Anal. Calcd. for $C_8H_{16}S_3$: C, 46.11, H, 7.74, S, 45.15, M_D 60.94. Found: C, 46.18, H, 7.67, S, 45.96, M_D 60.47.

Identification of 2-n-butylmercaptodithiane-1,4 (VII). A mixture of VII (58 g., 0.28 mole) and *p*-toluenesulfonic acid (1 g.) was heated slowly, with stirring, in a flask fitted with a distillation column. Temperature and pressure were regulated to remove from the distillation flask any material with boiling point lower than the starting material. Decomposition began at 170° and heating was continued for 1 hr., with a maximum pot temperature of 205°. A small amount of VII was distilled to sweep lower boiling materials from the reaction flask. The distillate and trapped (−70°) products were diluted with ethyl ether and were washed quickly with 10% sodium hydroxide.

Distillation of the organic layer gave VIII (11 g., 0.08 mole, 30% yield), identical with authentic VIII obtained by reaction of V with chlorodimethylacetal.[3]

A sample (1.8 g.) of VIII, obtained by acid-catalyzed decomposition of VII, was oxidized with peracetic acid at 0–5° to give 1,4-dithiene tetroxide (IX, 2.5 g.). IX was insoluble in organic solvents. A portion (0.5 g.) was recrystallized from concentrated nitric acid to give a white powder (0.3 g.), m.p. >280°.

Anal. Calcd. for $C_4H_6S_2O_4$: C, 26.36, H, 3.32, S, 35.19. Found: C, 26.36, H, 3.47, S, 34.97.

The sulfone (IX, 0.5 g.), was refluxed with zinc dust in acetic acid for 1 hr. to produce 1,4-dithiane tetroxide (X, 0.3 g.), which was washed with ethanol and dried, m.p. >280°.

Anal. Calcd. for $C_4H_8S_2O_4$: C, 26.08, H, 4.38, S, 34.81. Found: C, 26.01, H, 4.32, S, 34.77.

Infrared spectra of IX and X were identical with those of samples prepared in a similar way from authentic[3] VIII.

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The Nature of the Alkyl Groups in Nidulin

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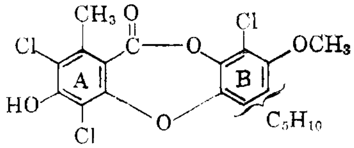
In 1954, Dean, Roberts, and Robertson, after extensive chemical investigation, proposed structure (I) for nidulin, the principal metabolic product of the mold *Aspergillus nidulans*.[1]



I

The 60-Mc NMR spectra of nidulin, *O*-methylisonidulin, and the product of the successful hydrogenation of nidulin, dihydronidulin,[2] are reproduced in Fig. 1.

The secondary splittings of the vinyl methyl doublet-of-quartets signal (at 278 c.p.s. in nidulin and 304 c.p.s. in *O*-methylisonidulin) were found to be 1.11 ± .04 c.p.s. for nidulin and 1.52 ± .05 c.p.s. for *O*-methylisonidulin. The major splittings of these signals were essentially identical: 6.76 ± .08 c.p.s. for *O*-methylisonidulin and 6.77 ± .08 c.p.s. for nidulin. These results may be seen qualitatively in a slow sweep of the vinyl region of each spectrum in Fig. 1.

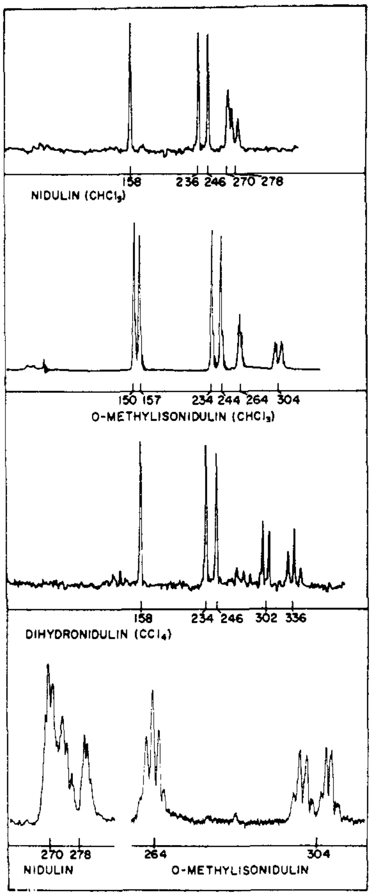


Figure 1

As a consequence of the detailed analysis of the NMR spectra of nidulin, *O*-methylisonidulin, and dihydronidulin, the nature of the five remaining carbons can be determined.

The appearance of two unsplit methyl peaks in the aromatic methyl (*ca.* 250 c.p.s.) region of the spectra of each of these compounds can have but one interpretation: that in nidulin there are two aromatic methyl groups. The previous authors have demonstrated the existence of one such methyl group attached to the A-ring.[1] Since it is known to be the only methyl group on the A-ring, the other aromatic methyl group must be attached to the B-ring. Hence, the previously undetermined five-carbon residue consists of a methyl group and a C_4H_7 fragment.

The presence of a double bond in the C_4H_7 fragment is substantiated by a quartet-of-quartets signal, proportional to a single proton in area, in the vinyl hydrogen portion of the spectrum. Although the fine structure of this signal can be observed only on slow, high-gain sweeps, its position

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[1] F. M. Dean, J. C. Roberts, and A. Robertson, *J. Chem. Soc.*, **1954**, 1432–9.

[2] D. S. Noyce, personal communication.

can be seen in Fig. 1 below the chloroform spinning sideband in the O-methylisonidulin spectrum. Also, in agreement with the presence of an olefin are the two three-proton signals in the vinyl methyl regions of the spectra of nidulin (270 and 278 c.p.s.) and O-methylisonidulin (264 and 304 c.p.s.). From the information given thus far, it is easily deduced that the C_4H_7 group is a 2-but-2-enyl group and that the sole difference between nidulin and O-methylisonidulin, aside from the methylated hydroxyl group of the A-ring, is that of a *cis-trans* isomerization about the double bond of the 2-but-2-enyl group.

Recent work with substituted 2-butenes,[3-5] which is summarized in Table I, has indicated the generality that spin-spin coupling constants linking vinyl methyl groups across double bonds are greater in magnitude when the methyls are *trans* to one another than when they are *cis* disposed. Measurements were made of the secondary splittings of the vinyl methyl doublet-of-quartets in the spectra of nidulin and O-methylisonidulin. Such splittings should represent solely the interactions between the vinyl methyl groups across the double bond. Since nidulin was found to possess a splitting constant of 1.11 ± .04 c.p.s. and O-methylisonidulin a splitting constant of 1.52 ± .05 c.p.s., the 2-but-2-enyl group in nidulin is assigned the *cis*-configuration (II).

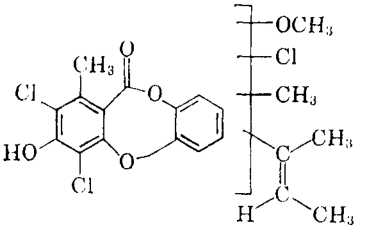
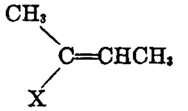


TABLE I

METHYL-TO-METHYL SPLITTING CONSTANTS IN 2-SUBSTITUTED 2-BUTENES



$$\underset{X}{\overset{CH_3}{C}}{=}CHCH_3$$

X	Relative position of the methyls (c.p.s.) *cis*	*trans*	Ref.
—Br	1.12 ± .04	1.59 ± .03	3
—COOH	1.17 ± .06	1.46 ± .06	4
—$COOCH_3$	1.20 ± .04	1.51 ± .05	4
—C_6H_5	1.00 ± .03	1.51 ± .04	5
-p-C_6H_4—OCH_3	0.97 ± .05	1.39 ± .06	5

EXPERIMENTAL

Isolation and purification of nidulin. A stock culture of *Apergillus nidulans* (NRRL, No. 2006) was obtained from the Agricultural Research Service of the U. S. Department of Agriculture, 1815 N. University Street, Peoria 5, Ill. This fungus was grown for the production of nidulin according to the method of Dean, Roberts, and Robertson.[1] Their methods were also applied in a general way to the isolation and purification of nidulin. The nidulin so obtained had m.p. 180–181° (lit.[1] m.p. 180°) and an ultraviolet absorption band at 268 mμ (log ε 3.95) in acidified ethanol. In basic ethanol, the absorption maximum was shifted to 323 mμ (log ε 4.27).

Anal. Calcd. for $C_{20}H_{17}O_5Cl_3$: C, 54.13; H, 3.86; Cl, 23.97. Found: C, 54.22; H, 3.77;Cl, 23.91.

O-Methylnidulin. This substance was prepared according to either procedure of Dean, Roberts, and Robertson[1]; *i.e.*, by using either diazomethane or methyl iodide and potassium carbonate in acetone as methylating agents. Our material had m.p. 143–145° (lit.[1] m.p. 144–145°).

O-Methylisonidulin (*O-methyldehydronidulin*). The isomerization of O-methylnidulin was effected[1] by treating it for a short time with nitric acid in acetic acid solution while warming the solution on a steam bath. After repeated crystallizations from methanol-chloroform mixtures, however, the pure material had m.p. 172–173° (lit.[1] m.p. 168°).

Anal. Calcd. for $C_{21}H_{19}O_5Cl_3$: C, 55.10; H, 4.18; Cl, 2324. Found: C, 55.28; H, 4.21; Cl, 23.11.

Dihydronidulin. Nidulin (340 mg., 0.78 mmole.) was dissolved in 20 ml. of glacial acetic acid in the flask of a small hydrogenation apparatus. Platinum dioxide catalyst was added (20 mg.), and the ensuing reaction was followed eudiometrically at room temperature and atmospheric pressure. After the initial uptake of the expected catalyst blank, 0.78 mmole of hydrogen gas was absorbed by the substrate and the rate of hydrogen uptake fell off to essentially zero. The reaction solution was diluted with excess water. The ethereal solution was washed with water, saturated with aqueous sodium bicarbonate, and again with water. After a treatment with anhydrous magnesium sulfate, the ethereal solution was taken to dryness. The residue was crystallized from hexane, giving dihydronidulin as long, transparent needles of m.p. 147-150°. Its ultraviolet spectrum in acidified ethanol had an absorption band at 268 mμ (log ε 3.95). In basic ethanol, this band is replaced by one at 322 mμ (log ε 4.27).

Anal. Calcd. for $C_{20}H_{19}O_5Cl_3$: C, 53.98; H, 4.30; Cl, 23.86. Found: C, 53.73; H, 4.19; Cl, 23.60.

The NMR spectra were observed at 60 Mc on a Varian Associates high resolution spectrometer (Model V-4300 B), equipped with a super-stabilizer (Model V-K3506) and a homogeneity control unit (Model V-4365). The spectra were calibrated with respect to an external benzene reference standard by the audio-sideband technique with the aid of a Hewlett-Packard frequency counter.

NOTE ADDED IN PROOF: The complete structure of nidulin has recently been deduced from infrared spectral evidence.[6]

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[3] J. H. Richards and W. F. Beach, *J. Org. Chem.*, in press.

[4] R. R. Frazer, *Can. J. Chem.*, 38, 549 (1960).

[5] J. H. Richards and W. F. Beach, unpublished work.

[6] W. F. Beach and J. H. Richards *J. Org. Chem.*, 26, 1339 (1961).