ary atom which is greater than that for a tertiary atom. Second, the steric factors for these reactions are at most 10^{-3}. Dorfman and Gomer[3] reached a similar conclusion about the magnitude of the steric factors from the results of their studies of a number of similar methyl radical reactions.

(3) L. M. Dorfman and R. Gomer, *Science*, **110**, 439 (1949).

DIVISION OF CHEMISTRY A. F. TROTMAN-DICKENSON
NATIONAL RESEARCH COUNCIL E. W. R. STEACIE
OTTAWA, CANADA

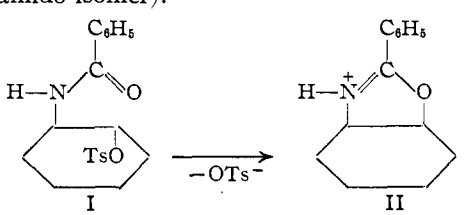
RECEIVED MARCH 29, 1950

THE NEIGHBORING BENZAMIDO GROUP IN ADDITION AND SUBSTITUTION

Sir:

Neighboring groups which participate in nucleophilic replacement processes with relatively large driving forces[1] can be expected to participate in addition[2] to the olefinic linkage which is initiated by electrophilic attack of some reagent on the multiple linkage.

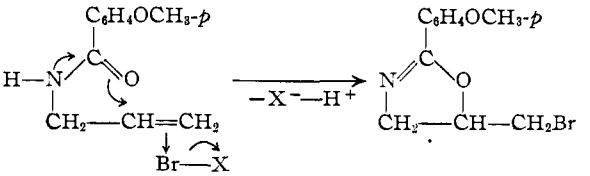
The benzamido and other acylamino groups are examples of so-called complex[2,3] neighboring groups with rather large driving forces. Benzamido can be compared with acetoxy from the first order rate of ionization of *trans*-2-benzamidocyclohexyl *p*-toluenesulfonate (I) in absolute ethanol at 74.51°, 1.78×10^{-3} sec.$^{-1}$, which is *ca.* 200 times the value for the *trans*-2-acetoxycyclohexyl ester[4] (and some 1000 times that of the *cis*-benzamido isomer).



I II

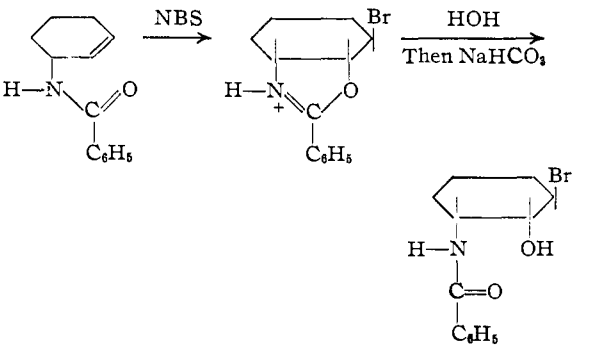
Solvolysis of I in ethanol or acetic acid produces the oxazolinium ion II as the first product[3] and this may be isolated either as the water-soluble *p*-toluenesulfonate, m. p. 160–161°, as the picrate, m. p. 155.5°, or as the free oxazoline, m. p. 47°. For example, oxazolinium toluenesulfonate is obtained in 95% yield from heating I several minutes in anhydrous acetic acid.

The acylamino group turns out to participate in addition in a very useful manner. For example, N-*p*-methoxybenzoylallylamine (III) gives, on treatment in acetic acid with N-bromosuccinimide, (which, incidentally, we have used for several years as a positive bromine source in hydroxylic solvents) a 95% crude yield of the bromoöxazoline IV, m. p. 91–91.5°.



IIII IV

This reaction is interesting theoretically and on the practical side constitutes a way for setting up three functional groups with a definite stereochemical relation. We illustrate with the cyclohexenyl case



DEPARTMENT OF CHEMISTRY S. WINSTEIN
UNIVERSITY OF CALIFORNIA LEON GOODMAN
LOS ANGELES 24, CALIFORNIA ROBERT BOSCHAN

RECEIVED FEBRUARY 25, 1950

THE STRUCTURE OF QUINAMINE[1]

Sir:

In 1945 quinamine, an indole alkaloid of the cinchona family,[2] was considered to have structure I.[3] In 1949 Robinson[4] suggested an alternate formulation II to account for the dihydroindole nature of quinamine (spectrum, coupling reaction with diazobenzenesulfonic acid). Very recently[5] structure III was proposed for quinamine based upon the elegant conversion of quinamine into cinchonamine (V) with lithium aluminum hydride.

We have now effected the reverse transformation of cinchonamine into quinamine with the aid of dilute peracetic acid. Since all attempts of converting indole derivatives into 2,3-epoxides by oxidation with peracids have so far failed, we should like to propose the expression IV for quinamine.

The action of peracetic acid results probably first in the formation of a β-hydroxyindolenine derivative (VI) in accordance with the general course of oxidation in the indole series.[6] Inter-

(1) I am indebted to Research Corporation, New York, for financial assistance of this work.

(1) Winstein and Grunwald, THIS JOURNAL, **70**, 828 (1948).

(2) Winstein, paper before Organic Division at the St. Louis meeting of the American Chemical Society, September, 1948.

(3) Winstein, paper at Eleventh National Organic Symposium, Madison, Wisconsin, June, 1949.

(4) Winstein, Hanson and Grunwald, THIS JOURNAL, **70**, 812 (1948).

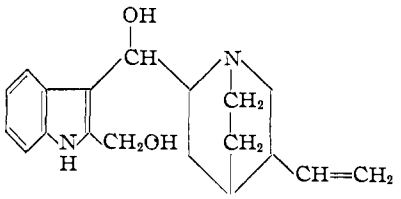
(2) Henry, Kirby and Shaw, *J. Chem. Soc.*, 524 (1945).

(3) Kirby and Shaw, *ibid.*, 528 (1945); Kirby, *ibid.*, 725 (1949).

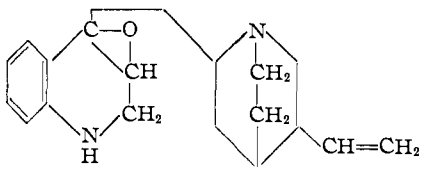
(4) Robinson, Festschrift Paul Karrer, Zürich, 1949, p. 40; *J. Chem. Soc.*, in press (quoted from ref. 5).

(5) Goutarel, Janot, Prelog and Taylor, *Helv. Chim. Acta*, **33**, 150 (1950).

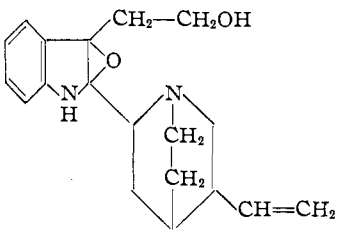
(6) Witkop, THIS JOURNAL, **72**, 1428 (1950).



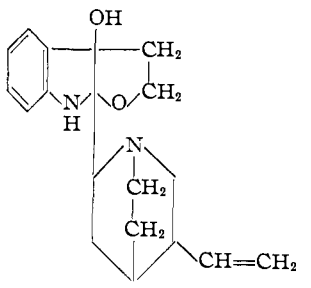
I Quinamine (Kirby 1945)



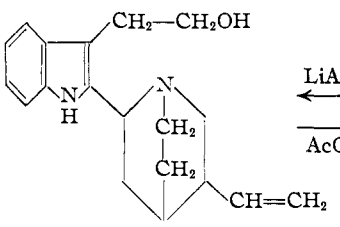
II Quinamine (Robinson, 1949)



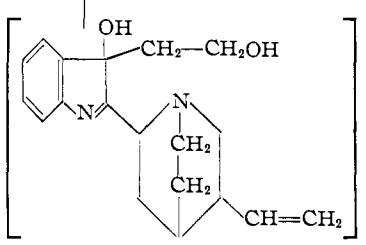
III Quinamine (Goutarel, Janot, Prelog, Taylor, 1950)



IV Quinamine



V Cinchonamine (Goutarel, Janot, Prelog, Taylor, 1950)



VI

nal addition of the β-hydroxyethyl chain to the reactive —C=N— double bond in VI leads to quinamine (IV). Further oxidation of the latter with rupture of the indole ring, which is usually observed under similar conditions, cannot occur. The removal of the hydroxyl group in IV by the action of lithium aluminum hydride[5] is analogous to the similar conversion[7,8] of 11-hydroxytetrahydrocarbazolenine[9] to tetrahydrocarbazole; opening of the oxide ring and loss of water results in cinchonamine (V).[5]

The quinamine (IV), obtained from 50 mg. of cinchonamine with peracetic acid in good yield, formed silky needles, m. p. 171–173°; calcd. for $C_{19}H_{24}N_2O_2$: C, 73.0; H, 7.77. Found: C, 72.83; H, 8.04. Comparison with an authentic specimen with regard to mixed melting point and ultraviolet and infrared absorption spectra confirmed the identity. Whether a second compound obtained in small yield as colorless cubes from ether, m. p. 143–145°, possibly isomeric with quinamine, has the other configuration at the β-indole position and is related to conquinamine[10] has not yet been established.

11-Hydroxytetrahydrocarbazolenine, under the action of alcoholic alkali, rearranges to *spiro*-[cyclopentane-1,2′-ψ-indoxyl].[9] Quinamine, under similar conditions, forms the yellow isoquinamine[3] which is, as Sir Robert Robinson and Dr. Prelog independently concluded, clearly an indoxyl derivative: ultraviolet spectrum, λλ max. (log ε): 228 mμ (4.427); 398 mμ (3.513); λλ min. (log ε): 250 mμ (3.985); 287 mμ (2.888). Infrared spectrum: 5.88 μ (carbonyl of five-membered ring), 6.18μ (Ph—NH—C—(R_1R_2)—). Reduction with lithium aluminum hydride furnishes *allo*dihydroisoquinamine, colorless needles, m. p. 172–174°. Attempts to convert this compound to cinchonamine (V) by an acid-catalyzed Wagner–Meerwein rearrangement[11] are in progress.

The conclusions as to the structure of quinamine were also reached independently by Prof. Prelog after he had been informed of the relevant facts summarized briefly above.

Acknowledgment.—I am indebted to Dr. Raymond-Hamet (Paris) for a sample of cinchonamine. Dr. Prelog (Zürich), as well as Drs. Sharp and Shaw (The Wellcome Laboratories of Tropical Medicine, London), through the courtesy of Dr. T. A. Henry, kindly placed at my disposal two samples of quinamine.

(7) Witkop and Patrick, some novel aspects of the chemistry of β-hydroxindolenines, *Experientia*, in press.

(8) Witkop and Patrick, THIS JOURNAL, in preparation.

(9) Patrick and Witkop, *ibid.*, **72**, 633 (1950).

(10) Hesse, *Ann.*, **209**, 62 (1881).

(11) *Cf.* Witkop, THIS JOURNAL, **72**, 614 (1950).

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RECEIVED MARCH 6, 1950

OROTIC ACID, A GROWTH FACTOR FOR *LACTOBACILLUS BULGARICUS*

Sirs:

Certain strains of *Lactobacillus bulgaricus* grow readily on a synthetic medium containing yeast extract as the source of an unknown nutritive essential (LBF).[1] We have found that other strains of the same species are incapable of growth on such a medium and require much larger amounts of natural material to furnish another growth factor(s). Using one such strain identified

(1) Williams, Hoff-Jorgensen and Snell, *J. Biol. Chem.*, **177**, 933 (1949).