〔Added after submitting paper〕 This paper was read at the 82th Annual Meeting of Pharmaceutical Society of Japan (Shizuoka: Nov. 3, 1962. cf. the abstract of the 82th Annual Meeting of Pharmaceutical Society of Japan, p. 96~102).

After submission of this paper, the report of the nuclear magnetic resonance spectra of morphine type alkaloids (T. Rüll: Bull. Soc. chim. France, **1963** (3), 586.) was seen. In this report the spectra of eleven compounds, including I, V, IX, XI, XIV, XV, XVII, XIX, and XX, were measured and the C ring conformations of these compounds were discussed.

〔Chem. Pharm. Bull.
12 (1) 112 ~ 118〕

UDC 547.655.1.07

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Mannich Compounds of 2-Naphthol Derivatives.[1]

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The introduction by Mannich reactions[2] of alkylating grouping like bis-(2-chloroethyl)aminomethyl- or the aziridinomethyl group into estrone occurred exclusively in the 2-position of aromatic ring, even when a large excess of reagents over the theoretically necessary was used. Substitution in 4-position could be enforced only when the 2-position was blocked by a methyl group. The results confirmed observations made earlier by Patton[3] who found that estrone or estradiol would react in the Mannich reaction only to give 2-aminomethyl derivatives while from equilenine exclusively 4-substituted substances were obtained. Because of the formal similarity of these aromatic steroids with 5,6,7,8-tetrahydro-2-naphthol and 2-naphthol respectively a study of the Mannich reaction with these two substances and some of their derivatives were undertaken.

It is known from a paper by Shriner, *et, al.*[4] that 2-naphthol (I) itself reacts with formaldehyde and morpholine exclusively in the 1-position giving 1-(morpholinomethyl)-2-naphthol (II). When, however, 5,6,7,8-tetrahydro-2-naphthol (XVI) was submitted to the same reaction only 3-(morpholinomethyl)-5,6,7,8-tetrahydro-2-naphthol (XV) was isolated, in agreement with Cohen, *et al.*[5] who condenced XVI with formaldehyde and piperidine and obtained 3-(piperidinomethyl)-5,6,7,8-tetrahydro-2-naphthol. It was now found that it is possible to prepare the isomer (XI) of compound (II) by an indirect route. From 2-hydroxy-3-naphthoic acid (VI) the acid chloride was obtained with thionyl chloride and then reacted with morpholine. The carbonyl group in the morpholide thus prepared was easily reduced as in other amides[6] with lithium aluminum hydride to a methylene group and 3-(morpholinomethyl)-2-naphthol (XI) isomeric to the Mannich compound from 2-naphthol was obtained. A similar sequence of reactions carried out with 3-hydroxy-

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1) This work was supported by Grant No. 4550 of the U.S. Public Health Service, an Institutional Grant No. EIN-56 of the American Cancer Society and a Grant from the Massachusetts Division of the American Cancer Society.

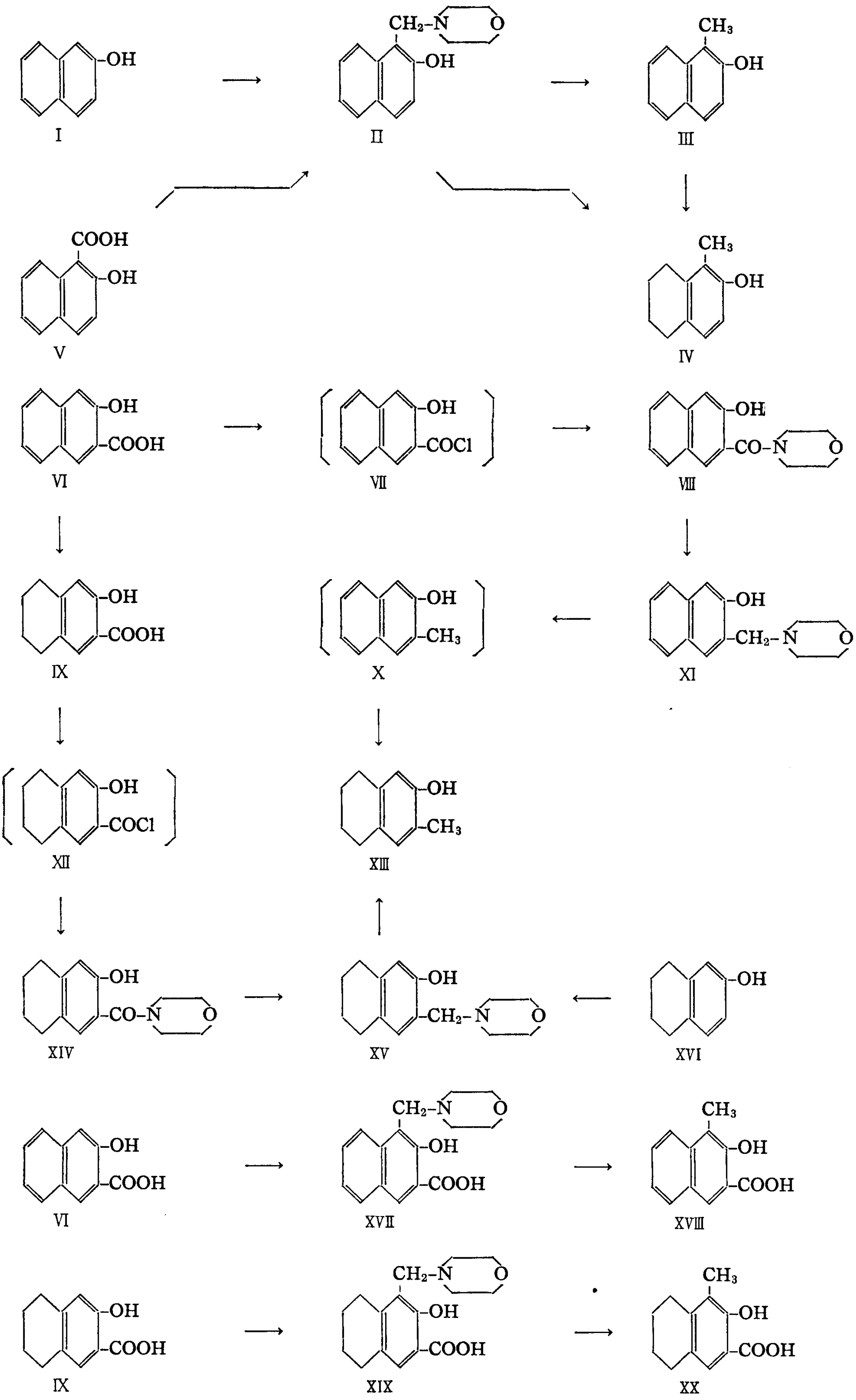
2) V.S. Gandhi, E. Schwenk: to be published.

3) T.L. Patton: Chem. & Ind. 923 (1959), J. Org. Chem., **25**, 2148 (1960).

4) R.L. Shriner, G.F. Grillot, W.O. Teeters: J. Am. Chem. Soc., **68**, 946 (1946).

5) A. Cohen, R.A. Hall, B. Heath-Brown, W.M. Parker, A.H. Rees: Brit. J. Phar. & Chemotherapy, **12**, 194 (1957).

6) N.G. Gaylord: "Reduction with Complex Metal Hydride" p. 566 (1956), Interscience Publishers, New York.


CH₂-N O
CH₃
-OH
COOH
-COOH
-COCl
-CO-N O
-CH₂-N O
-CH₃
I
II
III
IV
V
VI
VII
VIII
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X
XI
XII
XIII
XIV
XV
XVI
VI
XVII
XVIII
IX
XIX
XX

5,6,7,8-tetrahydro-2-naphthoic acid (IX) afforded 3-(morpholinomethyl)-5,6,7,8-tetrahydro-2-naphthol (XV), identical with the compound isolated, when 5,6,7,8-tetrahydronaphthol was submitted to Mannich reaction.

As far as can be seen from the literature,[7,8] Mannich reactions have not been carried out with phenolcaboxylic acids but treatment of either 3-hydroxy-2-naphthoic acid (VI) or 3-hydroxy-5,6,7,8-tetrahydro-2-naphthoic acid (IX) in a Mannich reaction with formaldehyde and morpholine resulted in reaction of the carbonyl groups and exclusive substitution in 4-position affording 3-hydroxy-4-(morpholinomethyl)-2-naphthoic acid (XVII) and 3-hydroxy-4-(morpholinomethyl)-5,6,7,8-tetrahydro-2-naphthoic acid (XIX), respectively. Both substances precipitated from the reaction mixture in excellent purity because of their insolubility. In the reaction with formaldehyde and morpholine, 2-hydroxy-1-naphthoic acd (V), however, lost the carboxyl group and substitution in its place gave the known 1-(morpholinomethyl)-2-naphthol (II). This reaction occurs even when the substances are left without heating at room temperature. It was not possible to split the carboxyl group out of VI or IX in the usual manner. These two substances (XVII, XIX) are also extremely alike in their properties and almost insoluble in most solvents. Only dimethylformamide allowed recrystallization and gave pure material. Alkali, bicarbonate and pyridine, as well as acids dissolve both compounds easily but dilution with water does not precipitate them. Even their melting points are identical, but a mixed melting points gives a depression of twenty degrees. Analysis and infrared spectra however leave no doubt their being different entities. Concentrated hydrochloric acid converts the two into hydrochlorides, which can be recrystallized from water, acetone or methanol and which are found to be identical by analysis, melting point and finallly by infrared spectra. They are evidently the hydrochloride or XVII, because both of them could be introduced into the free amine (XVII) by alkali. Dissolving in concentrated hydrochloric acid therefore must be connected with a dehydrogenation of the hydrogenated ring in XIX.

All these morpholinomethyl derivatives lose the morpholine residue when submitted to reduction. Patton[2] has shown that heating of such aminomethyl compounds in alcoholic solution with Raney nickel affords corresponding methyl derivatives and other methods for this hydrogenolysis are enumerated by Hellmann and Opitz.[8] They all employ quite severe reaction conditions. In the present work a method was used which was described by the senior author[9] years ago and which requries no heating, and moreover the reaction was completed in very short time. It consists in the reaction of Raney nickel alloy with the alkaline solution on the compounds under investigation. Accordingly the aminomethyl compounds prepared in this work were treated at room temperature and under cooling of their solution in 10% alkali with Raney nickel alloy. The corresponding methyl compounds were obtained. When however the reduction of the naphthalene derivatives was carried out under heating, hydrogenation occurred also at the non-substituted ring and tetralol derivatives can be isolated directly. The ease with which hydrogenolysis occurs under these conditions is remarkable.

In this manner II gave the known 1-methyl-2-naphthol (III), which was converted by further reduction under boiling into 1-methyl-5,6,7,8-tetrahydro-2-naphthol (IV). 3-Methyl-5,6,7,8-tetrahydro-2-naphthol (XIII) was prepared by two step reduction of XI, which could also be made directly from XV by cold reduction. Finally XVII gave at room temperature 3-hydroxy-4-methyl-2-naphthoic acid (XVIII), which is yellow as is VI, and XIX was reduced to the white 3-hydroxy-4-methyl-5,6,7,8-tetrahydro-2-naphthoic acid (XX).

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[7] B. Reichert : "Die Mannich-Reaktion" (1959) Springer, Berlin.

[8] H. Hellmann, G. Opitz : "α-Aminoalkierung" (1960) Verlag Chemie, G.m.b.H., Weinheim.

[9] D. Papa, E. Schwenk, H. Breiger : J. Org. Chem., **14**, 366 (1949).

The 1-(morpholinomethyl) compounds here described couple with diazotized 2-amino-4-aminoanisol to deep-red azo dyestuffs, just as the compounds with an unsubstituted 1-position. Evidently the morpholinomethyl residue is easily eliminated in this reaction, which is not the case when the substituent in 1-position is a methyl group. The ultraviolet spectra of the naphthalene derivatives in this work show a high peak in the 300 mμ region, while a peak is shifted to about 280 mμ in the case of the corresponding tetrahydro derivatives. In the caboxylic acid derivatives this peak is moved to 238~250 mμ. The infrared spectra of the morpholino derivatives present an indistinct phenolic OH band due to hydrogen bonding of the OH group with the N of morpholine residue. This disappearance of the phenolic absorption band in Mannich compounds has been emphasized by Patton[2] before. All these compounds display a band in the 1110 cm^{-1} region due to $-CH_2-O-CH_2-$ grouping in the morpholine residue and bands from 738~870 cm^{-1} to be ascribed to a tetra or penta substituted aromatic ring.

Experimental*4

1-(Morpholinomethyl)-2-naphthol (II)——a) From 2-naphthol: This substance was prepared from I according to Shriner, *et al.*[4] and was recrystallized from MeOH m.p. 122~123°(Lit. m.p. 115~116°). *Anal.* Calcd. for $C_{15}H_{17}NO_2$: C, 74.03; H, 7.04; N, 5.76. Found: C, 73.79; H, 6.92; N, 5.78.

b) From 2-hydroxy-1-naphthoic acid (V): 3 g. of this substance were dissolved in 9.2 ml. of 95% EtOH and a cold mixture of 2 ml. morpholine and 2 ml. of 38% CH_2O solution was added. A white precipitate formed about 10 min. after heating under reflux. Heating was continued for 50 min. and then the material was filtered and washed with H_2O.

The result was the same when the mixture of reactants was left to stand at room temperature for one half to one hour. After recrystallization from MeOH 1.86 g. of colorless plates was obtained, m.p. 119~121°.

1-Methyl-2-naphthol (III)——1 g. of II was dissolved in 10 ml. 10% KOH and 5 g. Raney Ni alloy was added to the heated and magnetically stirred solution in small portions, so that the solution was kept boiling. The alloy was added in the course of 1/2 hr. and heating continued for one more hr. The reaction mixture was filtered hot over a celite pad, care being taken that the pad remained wet all the time because the nickel residue in pyrogenic, and the residue was washed well with H_2O.

The filtrate was immediately acidified with HCl to congo blue acidity and the finely crystallized substance filtered hot, washed well with H_2O and dried over P_2O_5 in vacuum. Recrystallization from $CHCl_3$-hexane gave white needles, m.p. 105~111°. UV λ_{max} mμ (ε): 337 (3,700), 299 (3,700), 279 (3,600), 229 (67,700). IR: ν_{max} 805 cm^{-1} (1,2,3,4-arom. substit.). *Anal.* Calcd. for $C_{11}H_{10}O$: C, 83.51; (4,600), 268 H, 6.37. Found: C, 83.45; H, 6.51.

1-Methyl-5,6,7,8-tetrahydro-2-naphthol (IV)——When III was once more submitted to reduction as above, another product was obtained, which however is better prepared in the following way. 5 g. of II were dissolved in 500 ml. of 10% KOH, heated to boiling and under stirring reduced with 25 g. Raney Ni as outlined before. The hot solution was filtered from the Ni residue, acidified and the white crystalline precipitate was filtered. It was immediately dissolved in 500 ml. of 10% KOH, boiled and once more reduced with 25 g. Raney Ni alloy as above. The filtered reaction mixture was acidified with HCl to congo acidity, filtered hot and the white crystalline material was washed with H_2O. After drying in vacuum over P_2O_5 an yield of 1.9 g. was obtained. Recrystallized from Me_2CO and H_2O, m.p. 117~118°. UV: λ_{max} 282 mμ (ε 3,000). IR ν_{max} cm^{-1}: 3327 (-OH), 804 (1,2,3,4-arom. substit.). *Anal.* Calcd. for $C_{11}H_{14}O$: C, 81.41; H, 8.70. Found: C, 81.08; H, 8.91.

3-Hydroxy-2-naphthoic Acid Morpholide (VIII)——To a suspension of 5 g. 3-hydroxy-2-naphthoic acid (VI) in 50 ml. benzene in a round bottom flask with reflux condenser and $CaCl_2$ tube were added 10 ml. thionyl chloride and the mixture was heated on a steam bath to complete solution. Gas started to evolve immediately and after about 1 hr. the flask was left overnight at room temperature. The excess thionyl chloride was distilled off in vacuum and the volume was reduced to about on ethird. In the cold room the chloride of the acid crystallized and could be filtered and washed with petr. ether. It was dissolved in 25 ml. pyridine and 5 ml. morpholine was added while the flask was cooled with H_2O from the outside. Pyridine hydrochloride crystallized and several hours later the mixture was poured on ice and HCl. The precipitate was collected on a filter, washed well with H_2O and dried in vacuum over P_2O_5. The dried morpholide was recrystallized from Me_2CO or from benzene-pentane; m.p.

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*4 Melting points were taken on a Fisher stage or Hershberg apparatus and are not corrected. The UV spectra were determined in $CHCl_3$ solution, while for IR spectra KBr plachets were used.

222~224°. UV λ_{max} mμ (ε) : 288 (2,000), 277 (3,900), 227 (68,500). IR ν_{max} cm^{-1} : 3069 (-OH), 879 (1,2,4,5-arom. substit.). *Anal.* Calcd. for $C_{15}H_{15}NO_3$: C, 70.05; H, 5.88; N, 5.45. Found : C, 69.42; H, 5.64; N, 5.08.

3-(Morpholinomethyl)-2-naphthol (XI)——In a three necked flask equipped with a stirrer 1.2 g. of lithium aluminum hydride was placed and 50 ml. of anhyd. Et_2O was added. The amide (VIII) (0.8 g.) was dissolved in anhyd. tetrahydrofuran (95 ml.) at room temperature and added drop by drop with stirring at room temperature to Et_2O solution. After complete addition the mixture was stirred and refluxed for approximately 22 hr. It was then cooled in an ice bath and dropwise 35 ml. of Me_2CO was added followed by 25 ml. of H_2O. Precipitated alumina was filtered under suction through filter aid and the pad was washed thoroughly with methylene chloride (approx. 150 ml.). The filtrate and methylene chloride washings were transferred to a separatory funnel and the upper layer was separated. The organic extract was dried over anhyd. Na_2SO_4. Removal of the solvent gave a gummy residue which crystallized in form of needles. After recrystallization from EtOH and a charcoal treatment, the substance was obtained in form of colorless plates. Yield, 0.67 g., m.p. 108~109°. UV λ_{max} mμ (ε) : 335 (3,500), 289 (2,900), 278 (4,500), 267 (4,100), 228 (120,000). IR : ν_{max} 879 cm^{-1} (1,2,4,5-arom. substit.). *Anal.* Calcd. for $C_{15}H_{17}NO_2$: C, 74.00; H, 7.04; N, 5.75. Found : C, 73.47; H, 7.06; N, 5.73. The known isomer of this compound, 1-(morpholinomethyl)-2-naphthol (II) described above gave with the new isomer a melting point depression of 30°.

3-Hydroxy-5,6,7,8-tetrahydro-2-naphthoic Acid (IX)——This substance was made by reducing 3-hydroxy-2-naphthoic acid (VI) with Raney Ni alloy in the presence of alkali,[9] m.p. 179~180°. *Anal.* Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found : C, 68.90; H, 6.08.

3-Hydroxy-5,6,7,8-tetrahydro-2-naphthoic Acid Morpholide (XIV)——This substance was prepared from IX in the same manner as described for the corresponding naphthalene derivatives. After drying in vacuum over P_2O_5 the substance was recrystallized several times from benzene-hexane and showed m.p. 195° after softening at 186°. UV : λ_{max} 295 mμ (ε 3,500). IR : ν_{max} 866 cm^{-1} (1,2,4,5-arom. substit.). *Anal.* Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.32; N, 5.35. Found : C, 68.81; H, 7.21; N, 5.27.

3-(Morpholinomethyl)-5,6,7,8-tetrahydro-2-naphthol (XV)——600 mg. of the morpholide (XIV) was reduced using 1.0 g. of $LiAlH_4$ in 50 ml. of Et_2O, and 80 ml. of tetrahydrofuran according to the method described above in the experiment with the corresponding naphthalene derivative. Removal of the solvent gave a gummy residue which crystallized from Et_2O-pentane in the form of flat needles. Recrystallized from aq. EtOH (50%) as fine needles, 450 mg., m.p. 88~90°. UV : λ_{max} 285 mμ (ε 3,220). IR : ν_{max} 865 cm^{-1} (1,2,4,5-arom. substit.). *Anal.* Calcd. for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.55; N, 5.66. Found : C, 73.00; H, 8.79; N, 5.51.

3-(Morpholinomethyl)-5,6,7,8-tetrahydro-2-naphthol (XV) by Mannich Reaction from tetralol (XVI)——The reaction was carried out using 2.22 g. of tetralol (XVI) in EtOH (9.0 ml.). Morpholine (20 ml.) and 20 ml. of 38% CH_2O solution were mixed separately, cooled, added to the tetralol solution and refluxed for 4 hr. The reaction mixture was left overnight in the cold room and was then completely crystallized. The crystals were filtered and washed with ice cold EtOH with increasing H_2O additions and finally with H_2O. After drying in vacuum over P_2O_5 the yield was 1.7 g. Recrystallization from EtOH and H_2O gave pure substance, m.p. 88~90°, identical with the substance obtained in the foregoing experiment.

3-Methyl-5,6,7,8-tetrahydro-2-naphthol (XIII)——a) From XV : To a solution of 500 mg. of XV dissolved in 50 ml. of 10% KOH and heated to boiling, 5 g. of Raney Ni were added in small portions during about 1 hr. Heating was continued for 1 hr. more and then filtered hot over a pad of celite, care being taken by washing with H_2O that the Ni residue did not become dry. The hot filtrate was acidified to blue congo reaction with HCl, the crystalline precipitate was filtrated immediately and was washed with H_2O. It was dried over P_2O_5 in vacuum and then weighed 50 mg. After recrystallization from MeOH and H_2O white needles were obtained, m.p. 91~93°. UV : λ_{max} 283 mμ (ε 3,000). IR ν_{max} cm^{-1}: 3360 (-OH), 870 (1,2,4,5-arom. substit.). *Anal.* Calcd. for $C_{11}H_{10}O$: C, 81.41; H, 8.70. Found : C, 81.08; H, 8.91.

b) From XI : 200 mg. of XI were dissolved in 10 ml. of 10% KOH and 1 g. of Raney Ni alloy was added under stirring in small portions in the course of one half hour. Heating was avoided by outside cooling with H_2O and stirring was continued for another half hour at room temperature. Filtration and acidification with HCl to congo-blue acidity a white precipitate, which was filtered, washed with H_2O and recrystallized from aq. MeOH to give colorless needles, m.p. 149~155°, which seems to be crude 3-methyl-2-naphthol (X). 30 mg. of the crude material were dissolved in 3.0 ml. of 10% KOH and 150 mg. of Raney Ni were added to the boiling solution in small portions over a period of half an hour. Stirring was continued for another half hour. The reaction mixture was then filtered and the filtrate acidified with HCl to blue congo reaction. The precipitate was filtered, washed with H_2O and recrystallized from aq. MeOH to give XIII as colorless plates, m.p. 90~92°, which were identical with the substance obtained above in all respects.

3-Hydroxy-4-(morpholinomethyl)-2-naphthoic Acid (XVII)——1.3 g. of 3-hydroxy-2-naphthoic acid (VI) was dissolved in 4 ml. of 95% EtOH and a separately prepared cold mixture of 0.9 ml. of morpholine and 0.9 ml. of CH_2O solution (38%) was added. The solution was heated to reflux and soon separation of crystals began. It is good to stir the reaction mixture because it lumps considerably. After half an hour of boiling the precipitate was filtered hot and washed well with 95% EtOH. It was dried over P_2O_5 in vacuum and the yellowish crystal powder which then weighed 1.9 g. was pure enough for analysis. The substance was soluble in dilute AcOH or HCl, alkali or bicarbonate and in pyridine but could not be recrystallized from the usual solvent, m.p. 238~240°. UV λ_{max} mμ (ε) : 238 (51,800), 276 (5,400), 287 (5,700). IR ν_{max} cm^{-1} : 3428 (-OH), 1652 (C=O). *Anal.* Calcd. for $C_{16}H_{17}NO_4$: C, 66.86; H, 5.97; N, 4.88. Found : C, 66.14; H, 6.07; N, 5.10.

3-Hydroxy-4-methyl-2-naphthoic Acid (XVIII)——400 mg. of XVII were dissolved in 40 ml. of 10% KOH and 4.0 g. of Raney Ni alloy added in small portions with continuous stirring. Warming was avoided by immersion in a cold water bath. The addition of the alloy was finished after half an hour and the reaction mixture was left with occasional shaking for another half hour to complete the reduction. It was filtered over a celite pad and care was taken that the Ni residue did not become dry. The fiiltrate was acidified to congoblue reaction with HCl and a yellowish crystalline material separated which filtered and recrystallized from MeOH and H_2O, yield 230 mg. Even after several recrystallizations the substance remained yellow, m.p. 245~246°. UV λ_{max} mμ (ε) : 299 (2,100), 285 (4,100), 276 (8,700), 239 (44,500). IR ν_{max} cm^{-1} : 3308 (-OH), 1665 (C=O), 738 (1,2,3,4-arom. sustit.). *Anal.* Calcd. for $C_{12}H_{10}O_3$: C, 71.31; H, 4.98. Found : C, 71.15; H, 4.90.

3-Hydroxy-4-(morpholinomethyl)-5,6,7,8-tetrahydro-2-naphthoic Acid (XIX)——2.3 g. of 3-hydroxy-5,6,7,8-tetrahydro-2-naphthoic acid (IX) were dissolved in 7 ml. of 95% EtOH and a cold mixture of 1.6 ml. morpholine and 1.6 g. of 38% CH_2O solution was added. The mixture was heated under reflux and soom crystalline material came out. Heating was continued for 1 hr. Filtered after standing overnight in the cold room and washed well with EtOH and H_2O. After drying overnight over P_2O_5 in vacuum the yield was 1.5 g. of a yellowish crystalline powder. It could only be recrystallized from dimethylformamide with H_2O. The substance was soluble in alkali, bicarbonate and pyridine as well as in AcOH or HCl and from these solutions was not precipitated with H_2O, m.p. 238~240°. Mixed melting point with VI gave a depression to 219~220°. UV : λ_{max} (ε) 238 mμ (14,700). IR ν_{max} cm^{-1}: 3445 (-OH), 1640 (C=O). *Anal.* Calcd. for $C_{16}H_{21}NO_4$: C, 65.94; H, 7.27; N, 4.80. Found : C, 65.18; H, 7.10; N, 5.01.

Hydrochloride of XVII——a) From XVII : When 10 ml. of conc. HCl were added to 1.7 g. of XVII a colorless solution resulted first but suddenly crystallization started. After filtration and washing with little ice H_2O the substance could be recrystallized from H_2O but a small amount of HCl was necessary to avoid hydrolysis. Recrystallization from MeOH or Me_2CO gave white needles, yield 1.25 g., m.p. 187~189°. An analytical sample was dried in vacuum over P_2O_5 but this hydrochloride could not obtained free of H_2O. *Anal.* Calcd. for $C_{16}H_{17}NO_4 \cdot HCl \cdot H_2O$: C, 56.21: H, 5.90; N, 4.10; Cl, 10.38. Found : C, 55.66; H, 5.78; N, 4.20; Cl, 10.38.

b) From XIX : When 1.5 g. of XIX was treated with concentrated HCl as described above, the hydrochloride, m.p. 187~189° was obtained. Yield 1.3 g. This hydrochloride was identical with that from XVII in their IR spectra.

An theoretical amount of $KHCO_3$ was added to a solution of the hydrochloride from XIX in H_2O at room temperature and the resulting precipitate was collected by filtration, washed well with H_2O and dried. IR spectra of this material showed that indeed it was XVII not XIX. XVII was also obtained from the hydrochloride from XVII by the same treatment.

3-Hydroxy-4-methyl-5,6,7,8-tetrahydro-2-naphthoic Acid (XX)——750 mg. of XIX were dissolved in 30 ml. of 10% KOH and heated to boiling. 3 g. of Raney Ni alloy were added in small portions while the reaction mixture was magnetically stirred. When after half an hour all of the alloy had been added, heating was continued for 1 hr. and H_2O which had boiled off was replaced. The reaction mixture was filtered hot over a celite pad and the filtrate acidified with conc. HCl to congo reaction. The white precipitate was filtered hot and washed with H_2O. Yield 350 mg. Recrystallized from MeOH or Me_2CO and H_2O. The same substance was obtained when XVII was reduced in hot alkaline solution with Raney Ni alloy, m.p. 237~238°. UV : λ_{max} 250 mμ (ε 10,100). IR ν_{max} cm^{-1} : 3223 (-OH), 1661 (C=O). *Anal.* Calcd. for $C_{12}H_{14}O_3$: C, 69.91; H, 6.84. Found : C, 69.71; H, 6.78.

The authors are especially grateful to Mrs. Erszebet Joachim for assistance with the chemical work and the ultraviolet spectra. They wish to thank also Dr. N. McNiven and Mr. D.F. Horgan for the infrared spectra.

Summary

The Mannich reactions of some 2-naphthol and its tetrahydro compounds were studied. The Mannich reaction of 2-naphthol (I) by morpholine gave 1-(morpholinomethyl) compound (II), which was also obtained by same reaction of 2-hydroxy-1-naphthoic acid (V). On the other hand, the Mannich reaction of 2-tetralol (XVI) gave 3-(morpholinomethyl) derivative (XV). 2-Hydroxy-3-naphthoic acid (VI) and its tetrahydro compound (IX) were introduced into 1-(morpholinomethyl) derivatives, XVII and XIX, respectively. Some transformations of these Mannich compounds were also studied.

(Received September 27, 1963)