then reconverted to **2** in 51% yield by treatment with methylene bromide and potassium carbonate in dimethylformamide at 100°, in a reaction constituting a partial synthesis of deoxynybomycin.

The question of which aromatic methyl of **2** bears a hydroxyl substituent in nybomycin was resolved conclusively by spin decoupling carried out on nybomycin in trifluoroacetic acid. Irradiation of the aromatic methylene signal at δ 5.58 sharpened the ring-proton absorption at δ 7.69, while irradiation of the aromatic methyl signal at δ 2.87 sharpened the ring-proton absorption at δ 7.16. The position of the latter signal is at the precise position expected for the pyridone ring proton of a 4-methyl-2-quinolone bridged 1,8 by a methylene bridge.[10-12] Hence, the aromatic methyl is on the same ring as the methylene bridge, as shown in **1**. In the accompanying report[10] we describe the total synthesis of deoxynybomycin (**2**).

Acknowledgment. This investigation was supported in part by Public Health Service Research Grants No. AI 01278 and AI 04769 from the National Institute of Allergy and Infectious Diseases. We also thank the Upjohn Co. for a sample of nybomycin.

(10) See accompanying manuscript: R. M. Forbis and K. L. Rinehart, Jr., *J. Amer. Chem. Soc.*, **92**, 6995 (1970).

(11) Both the pyridone ring proton and the methyl group protons in 2-lepidones are remarkably constant in their chemical shifts so long as the character of the N-substituent is unchanged (see Table I, accompanying report).[10] That it is in fact the 6-methyl which is found at δ 2.90 in the spectrum of **2** was verified by reduction of **1** with 47% deuterium iodide at reflux; the nmr spectrum of the product (**12**) shows a two-proton singlet at δ 2.98 (Ar-CH_2D) and a three-proton signal at δ 2.90.

(12) Upon standing in trifluoroacetic acid, nybomycin forms a trifluoroacetate ester (**13**), whose nmr spectrum retains the singlet peaks at δ 2.87 (3 H), 6.82 (2 H), and 7.16 (1 H), for the protons on the oxazolinopyridone rings, but shows shifted singlets at δ 4.45 (3 H), 6.03 (2 H), and 7.46 (1 H), for the protons on the trifluoroacetate-substituted ring.

(13) National Science Foundation Cooperative Graduate Fellow.

(14) National Science Foundation Predoctoral Fellow.

*Address correspondence to this author.

Kenneth L. Rinehart, Jr.,* Graham Leadbetter
Richard A. Larson,[13] Richard M. Forbis[14]
Department of Chemistry, University of Illinois
Urbana, Illinois 61801

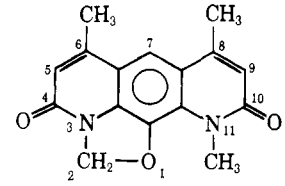
Received August 31, 1970

Nybomycin. IV. Total Synthesis of Deoxynybomycin[1]

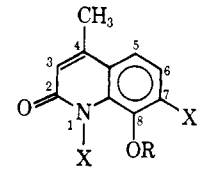
Sir:

Umezawa, *et al.*,[2] recently reported the isolation of the antibiotic deoxynybomycin from *Streptomyces hyalinum* n. sp. Hamada *et* Yakayama. That compound, which we assigned structure **1**,[1,3] had earlier been reported as a degradation product of the antibiotic nybomycin.[4] We report here the unambiguous synthesis of 6,8,11-trimethyl-4,10-dioxo-2*H*,4*H*,10*H*,-11*H*-pyrido[3,2-*g*]oxazolo[5,4,3-*ij*]quinoline (**1**) and its complete identity with deoxynybomycin.

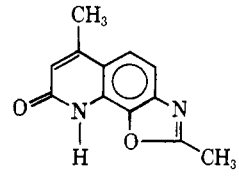
Our synthetic route began with the acylation of commercially available *o*-anisidine with diketene[5] to



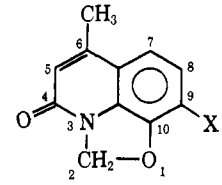
1



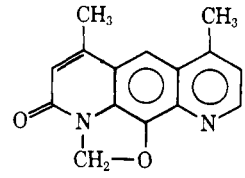
2, R = CH_3; X = H
3, R = X = H
4, R = H; X = NO_2



5



6, X = NO_2
7, X = NH_2



8

give *o*-methoxyacetoacetanilide ($C_{11}H_{13}NO_3$, mp 83–84°, 85% yield),[6,7] which cyclized in polyphosphoric acid[8] at 100° to **2** ($C_{11}H_{11}NO_2$, mp 187–188°, 80% yield).[6,7] Demethylation of **2** with refluxing 48% hydrobromic acid gave **3** ($C_{10}H_9NO_2$, mp 248–250°, 94% yield),[6,7] which was nitrated[9] in nitric acid–acetic anhydride at 3° to give a mixture of two isomers, from which **4** [$C_{10}H_8N_2O_4$, mp 284° dec; nmr, H-5 at δ 8.34, H-6 at δ 7.77, J_{56} = 9 Hz][6,7] could be isolated in 39% yield. A second isomer, the 5-nitro analog (mp 205–207°, 29% yield; nmr, H-6 at δ 7.82, H-7 at δ 7.40, J_{67} = 8.5 Hz),[6,7] was also isolated. The obvious ortho coupling in the nmr spectra of both isomers served to eliminate the other possible isomers—the 3-nitro and 6-nitro analogs. Assignment of structures to the nitroquinolones isolated was achieved by formation of a benzoxazole derivative from **4**.[10] Reduction of the nitro group in the higher melting isomer followed by treatment with acetic anhydride at 200° in a sealed tube yielded the oxazoloquinolone **5** ($C_{12}H_{10}N_2O_2$, mp 236–238°, 32% yield);[6,7] similar treatment of the lower melting isomer produced no benzoxazole.

Insertion of the methylene bridge into **4** was carried out with methylene bromide and powdered potassium carbonate in dimethylformamide at 100° to afford the bridged quinolone **6** ($C_{11}H_8N_2O_4$, mp 293–295°)[6,7] in 54% yield. Hydrogenation of **6** over platinum oxide gave the aminoquinolone **7** ($C_{11}H_{10}N_2O_2$, mp 224–226°, nearly quantitative yield).[6,7] A modified Doebner–Miller reaction,[11] involving treatment of the hydro-

(1) Paper III: K. L. Rinehart, Jr., G. Leadbetter, R. A. Larson, and R. M. Forbis, *J. Amer. Chem. Soc.*, **92**, 6994 (1970).

(2) H. Naganawa, T. Wakashiro, A. Yagi, S. Kondo, T. Takita, M. Hamada, K. Maeda, and H. Umezawa, *J. Antibiot.*, **23**, 365 (1970).

(3) K. L. Rinehart, Jr., R. A. Larson, R. M. Forbis, and G. Leadbetter, Abstracts, 5th International Symposium on the Chemistry of Natural Products, IUPAC, London, July 1968, p 79.

(4) K. L. Rinehart, Jr., and H. B. Renfroe, *J. Amer. Chem. Soc.*, **83**, 3729 (1961).

(5) A. B. Boese, *Ind. Eng. Chem.*, **32**, 16 (1940).

(6) Microanalyses agree with the molecular formula shown.

(7) Low-resolution mass spectral data agree with the molecular formula shown.

(8) A. K. Mallams and S. S. Israelstam, *J. Org. Chem.*, **29**, 3548 (1964).

(9) R. E. Buckles and M. P. Bellis in "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963, p 722.

(10) W. Theilacker, *J. Prakt. Chem.*, [2] **153**, 54 (1939).

(11) K. N. Campbell and I. J. Schaffner, *J. Amer. Chem. Soc.*, **67**, 86 (1945).

chloride salt of **7** with methyl vinyl ketone, ferric chloride, and zinc chloride in ethanol, followed by polyphosphoric acid at 110°, gave the strongly fluorescent pyridoquinolone **8** ($C_{15}H_{12}N_2O_2$, mp 235–238°)[6,7,12] in 34% yield. Methylation of **8** with dimethyl sulfate in refluxing benzene gave its methosulfate which was not purified but treated directly with potassium hydroxide and potassium ferricyanide at 3° for 7 hr[13] to give **1** ($C_{16}H_{14}N_2O_3$)[6] in 21% yield (from **8**).

The synthetic sample of **1**, prepared by the route described, was identical with authentic deoxynybomycin, prepared from nybomycin, in the following characteristics: melting point behavior, thin layer chromatographic behavior, infrared spectrum (Nujol and KBr), nmr spectrum (trifluoroacetic acid), mass spectrum. As seen in Table I, both the ring protons and those of the methyl substituent appear at about 0.1-ppm higher field in the methylene-bridged quinolones, a correlation of use in assigning the structure of nybomycin.[1]

Table I. Chemical Shifts (δ) of Quinolone Ring Substituents[a]

Compd	5-H	6-CH_3	2-CH_2	3-H	4-CH_3
2				7.26	2.89
3				7.30	2.90
4				7.40	2.91
6	7.26	2.82	6.83		
7	7.21	2.81	6.72		
8	7.16	2.89	6.90		
1	7.18	2.90	6.85	7.38[b,c]	2.98[b,d]

[a] Spectra obtained on trifluoroacetic acid solutions at 100 MHz. [b] Corresponding protons, but numbering system changed; see formulas in text. [c] 9-H. [d] 8-CH_3.

Acknowledgment. This work was supported in part by Public Health Service Grants No. AI 01278 and AI 04769 from the National Institute of Allergy and Infectious Diseases.

(12) High-resolution mass spectral data agree with the molecular formula shown.

(13) E. A. Prill and S. M. McElvain in "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., Wiley, New York, N. Y., 1943, p 419.

(14) National Science Foundation Predoctoral Fellow.

*Address correspondence to this author.

Richard M. Forbis,[14] Kenneth L. Rinehart, Jr.*
Department of Chemistry, University of Illinois
Urbana, Illinois 61801
Received August 31, 1970

Photochemical Reaction of Bis(1,3-diketonato)nickel(II) Chelates

Sir:

As a part of our general investigation of the photochemical reactions of transition metal chelates,[1,2] we have studied the photoreduction of a series of bis(1,3-diketonato)nickel(II) complexes in ethanol. To our knowledge there are no reports in the literature of photochemical reactions of nickel(II) complexes. Previous studies of divalent nickel complexes have reported no photosensitivity[3] in the ultraviolet region. However, exposure of degassed ethanol solutions of these neutral 1,3-diketonato chelates to 254-nm radiation does result in a photochemical reaction. The reaction is accompanied by a change from the initial light green solution to a colorless or brownish solution containing a dispersed black solid. In addition, a greyish-white metallic nickel film is formed on the irradiated cell face. The other major product is the protonated ligand which has been isolated and identified spectrally. The amount of metallic nickel formed as well as the amount of nickel(II) remaining in solution was determined by atomic absorption spectroscopy for a series of bis(acetylacetonato)nickel(II), $Ni(AA)_2$, solutions. These determinations resulted in a molar ratio of 0.8 ± 0.3 for the moles of metallic nickel produced to the moles of chelated nickel consumed. Thus the overall reaction may be written as

$$Ni(AA)_2 \xrightarrow[EtOH]{h\nu} Ni + 2HAA + \text{oxidized solvent} \qquad (I)$$

Quantitative measurement of the protonated ligand produced during the photolysis has been hindered by the heterogeneous nature of the solution.

The rate of the photoreduction was studied as a function of the initial concentration of chelate in a series of optically dense solutions, *ca.* 10^{-3}–10^{-2} *M*. The rate of formation of metallic nickel was found to be independent of the chelate concentration.

The light intensity dependence was determined by irradiating 5×10^{-3} *M* solutions of the various chelates. The reduction has a first-order dependence on the incident light intensity as evidenced by an average slope of 0.8 ± 0.2 for plots of the log of the initial rate *vs.* the log of the average intensity. The range of light intensity studied was from 5×10^{15} quanta/sec to 2.4×10^{16} quanta/sec. Thus the rate equation for optically dense solutions can be written as

$$d(Ni^0)/dt = \phi I_a^{0.8\pm0.2} \qquad (II)$$

A resonable mechanism involves a one-electron reduction to a Ni(I) intermediate followed by a second one-electron reduction to Ni^0. In this mechanism, the first step is a primary photochemical reaction, while the second step is a thermal reaction. This tentative mechanism is supported by the appearance of a black solid dispersed in the solution. The black substance is believed to be the Ni(I) intermediate. It is extremely reactive and disappears immediately when exposed to the atmosphere.

The results of quantum yield determinations for the chelates studied are summarized in Table I. Each average quantum yield was calculated from at least four independent determinations. The rate of the photoreduction is relatively independent of the presence of water, as evidenced by the similar quantum yields in ethanol and ethanol–water.

(1) H. D. Gafney, R. L. Lintvedt, and I. S. Jaworiwsky, *Inorg. Chem.*, **9**, 1728 (1970).

(2) H. D. Gafney and R. L. Lintvedt, submitted for publication.

(3) A. W. Adamson, W. L. Waltz, E. Zinato, D. W. Watts, P. D. Fleischauer, and R. D. Lindholm, *Chem. Rev.*, **68**, 541 (1968), and references therein.