The reaction mixture was filtered and the filter cake was washed with 20 ml. of acetone. The combined filtrate and washings were poured into 400 ml. of cold 10% aqueous sodium carbonate. The resulting basic mixture was extracted with 300 ml. of methylene chloride. The methylene chloride layer was evaporated to dryness *in vacuo* to give a sirupy mixture of mono- and diacetone derivatives (XI and XII). The crude mixture was partitioned in the solvent system hexane-methanol-water (7:7:2) (336 ml.) to give 5.8 g. (32%) of crude monoacetone derivative (XI) in the methanol-water layer and 5.4 g. (32%) of crude diacetone derivative (XII) in the hexane layer which was satisfactory for the Friedel-Crafts cyclization.

Trituration of the crude monoacetone derivative (XI) with cold hexane caused the sirup to crystallize. Recrystallization from 50 ml. of hexane and 3 ml. of absolute ethanol gave 2.85 g. of a white crystalline material, m.p. 101–102°, the infrared spectrum of which was essentially identical with that of the analytical sample. No effort was made to obtain a second crop.

The analytical sample, prepared from a similar run, melted at 103–104° after two recrystallizations from Skellysolve B[6]–ethanol and had $\lambda_{max(\mu)}^{KBr}$ 2.94 (NH, OH), 7.24 (CH_3), 9.50 (C—O—C), 12.34 (1,3,4-trisubstituted benzene).

Anal. Calcd. for $C_{16}H_{25}NO_4$: C, 65.1; H, 8.53; N, 4.74. Found: C, 65.0; H, 8.72; N, 4.39.

To 0.2 g. (0.61 mmole) of crystalline *N*-(3,4-*O*-isopropylidene-1-D-ribityl)-3,4-xylidine (XI) was added a solution of 1 ml. of pyridine and 1 ml. of acetic anhydride. The solution was allowed to stand for 2 days protected from moisture and then was poured into 100 ml. of ice water. The oil which separated was extracted with 50 ml. of methylene chloride. The extract was washed with 50 ml. of 5% sodium bicarbonate solution and 50 ml. of water, and dried over magnesium sulfate. The solulion was concentrated *in vacuo;* yield, 0.35 g. of *N,O,O*-triacetyl derivative of XI as a tan, viscous oil which did not crystallize; $\lambda_{max(\mu)}^{film}$ 5.74 (acetate C=O), 6.01 (amide C=O), 8.15 and 9.35 (acetate C—O—C). The relative intensities of the amide and acetate carbonyl absorption were almost equal.

A small portion of the crude diacetone derivative (XII) was acetylated in the manner described above for the monoacetone derivative (XI). The infrared spectrum of the *O*-diacetate showed an *O*-acetate/*N*-acetate intensity ratio of 1:17 in the C=O region, indicating less than 5% contamination by the monoacetone derivative.

An analytical sample of the diacetone derivative (XII) was obtained by distillation of the crude material after one partition treatment, b.p. 135–140° (0.025 mm.); $\lambda_{max(\mu)}^{film}$ 2.96 (NH), 7.31 (CH_3), 9.31 (C—O—C).

Anal. Calcd. for $C_{19}H_{29}NO_4$: C, 68.0; H, 8.71; N, 4.18. Found: C, 67.9; H, 8.83; N, 4.64.

A small portion of the distilled product was acetylated, using acetic anhydride and pyridine. The infrared spectrum showed only a trace amount of *O*-acetate compared to *N*-acetate.

3,4-Dihydro-4,4,6,7-tetramethyl-1-(1-D-ribityl)carbostyril (VI). To a stirred solution of 5.3 g. (1.6 mmoles) of *N*-(2,3:4,5-di-*O*-isopropylidene-1-D-ribityl)-3,4-xylidine (XII) in 13 ml. of dry pyridine was added dropwise 2.3 g. (1.9 mmoles) of 3-methylcrotonyl chloride with ice cooling. The addition time was 5 min. A precipitate formed and the resulting mixture was stirred with ice cooling for 2 hr. and then stirred at 30° for 18 hr. protected from moisture. The volatile materials were removed *in vacuo* and the residue dissolved in 50 ml. of methylene chloride. The methylene chloride solution was washed with 50 ml. of saturated sodium bicarbonate solution and concentrated *in vacuo*. The residue was dissolved in a small amount of toluene and then concentrated *in vacuo*. This procedure was repeated several times. The last traces of solvents were removed *in vacuo* at 60° at 0.1 mm. to yield 7.0 g. (theory 6.7 g.) of crude *N*-(2,3:4,5-di-*O*-isopropylidene-1-D-ribityl)-3-methyl-3′,4′-crotonoxylidide (IX); $\lambda_{max(\mu)}^{film}$ 6.05 (amide C=O), 6.13 (shoulder, >C=C<), 7.30 (CH_3), 9.37 (C-O—C), no ester C=O in the 5.8 region.

The crude IX (7.0 g., 1.6 mmoles) was dissolved in 80 ml. of Skellysolve C[6] and treated with 8.0 g. (0.060 mole) of powdered, anhydrous aluminum chloride. The mixture was stirred under reflux on the steam bath for 2 hr. The resulting mixture was decomposed with ice and the Skellysolve C decanted from the gummy residue. The residue was suspended in 125 ml. of chloroform and heated to boiling with 100 ml. of 6*N* hydrochloric acid. The mixture was cooled, shaken vigorously, and the chloroform layer separated. The aqueous layer was extracted with 25 ml. of chloroform. The combined chloroform solutions were washed with 3*N* hydrochloric acid, dried over magnesium sulfate, and concentrated *in vacuo;* weight 6.5 g. The infrared spectrum of this material showed that not all of the isopropylidene groups had been removed. The residue was dissolved in 150 ml. of methanol, treated with 6 ml. of 6*N* hydrochloric acid; the solution was heated under reflux on the steam bath for 1 hr. and then concentrated *in vacuo*. The residue (5.72 g.) was dissolved in 110 ml. of hot 50% aqueous ethanol, treated with Norit, filtered, and chilled. The crystals were collected and dried *in vacuo;* yield 0.35 g., m.p. 69–71°. The filtrate was concentrated and a second crop of 0.75 g., m.p. 60–70°, was obtained; total yield 1.10 g. (20.4%). Recrystallization of the first crop from aqueous alcohol with use of Norit gave white crystals that softened at 85°, partially melted at about 100°, then melted at 115–200°; $\lambda_{max(\mu)}^{KBr}$ 2.95 (OH), 6.05 (lactam C=O), 8.92, 9.59 (C—O—), 11.37 (1,2,4,5-tetrasubstituted benzene), no C=C at 6.13.

Anal. Calcd. for $C_{18}H_{27}NO_5$: C, 64.1; H, 8.07; N, 4.15. Found: C, 64.5; H, 8.16; N, 4.01.

The filtrate from the second crop was concentrated to obtain a third crop; however, only an oil separated. The infrared spectrum of this oil was similar to that of the product.

Paper Chromatography	R_f in Solvent System A	R_f in Solvent System B
Analytical sample	0.87	0.00
Second crop	0.86	0.00
Oil	0.88	0.58
		0.71
Mother liquor	0.00	0.00
	0.85	

The oil contained little or no product. The mother liquor may have had additional product.

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Action of Hydroxylamine, Hydrazine Hydrate, and Phenylhydrazine on 2-Acetoaceto-1-naphthol

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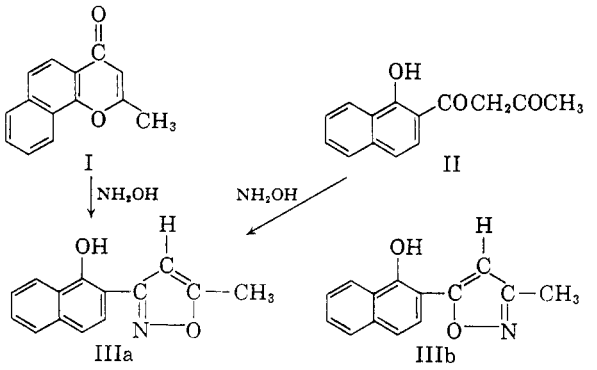
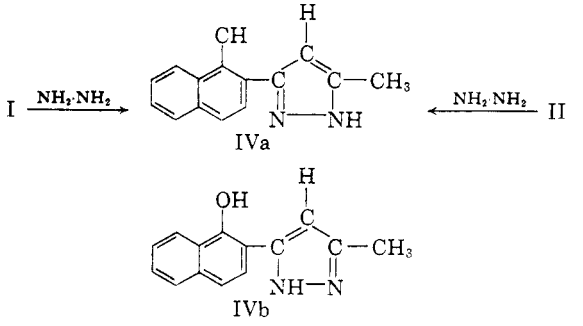
Recently Schönberg, Fateen, and Sammour[1] have reported the reaction of I with hydroxylamine

hydrochloride, hydrazine hydrate, and phenylhydrazine hydrochloride. They have shown that I reacts with hydroxylamine hydrochloride in boiling pyridine to give an isoxazole derivative IIIa or IIIb.

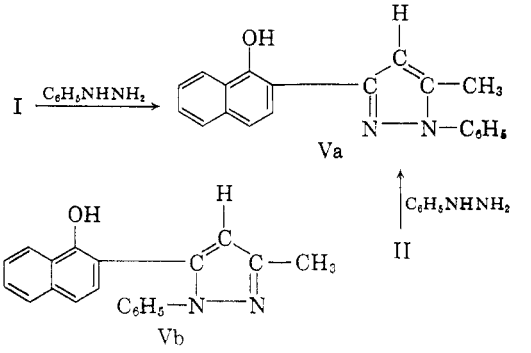
The author has found that 2-acetoaceto-1-naphthol (II) reacts with hydroxylamine hydrochloride in boiling ethyl alcohol leading to the same 2-[5(or 3)-methyl-3(or 5)-isoxazolyl]-1-naphthol (IIIa or IIIb). An alcoholic solution of the product gives a violet color with alcoholic ferric chloride solution. It yields a monobenzoyl derivative. IIIa or IIIb was recovered unchanged when boiled with 10% sodium hydroxide for one hour, followed by acidification with dilute hydrochloric acid. The stability towards alkali was to be expected as, according to Claisen,[2] 3,5-disubstituted isoxazoles are very resistant to alkaline degradation.



The action of hydrazine hydrate on 2-acetoaceto-1-naphthol (II) in alcohol leads to 2-[5(or 3)-methyl-3(or 5)-pyrazolyl]-1-naphthol (IVa or IVb). It is identical with that obtained when hydrazine hydrate is allowed to react with I. The product gives a green color with alcoholic ferric chloride and yields a dibenzoyl derivative.



The reaction of I with phenylhydrazine hydrochloride in pyridine gives a compound Va or Vb which was regarded as a pyrazole derivative. 2-[1-Phenyl-5(or 3)-methyl-3(or 5)-pyrazolyl]-1-naphthol (Va or Vb) was also obtained from the action of phenylhydrazine with 2-acetoaceto-1-naphthol (II) in alcohol. It gives a violet color with alcoholic ferric chloride solution.



EXPERIMENTAL

2-[5(or 3)-Methyl-3(or 5)-isoxazolyl]-1-naphthol (IIIa or IIIb). A mixture of 4 g. of hydroxylamine hydrochloride and 5 g. of 2-acetoaceto-1-naphthol[3] in 50 ml. of ethyl alcohol was refluxed for 4 hr., cooled, and diluted with water. The deposit formed (4.3 g., 85%) was filtered; on crystallization from benzene, it yielded yellowish crystals which were proved by melting point and mixture melting point (181°) and the violet color with alcoholic ferric chloride to be 2-[5(or 3)-methyl-3(or 5)-isoxazolyl]-1-naphthol (IIIa or IIIb). Its monobenzoyl derivative crystallized as colorless crystals from dilute ethyl alcohol (m.p. and mixture m.p. 126°).

2-[5(or 3)-Methyl-3(or 5)-pyrazolyl]-1-naphthol (IVa or IVb). 2-Acetoaceto-1-naphthol (3 g.), hydrazine hydrate (3 ml.), and ethyl alcohol (30 ml.) were heated under reflux for 20 min. and cooled, water was added, and the solid collected, washed, dried (3 g. 97%), and crystallized from benzene as colorless leaflets. The product was proved to be 2-[5(or 3)-methyl-3(or 5)-pyrazolyl]-1-naphthol (IVa or IVb) by melting point and mixture melting point (171°), the deep green color with alcoholic ferric chloride solution and lack of color with concd. sulfuric acid. The dibenzoyl derivative was prepared (Schotten-Baumann method) and crystallized from dilute alcohol as colorless crystals, (m.p. and mixture m.p. 144–145°). It dissolved in concd. sulfuric acid yielding a yellow solution.

2-[-Phenyl-5(or 3)-methyl-3(or 5)-pyrazolyl]-1-naphthol (Va or Vb). 2-Acetoaceto-1-naphthol (2 g.), phenylhydrazine (1 ml.) and ethyl alcohol (20 ml.) were heated under reflux for 2.5 hr., the solution concentrated to half its volume, and water added. The precipitate (1.8 g., 72%) was crystallized from petroleum ether (b.p. 100–120°) giving almost colorless crystals which were proved to be 2-[1-phenyl-5(or 3)-methyl-3(or 5)-pyrazolyl]-1-naphthol (Va or Vb) by melting point and mixture melting point (143°). Its alcoholic solution gives a violet color with alcoholic ferric chloride solution.

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