoxymorphine, m.p. 258–260°. Crystallization from ethanol followed by sublimation gave material melting at 260–261° (reported[2] m.p. 254–255°); $[\alpha]^{25}_{\mathrm{D}}$ −15.3° (*c* 0.44, methanol).

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(11) L. F. Small and D. E. Morris, THIS JOURNAL, **55**, 2874 (1933).

(12) R. Pschorr and A. Rollett, *Ann.*, **373**, 1 (1910).

(13) D. E. Morris and L. F. Small, THIS JOURNAL, **56**, 2159 (1934).

(14) We are indebted to Dr. Homeyer of the Mallinckrodt Chemical Works, St. Louis, Mo., for generously supplying this material.

(15) A. H. Homeyer and W. L. Shilling, *J. Org. Chem.*, **12**, 356 (1947).

(16) H. E. Fierz-David and L. Blangey, "Fundamental Processes of Dye Chemistry," Interscience Publishers, Inc., New York, N. Y., 1949, p. 262.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.8; H, 7.1. Found: C, 75.8; H, 7.0.

The perchlorate was prepared with ethanolic perchloric acid and crystallized from ethanol, m.p. 261–262° (dec.); $[\alpha]^{25}D$ −23.5 (*c* 0.44, water).

Anal. Calcd. fror $C_{17}H_{20}ClNO_6$: C, 55.2; H, 5.4. Found: C, 55.3; H, 5.4.

Treatment with diazomethane converted Δ^8-desoxymorphine to Δ^8-desoxycodeine.

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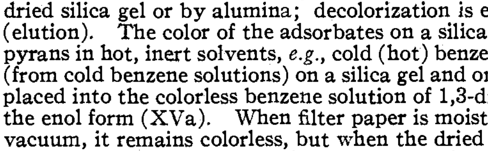
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, FOUAD I UNIVERSITY]

Some Adsorption Colors and their Significance for Thermochromic and Tautomeric Effects. II.[1] Experiments with Spiropyrans and with 1,3-Diketohydrindene

BY ALEXANDER SCHÖNBERG, AHMED MUSTAFA AND WAFIA ASKER

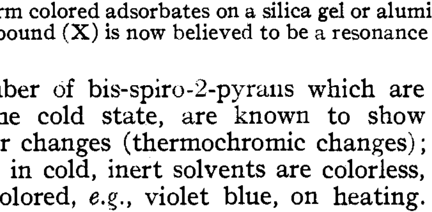
Some thermochromic spiropyrans are adsorbed from their colorless, cold, benzene solutions with the production of color by dried silica gel or by alumina; decolorization is effected by treating the colored surface active material with methyl alcohol (elution). The color of the adsorbates on a silica gel and alumina is similar to the color shown by the thermochromic spiropyrans in hot, inert solvents, *e.g.*, cold (hot) benzene solutions of (I) are colorless (violet); whereas the color of the adsorbate (from cold benzene solutions) on a silica gel and on alumina is blue. The results are presented in Table I. When alumina is placed into the colorless benzene solution of 1,3-diketohydrindene (XIV), a violet adsorbate is formed, believed to be due to the enol form (XVa). When filter paper is moistened with the colorless, benzene solution of (XIV) and allowed to dry in a vacuum, it remains colorless, but when the dried filter paper is exposed to water vapor, it turns violet (formation of XVa). A theory is advanced to explain the adsorption colors described in the above paragraphs. Free radicals (*e.g.*, XIIa and XIIIa) do not form colored adsorbates on a silica gel or alumina. The red dehydro-2-naphthol-1-sulfide previously regarded as the spiro compound (X) is now believed to be a resonance hybrid (compare XIa and XIb).

(a) A number of bis-spiro-2-pyrans which are colorless in the cold state, are known to show reversible color changes (thermochromic changes); their solutions in cold, inert solvents are colorless, but become colored, *e.g.*, violet blue, on heating. This phenomenon has been studied chiefly by Heilbron, Löwenbein and Dilthey[2] and their respective schools and they all agree that the color change is due to ionic dissociation with the formation of a heteropolar molecule (comp. I $\leftrightarrows$ II).[3] The observation of Schönberg, Mustafa and Asker,[4a] relative to the action of the Grignard reagent on such spiropyrans, are in good agreement with the supposed betaine structure (comp. II), as the observations of Dilthey and co-workers[4b] are.



I

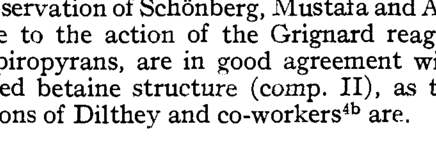
colorless solutions in the cold



II

violet-blue solutions on heating

It should, however be pointed out that the colored form has to be regarded as a resonance hybrid of many structures, *e.g.*, IIa.



IIa

Previously, it was thought that the colored forms might be regarded as free radicals, but this conception was rightly abandoned in view of the stability of the colored form toward oxygen[4]; also the thermostability of the colored forms is not in agreement with the free radical theory.

(b) We placed dried silica gel or alumina in cold, colorless, benzene solutions of some of the thermochromic bis-spiro-2-pyrans. From Table I, it is evident that the material acquired the same color, or a similar color, as shown by the thermochromic bis-spiro-2-pyrans in hot, inert solvents; coloration was effected instantaneously or within a few seconds, depending *inter alia*, on whether concentrated or diluted solutions were used; decolorization was effected by washing the colored, inorganic material with methyl alcohol.

These experiments are reminiscent of similar ones by E. Weitz and his school. According to Weitz and co-workers,[5] certain colorless compounds adsorbed on solid adsorbents are polarized by the strong, electric field present at the surface of the adsorbent to yield a colored compound, the color disappearing on elution. Thus the di- and triaminotriphenylmethanols (the colorless pseudobases of the corresponding Ph_3CH dyes) are adsorbed by silica gel and alumina, the color of the adsorbates corresponding to that of the dye salts (malachite green and crystal violet). The colorless compounds become colored as the result of polarization[6] on adsorption.

It is, however, possible that the adsorption color in the case of spiropyrans may be explained in a different way, namely, that there is an equilibrium between the colorless spiro form and the colored form not only in hot, but also in cold solutions. The colored form (its concentration in cold solutions is so small that the color cannot be detected) is adsorbed in preference. Thus, when the equilibrium in the solution is disturbed, the colored form

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[1] Schönberg and Asker, *Science*, **113**, 56 (1951), is to be regarded as Part I.

[2] See Mustafa, *Chem. Revs.*, **43**, 509 (1948).

[3] Dickinson and Heilbron, *J. Chem. Soc.*, 1699 (1927).

[4] (a) Schönberg, Mustafa and Asker, *ibid.*, 847 (1947); (b) Dilthey and Wizinger, *Ber.*, **59**, 1856 (1926).

[5] Weitz, *et al.*, *Z. Elektrochem.*, **46**, 222 (1940); **47**, 65 (1941); *Ber.*, **72**, 1740 (1939).

[6] Weitz and Schmidt, *ibid.*, **72**, 2099 (1939).