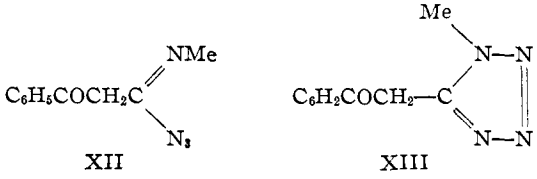
an incomplete reaction with triethylamine in heavy water, it contains no deuterium; (ii) the product (IV: Et in place of Me) from the reaction of N-ethyl-5-phenylisoxazolium fluoroborate with sodium acetate in heavy water contains only a small and variable amount of deuterium bound to carbon; (iii) the rate of the reaction of acetic acid with the α-ketoketenimine (X: R = C_6H_5, R′ = H, R″ = Et) in methylene chloride is depressed by addition of triethylamine.

The reactions of many other nucleophiles with isoxazolium salts[2] all receive ready rationalization in terms of the initial production of α-ketoketenimines. The great facility of the reactions is dramatically illustrated by the rapid combination of (I) with azide ion in aqueous solution to give (XII) (Found: C, 59.30; H, 5.06; N, 28.18)



XII XIII

[infrared spectrum (CH_2Cl_2)—4.69 μ, 5.90, 6.17; ultraviolet spectrum (EtOH)—348 mμ (6,000), 285(1,500), 245 (12,500)]. This substance is the only known simple iminoazide[8]; in hydroxylic solutions it cyclizes readily [$t_{1/2} \sim$ 100 min. in MeOH/H_2O: 1/1 at 27°] to the isomeric tetrazole (XIII)[9] [infrared spectrum (CH_2Cl_2)—5.90 μ; ultraviolet spectrum (EtOH)—285 mμ (1,600), 245(14,200)], which is hydrolyzed by hot 2 *N* sodium hydroxide to benzoic acid and 1,5-dimethyltetrazole, identical with an authentic sample.[10]

The reaction of the N-methyl-5-phenylisoxazolium cation (**I**) with acetate ion to give the enol ester (IV) exemplifies a process for converting a carboxylate group into a reactive ester group by a very rapid and smooth reaction, occurring under conditions of exceptional mildness. The adaptation of the reaction for use in a new method of peptide synthesis is described in an accompanying communication.[7]

We wish to express our appreciation of support by the National Science Foundation and the National Institutes of Health.

(8) *Cf.* J. H. Boyer and E. J. Miller, Jr., *J. Am. Chem. Soc.*, **81**, 4671 (1959).

(9) This substance was isolated, but described as having a different structure, by W. Stülcken, ref. 2.

(10) *Cf. Chem. Abs.*, **26**, 2199 (1932).

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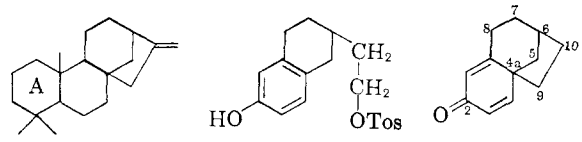
RECEIVED JANUARY 13, 1961

SYNTHESIS OF 4a,6-ETHANO-5.6 7,8-TETRAHYDRO-2(4a)-NAPHTHALENONE

Sir:

Recent investigations[1] have shown that the bicyclo[3,2,1]octane system is a structural unit common to a number of diterpene alkaloids and diterpenes, *e.g.*, phyllocladene (I). We have searched for a general approach to the synthesis of these compounds and wish to report the successful conversion of 6-hydroxy-2-(β-tosyloxyethyl)-1,2,3,4-tetrahydronaphthalene (II) to the compound in the title.



I II IV

Winstein and Baird[2a] first observed the conversion of *p*-(ω-tosyloxybutyl)-phenol (III) to spiro-(4,5)-deca-1,4-diene-3-one through so-called Ar_1 5 participation. Since then only a few examples of this type of reaction have been recorded[2b] and the application has been limited to simple *p*-substituted phenols.

Refluxing a dilute (0.01 *M*) solution of II in *tert*-butyl alcohol with a slight excess of potassium *t*-butoxide for six hours afforded in approximately 90% yield a colorless liquid,[3] $n^{26}D$ 1.5738 (found: C, 82.75, H, 8.17) λ_{max}^{MeOH} 246 mμ (ϵ 1.57 × 10^4) λ_{max}^{Chl} 6.02 μ, 6.17, 6.22 (shoulder); semicarbazone, m.p. 222–224° (found: C, 67.71, H, 7.52). In view of the elementary analyses and spectral evidence, this liquid is represented by formula IV. The yield appeared to be the highest ever reported for this type of reaction. Undoubtedly this smooth cyclization was effected by an advantageous orientation of the carbon atom carrying the tosylate group. Side reactions are suppressed by the tertiary C_6 atom, a structural feature not present in III.

Preparation of II.—The Reformatsky reaction of 6-methoxy-β-tetralone[4] with ethyl bromoacetate produced a β-hydroxy ester (V), b.p. 174–175° (0.75 mm.) (found: C, 66.73, H, 7.75). The ester (V) was dehydrated with thionyl chloride and pyridine to an unsaturated ester (VI), b.p. 135–137° (0.09 mm.) (found: C, 72.90, H, 7.60). The unsaturated ester was reduced catalytically to afford ethyl 6-methoxy-1,2,3,4-tetrahydronaphthalene-2-acetate (VII),[5] b.p. 127–128° (0.06 mm.), which was reduced with lithium aluminum hydride to the corresponding alcohol (VIII), b.p. 132–133° (0.07 mm.) (found: C, 75.81, H, 9.00). Pyrolysis of the methylmagnesium iodide complex of VIII at 175° effected demethylation,[6] affording a hydroxy phenol (IX), m.p. 88–90° (found: C, 75.12, H, 8.21). The phenol (IX) was converted to II[7] through the benzyl ether (X), m.p. 61–62° (found: C, 81.17, H, 7.82) and the benzyl ether tosyl ester (XI) m.p. 76–78° (found: C, 71.52, H, 6.50). Catalytic hydrogenolysis of XI with palladium on carbon proceeded without difficulty.

(1) For instance, see: K. Wiesner and Z. Valenta, *Fortschr. Chem. org. Naturstoffe*, **16**, 26 (1958); L. H. Briggs, B. F. Cain, B. R. Davis and J. K. Wilmshurst, *Tetrahedron Letters*, No. 8, 8 (1959).

(2) (a) S. Winstein and R. Baird, *J. Am. Chem. Soc.*, **79**, 756 (1957). (b) S. Doring and J. Harley-Mason, *Chem. and Ind.*, 1551 (1959), and references cited therein.

(3) This liquid was purified by silicic acid chromatography, then evaporative distillation at 60° (0.1 mm.).

(4) N. A. Nelson, R. S. P. Hsi, J. M. Shuck and L. D. Kahn, *J. Am. Chem. Soc.*, **82**, 2573 (1960).

(5) The corresponding acid melts at 91–92° (found: C, 71.02, H, 7.13).

(6) W. S. Johnson, E. R. Rogier and J. Ackerman, *ibid.*, **78**, 6322 (1956).

(7) II was sensitive to air oxidation and resisted crystallization. Purification was achieved by silicic acid chromatography.

The cyclization described in this Communication is of interest in gaining further understanding of Ar_1 participation. Moreover, IV is quite suitable for the further construction of ring A of many natural products. The introduction of a ketone group at C_{10}[2b] and the construction of ring A[8] are now in progress.[9,10]

(8) As an example of a conventional method for this purpose, see: G. Stork, H. J. E. Loewenthal and P. C. Mukharji, *ibid.*, **78**, 501 (1956).

(9) The author is grateful to Mr. John Carmody for his helpful technical assistance.

(10) This investigation was supported by a grant (RG-6646) from the National Institutes of Health, Public Health Service.

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RESTRICTED ROTATION IN AMINOBORANES

Sir:

In a recent publication concerning unsymmetrically substituted aminoboranes of the type $R_1R_2NBR_3R_4$ the tentative suggestion was made that such compounds may exhibit *cis-trans* isomerism.[1] This hypothesis was made, in the main, on the basis of the melting points and change of melting points of mixtures of constant composition and of their molecular weights. We are now, on the basis of other observations, in a position to offer definite proof of hindered rotation about a boron–nitrogen bond, leading to *cis* and *trans* conformations.

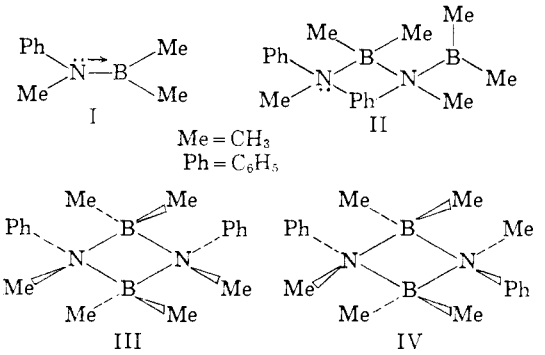
We have investigated the proton resonance spectrum of (methylphenylamino)-dimethylborane,[2] $(CH_3NC_6H_5)B(CH_3)_2$, and find that, at room temperature, the two methyl groups attached to boron are non-equivalent. When the temperature is raised above 100° these two groups become magnetically equivalent as rotation about the N–B bond evidently becomes more rapid.

The p.m.r. spectrum at room temperature, obtained in a Varian high-resolution n.m.r. spectrometer at 60 mc., shows four distinct peaks: (1) a complex phenyl peak, (2) a single sharp N-methyl peak at 4.15 ppm. to high field of the center of the phenyl peak, (3) a sharp peak, assigned to one B-methyl, at 6.64 ppm. above the phenyl, and (4) a sharp peak, assigned to the other B-methyl, at 6.92 ppm. above phenyl. No other peaks appear.

Peaks (3) and (4) are seen to be relatively close together. As the temperature is raised, each of these peaks broadens and they move closer together, finally merging into one at about 100°; at yet higher temperatures this single peak narrows. This is the characteristic behavior when the rate of intramolecular rotation varies with temperatures.[3]

The molecular weight of (methylphenylamino)-dimethylborane has been determined, presumably cryoscopically in benzene for a freshly distilled sample, and indicated a monomeric species.[2] However, since some aminoboranes are reported to form dimers slowly on standing[1,2,4,5] we have considered this possibility in our case.

Therefore, the structures considered for the interpretation of the spectrum are the monomer I, the chain dimer II, and the cyclic dimers III and IV.



Structure II is ruled out because the two methyl groups attached to nitrogen would be non-equivalent, giving two bands. Structure IV would have only one kind of methyl group attached to boron. An equilibrium between two or more forms also is excluded because of the observation of only three methyl resonances. Structure III is consistent with the room-temperature spectrum, but does not afford any explanation of the change of band shape as the temperature is raised. Thus it is concluded that our sample consisted of the monomeric form, I, in the whole temperature interval.

On the basis of the temperature variation, up to 118°, of the separation and shape for the resonances associated with methyl groups attached to boron, we make a preliminary estimate of the barrier to rotation as 15 ± 3 kilocalories per mole; the lifetime of the individual molecular states is about 10^{-2} second at 100°.

(1) K. Niedenzu and J. W. Dawson, *J. Am. Chem. Soc.*, **82**, 4223 (1960).

(2) B.p. 67° at 14.0 mm., prepared according to K. Niedenzu and J. W. Dawson, *ibid.*, **81**, 5553 (1959).

(3) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Company, Inc., New York, N. Y., 1959, pp. 218–224.

(4) H. J. Becher and J. Goubeau, *Z. anorg. allgem. Chem.*, **268**, 133 (1952).

(5) E. Wiberg, A. Bolz and P. Buchheit, *ibid.*, **256**, 285 (1948).

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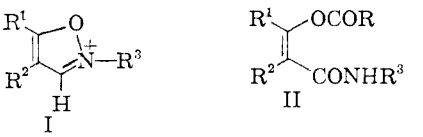
RECEIVED DECEMBER 12, 1960

A NEW SYNTHESIS OF PEPTIDES

Sir:

Carboxylates ($RCOO^-$) react rapidly and smoothly with 3-unsubstituted isoxazolium salts (I), under very mild conditions, to give enol esters (II).[1] We now record the application of this reaction as the carboxyl-activating step in a simple and practical new synthesis of peptides.



Clearly the activating reagent (I) may be varied, through specific choices for the groups R^1, R^2 and R^3, with a view to conferring a special degree of reactivity, or particular physical properties, on the reagent, the activated ester intermediate (II), or

(1) R. B. Woodward and R. A. Olofson, *J. Am. Chem. Soc.*, **83**, 1007 (1961).