

The biological conversion of the synthetic precursor, **4**, to 7-chloro-6-demethyltetracycline was carried out using *S. aureofaciens* V828 by the method previously described.¹ The product was identified by paper chromatography and represented a 7.9% yield (microbiological assay) based on precursor added to the fermentation. A control conversion of authentic **4** carried out simultaneously resulted in a yield of 8.4% of 7-chloro-6-demethyltetracycline.

The total synthesis of the naphthacenic precursor, **4**, and the biological conversion to 7-chloro-6-demethyltetracycline constitute a potential chemical-biological route to new tetracycline antibiotics involving, in the chemical steps, only aromatic chemistry.⁹ Investigation of this route as a source of semisynthetic new tetracycline antibiotics is in progress.

(9) L. H. Conover and co-workers [*J. Am. Chem. Soc.*, **84**, 3222 (1962)] recently have reported the total synthesis of (\pm) 6-demethyl-6-deoxytetracycline by an essentially aliphatic approach.

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RECEIVED MARCH 18, 1963

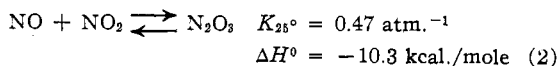
INFRARED ABSORPTION BY PEROXY-NITROGEN TRIOXIDE FREE RADICAL IN THE GAS PHASE

Sir:

We have observed a new absorption band with a maximum occurring at 1840 cm^{-1} , which we assign to the peroxy-free radical, OONO. This observation was made by means of a prism-grating spectrophotometer (Beckman IR-7) in conjunction with a pair of long path (80 m.) multireflection cells. Pressure of nitric oxide in the 270-l. sample cell was between 0.5 and 2.5 mm. and pressure of oxygen varied from 10 to 50 mm. Oxygen reacts slowly and irreversibly with nitric oxide at these pressures and at room temperature to produce nitrogen dioxide.



Nitrogen dioxide and nitric oxide react rapidly and reversibly to produce dinitrogen trioxide.



The peroxy-free radical presumably is formed by the rapid reversible reaction



The absorption spectra of NO, N_2O_3 , and OONO are given in Fig. 1. All three absorb infrared radiation in the same spectral region, but they can be distinguished on the basis of their behavior as a function of time and by differences in optical density where their absorption maxima do not overlap. When nitric oxide alone was placed in the absorption cell, and oxygen quickly added, the P branch of nitric oxide was instantly enhanced. Within a few minutes enough dinitrogen trioxide was formed by reactions 1 and 2 to cause a further and a different enhancement in this spectral region. By correcting for absorption due to NO and N_2O_3 , the difference spectrum shown in Fig. 1 was obtained. (This procedure is complicated to some extent by the noticeable adsorption of nitric oxide on the surface of the optical cell. This adsorbed material could be displaced either by added oxygen or nitrogen. The amount of nitric oxide actually present was given by the non-overlapped R branch.)

A series of runs was made with constant initial nitric oxide and varied pressures of added oxygen. The new absorption is linear in oxygen, as can be seen from

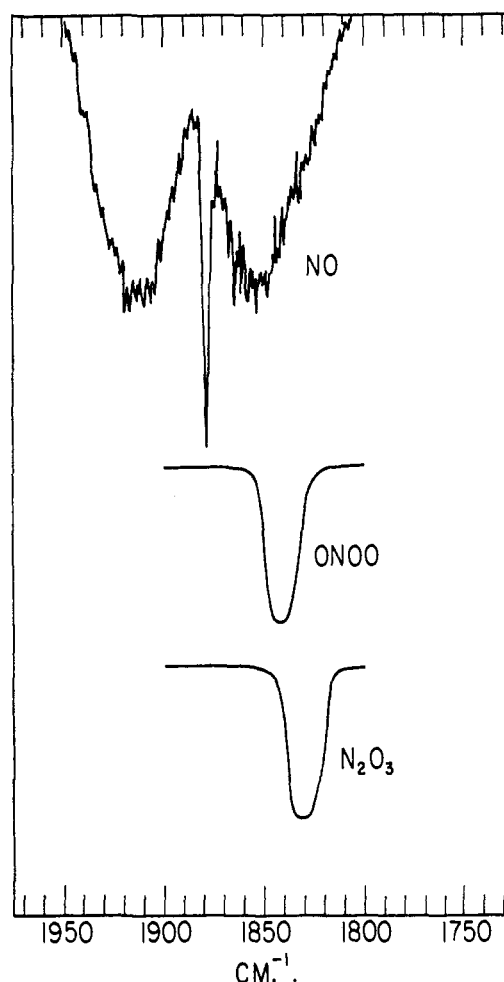


Fig. 1.—Absorption spectra as observed in this study.

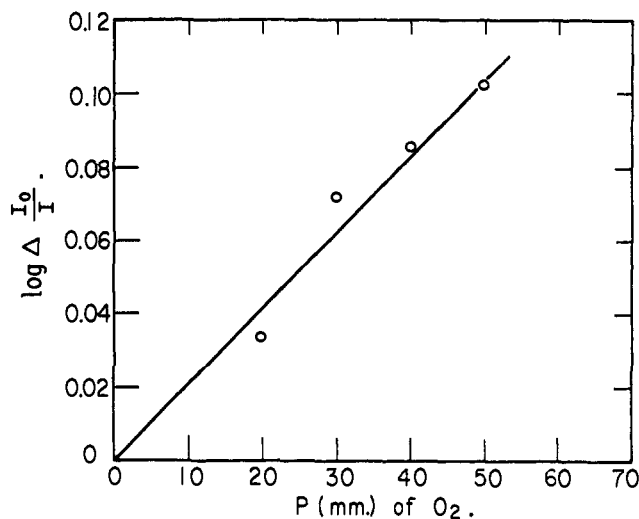


Fig. 2.—First-order dependence of optical density at 1840 cm^{-1} on oxygen for constant nitric oxide. Corrections have been made for absorption by NO and by N_2O_3 .

Fig. 2. Similarly, a series of runs was made with varied initial nitric oxide and constant oxygen. The optical density of the new band is linear in nitric oxide, Fig. 3.

The evidence cited in support of identifying the compound as NO_3 is the first-order dependence on both NO and O_2 , and the time behavior of the new band. The structural assignment OONO, rather than

that of the symmetrical nitrate radical $\text{O}-\text{N} \begin{matrix} \text{O} \\ \diagup \\ \text{O} \end{matrix}$, is

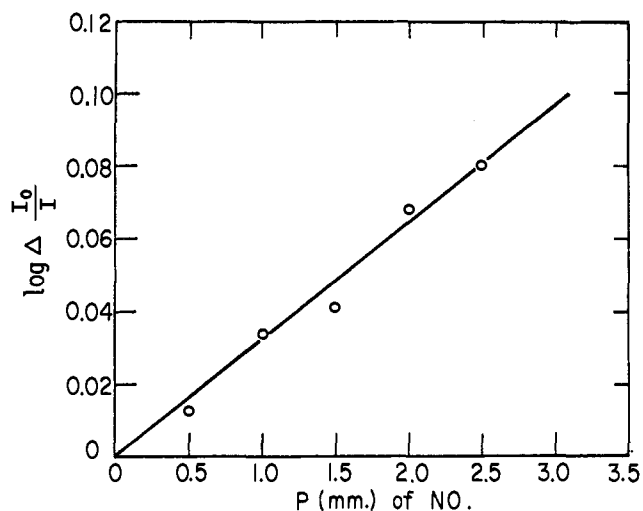


Fig. 3.—First-order dependence on nitric oxide for constant oxygen.

based on the absorption frequency. Nitric oxide contains a non-bonding electron, and its absorption maximum is only slightly shifted by bond formation, for example

Species	ω (cm. ⁻¹)	Ref.
NO	1876	
F-NO	1845	1
OO-NO	1840	(This work)
O ₂ N-NO	1830	2
Cl-NO	1800	3

A vibrational analysis of the symmetrical nitrate radical, with a reasonable assignment of force constants, indicates that the infrared active frequencies should be about 664 cm.⁻¹, 904 cm.⁻¹ and 1603 cm.⁻¹, none anywhere near the observed band at 1840 cm.⁻¹.

If one assumes that the Beer's law constant for OONO is the same as for N₂O₃ and if the entropy is estimated to be 68 cal./deg.-mole, the heat of reaction 3 is about -6 kcal./mole, and the equilibrium constant at 25° is about 3.4 × 10⁻³ atm.⁻¹. On the other hand, if one assumes the Beer's law constant for OONO to be the same as that for NO, then the heat of reaction 3 is about -9 kcal./mole, and the equilibrium constant at 25° is about 3.2 × 10⁻¹ atm.⁻¹. The true situation is probably somewhere between these two limits.

This work is believed to have significance with respect to the mechanism of nitric oxide oxidation and with respect to the role of nitric oxide as an oxidizing agent when it is in the atmosphere in trace amounts.

Acknowledgment.—This work was supported by the U. S. Public Health Service, Grant AP-104.

(1) P. J. H. Wolty, E. A. Jones and A. H. Nielsen, *J. Chem. Phys.*, **20**, 378 (1952).

(2) L. D'Or and P. Tarte, *Bull. soc. roy. sci. Liege*, **22**, 276 (1953).

(3) W. G. Burns and H. J. Bernstein, *J. Chem. Phys.*, **18**, 1669 (1950).

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RECEIVED APRIL 10, 1963

THE HYDROXYMETHYLENE KETONE-ALDO ENOL EQUILIBRIUM

Sir:

The enolization of β -keto aldehydes (I) may lead to two possible tautomeric enols: aldo enol (Ia) and hydroxymethylene ketone (Ib). The long-standing supposition that the hydroxymethylene ketone is the predominant if not the exclusive enol form at equilib-

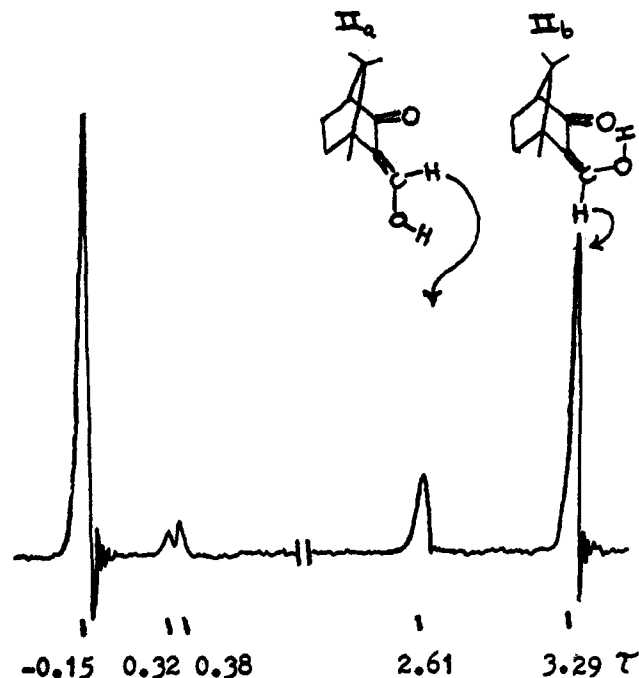
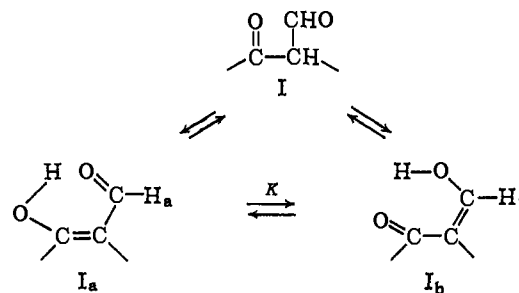


Fig. 1.—The low field part of the proton magnetic resonance spectrum of 3-formylcamphor (II).

rium apparently arises largely from the demonstration by Claisen nearly 70 years ago that 3-formylcamphor (II, no. 12) underwent numerous reactions each consistent with that anticipated for 3-hydroxymethylene-camphor.¹ Reactions of β -keto aldehydes, however, do not necessarily reflect the composition of their tautomeric equilibria.



The direction of enolization of a number of cyclic β -keto aldehydes has been estimated by n.m.r. spectroscopy. The equilibria between I and Ia, Ib are expected to be slow with regard to spectra averaging,² and the equilibrium between Ia and Ib fast.³ Consequently, the recorded spectrum should show unenolized I and a weighted average of enols Ia and Ib. From the observed averaged chemical shift of H_a and H_b (δ^0), the mole fraction of Ib at equilibrium is given by: $N_{Ib} = (\delta^0 - \delta_a)/(\delta_b - \delta_a)$ where δ_a and δ_b are the chemical shifts of H_a and H_b, respectively. Taking the δ of the aldehyde proton of salicylaldehyde (0.18 τ) and adding 0.61 p.p.m., the deshielding arising from the anisotropy of the benzene ring⁴ (assuming a planar molecule and standard bond lengths and angles), a value of 0.79 τ is obtained for δ_a . The n.m.r. spectrum of 3-formylcamphor (II) was measured with the

(1) L. Claisen, *Ann.*, **281**, 306 (1894); A. W. Bishop, L. Claisen and W. Sinclair, *ibid.*, **281**, 314 (1894).

(2) J. A. Pople, W. G. Schneider and H. S. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., New York, N. Y., 1959, chapter 17.

(3) The small change in the equilibrium position of the enol proton is undoubtedly a low activation energy process.

(4) Estimated from the tables of C. E. Johnson, Jr., and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).