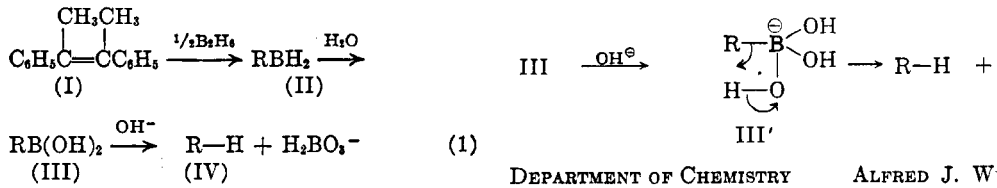
Communications TO THE EDITOR

Alkali-Catalyzed Dealkylation of Two Diastereomeric Benzyl Boranes

Sir:

In the course of an investigation of the monoalkyl boranes (II) prepared from the *cis* and *trans* isomers of α,α'-dimethylstilbene (I) by reaction with diborane, we have found that these organo-boranes (II) suffer cleavage (dealkylation) of the carbon-boron bond under the remarkably mild influence of dilute alkali in aqueous diglyme at room temperature, and moreover, that the alkane (IV, *meso* and *d,l*, respectively) obtained from each borane is produced with a high degree of stereospecificity. The over-all result of sequence (1) is the clean *cis* addition of two hydrogen atoms to the starting olefin.



(I) (II) (III) (IV)

(1)

R = 2,3-diphenyl-2-butyl-
a, *erythro*; b, *threo*

Since hydroboration is known to occur by *cis* addition to the olefinic linkage,[1] it is apparent that these dealkylations (II→IV) proceed with retention of configuration. The boronic acid (III), or a derivative, formed by hydrolysis of the borane, probably is an intermediate in this conversion.

Dealkylation of the *in situ*[2] hydroboration product of *cis*-dimethylstilbene occurred at room temperature within 1 hr. after bringing the diglyme solution to *p*H 9–10 by the addition of 3 *N* sodium hydroxide. Pure *meso*-2,3-diphenylbutane (IVa, 69%), m.p. 126.5–127.5°, was isolated as the total hydrocarbon fraction from chromatography on alumina, in hexane. It did not depress the melting point of authentic hydrocarbon,[3] m.p. 127–127.5.° No dealkylation was observed when the hydroboration product was treated with water alone, or with dilute acetic acid.

The adduct from *trans* I similarly underwent dealkylation, but at a slower rate, giving *d,l*-2,3-diphenylbutane (IVb) in 71% yield after 11 hr. with dilute sodium hydroxide at room temperature. This hydrocarbon, $n^{25}D$, 1.5538, m.p. 10°, and after flash distillation, $n^{25}D$, 1.5528, m.p. 10°, was identified by comparison with authentic material, $n^{25}D$, 1.5530, m.p. 10°, prepared by the method of Greene,[4] and shown to contain less than 5% *meso* isomer by quantitative infrared determination.[4]

Alkali fission of the carbon-boron bond is decidedly less general than its acid-catalyzed counterpart, protonolysis,[5] and appears to depend on the ability of the organic residue to sustain a negative charge. Thus, dibutyl acetyleneboronate[6] rapidly generates acetylene on shaking with aqueous bicarbonate, and α-toluene- and 2-thiopheneboronic[7] acids are smoothly converted to toluene and thiophene, respectively, by hot aqueous sodium hydroxide. In contrast, 1-butane-[8] and benzeneboronic[9] acids yield small amounts of the corresponding hydrocarbons only on fusion with alkali. This correlation, and the retention of configuration observed in the present work, suggest the S_Ei mechanism[10] shown in intermediate III′.

III III′

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RECEIVED AUGUST 21, 1961

(1) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 247 (1959).
(2) H. C. Brown and B. C. Subba Rao, *ibid.*, **78**, 5694 (1956).
(3) E. Ott, *Ber.*, **61**, 2137 (1928).
(4) F. D. Greene, *J. Am. Chem. Soc.*, **77**, 4869 (1955).
(5) H. C. Brown and K. Murray, *ibid.*, **81**, 4108 (1959).
(6) D. S. Matteson and K. Peacock, *ibid.*, **82**, 5760 (1960).
(7) J. R. Johnson, M. G. Van Campen, and O. Grummitt, *ibid.*, **60**, 111 (1938).
(8) H. R. Snyder, J. A. Kuck, and J. R. Johnston, *ibid.*, **60**, 105 (1938).
(9) A. D. Ainley and F. Challenger, *J. Chem. Soc.*, 2171 (1930).
(10) J. R. Johnson, H. R. Snyder, and M. G. Van Campen, Jr. *J. Am. Chem. Soc.*, **60**, 115 (1938).

Proton Magnetic Resonance Spectra of *cis*- and *trans*-4-*tert*-Butylnitrocyclohexane. Long Range Shielding by the Nitro Group[1]

Sir:

We wish to report the characterization of *cis*- and *trans*-4-*tert*-butylnitrocyclohexane by NMR and the observation of a long range magnetic shielding effect by the nitro group in the *cis* isomer. The *cis* and *trans* isomers are readily characterized from the NMR signal of the hydrogen on the number 1 carbon from the well demonstrated phenomenon of stronger spin-spin coupling between axial hydrogens on neighboring carbon atoms

(1) This investigation was supported by a research grant from the State of Washington Initiative 171 funds for Research in Biology and Medicine. The NMR spectra were determined by B. J. Nist, Department of Chemistry, University of Washington.

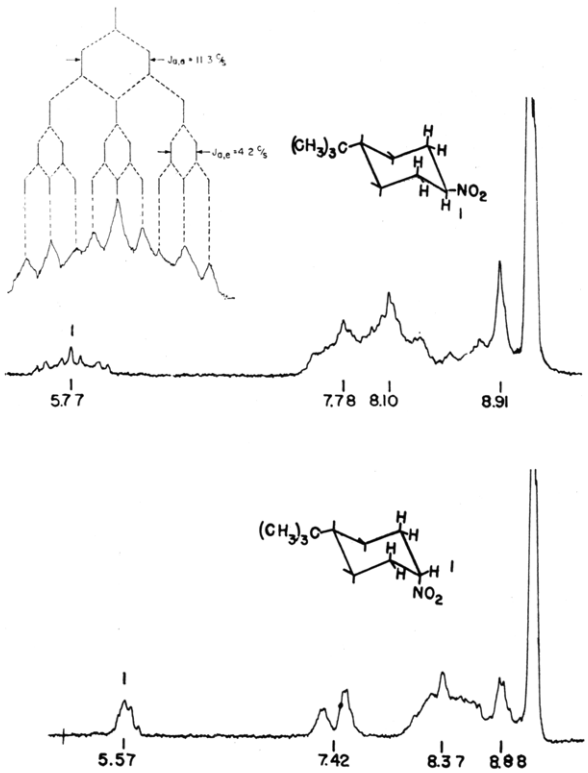
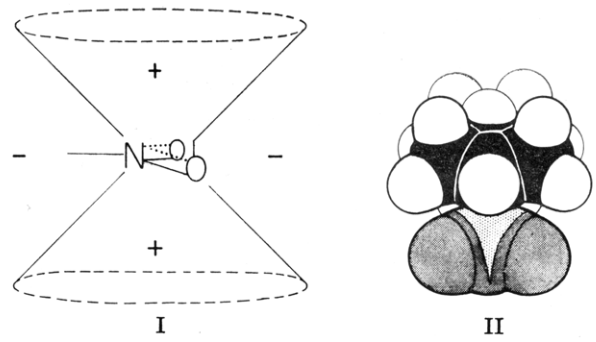


Figure 1



I II

Figure 2

than between neighboring hydrogen atoms in other orientations in fixed six-membered rings.[2] The NMR spectra are consistent with structures in which the cyclohexane ring is in a chair conformation with the *tert*-butyl group in equatorial orientation. In the *cis* isomer the 1-hydrogen is equatorial and its NMR signal, $\tau = 5.57$, shows essentially a singlet with only slight splitting by the four adjacent hydrogens. In the *trans* isomer the 1-hydrogen is axial and is adjacent to two identical axial and two identical equatorial hydrogens. This should give rise to a signal split into nine peaks with relative intensities of approximately 1:2:1:2:4:2:1:2:1. The theoretical spectrum, using the observed coupling constants of $J_{a,a} = 11.3$ c.p.s. and $J_{a,e} = 4.2$ c.p.s., is shown above the expanded observed signal of the 1-hydrogen.

The spectrum of the *cis* isomer shows that in addition to the 1-hydrogen the signal of two other hydrogen atoms experience a sufficient paramagnetic shift, $\tau = 7.42$, to be completey isolated from the signals of the other ring hydrogens. This cannot be due to the inductive effect of the nitro group through bonding orbitals because this effect would cause equal deshielding of the four hydrogens on C-2 and C-6. The observed effect can be explained on the basis of long range shielding effects of the nitro group, and the observation is consistent with a region of negative shielding extending in the plane of the trigonal nitrogen atom of the nitro group. This effect is similar to that observed for the carbonyl group.[3,4] The long range shielding effects of groups containing π-electron systems have been discussed.[5] Regions of positive and negative shielding have been mapped for the benzene ring.[5c] They have been approximated for the carbonyl group as positive in conical regions extending above and below the plane of the trigonal carbon and negative elsewhere,[3] but the boundaries in this case are not known with any degree of certainty. By analogy, regions of positive and negative shielding are roughly depicted for the nitro group in I. Drawing II illustrates that the equatorial hydrogens on C-2 and C-6 are both located in a region of negative shielding when the nitro group is perpendicular to the (C-1)–(C-4) longitudinal axis. This is the least sterically hindered position, but since the actual regions of paramagnetic and diamagnetic shielding around the nitro group are not known no definitive statement can be made at this time regarding hindrance to rotation.

The doublet at $\tau = 7.42$, therefore, consists of the superimposed signals of the equatorial hydrogens at C-2 and C-6, each signal being split into a doublet by the axial hydrogen on the same carbon atom, $J_{2,2} = J_{6,6} = 11.6$ c.p.s., a coupling constant which is slightly less than that observed for the methylene group in 21-acetoxy-20-one steroids[6] and in good agreement with the calculated and observed values in deuterated methane.[7] The fairly well defined doublet could not be due to the axial hydrogens on C-3 and C-5 because each is adjacent to two other axial and two equatorial hydrogen and

(2) (a) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. C. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958); (b) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill, 1959, Chap. 14; (c) A. C. Huitric and J. B. Carr, *J. Org. Chem.*, **26**, 2648 (1961); (d) A. C. Huitric, W. G. Clarke, Jr., K. Leigh, and D. C. Staiff, *J. Org. Chem.*, **27**, 715 (1962).

(3) L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, 1959, pp. 121–125.

(4) L. Crombie and J. W. Lowen, *Proc. Chem. Soc.*, 229, August 1961.

(5) (a) Ref. 3, Chap. 2 and 7; (b) J. A. Pople, *Proc. Roy. Soc.*, A **239**, 541, 550 (1957); (c) C. E. Johnson, Jr., and F. A. Bovey, *J. Chem., Phys.* **29**, 1012 (1958).

(6) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

(7) H. S. Gutowsky, M. Karplus, and D. M. Grant, *J. Chem Phys.*, **31**, 1278 (1959).

the resulting signal would be a multiplet with a width of about 30 c.p.s.

The nitro compounds were obtained by the oxidation of 4-*tert*-butylcyclohexanone oxime by the method described by W. D. Emmons and A. S. Pagano for the oxidation of cyclopentanone oxime.[8] The product was distilled and collected in one fraction, b.p. 70–90° at 0.4 mm. Analysis by gas chromatography gave 40% *trans*- and 18% *cis*-4-*tert*-butylnitrocyclohexane plus 42% of 4-*tert*-butylcyclohexanone. The yield of the combined nitro isomers was about 33% of theoretical. The ketone was removed by treatment with Girard T reagent and the nitro isomers were separated by recrystallization; m.p. 72.5–73.5° for the *cis*-isomer and 27–27.5° for the *trans*. *Anal.* Calcd. for $C_{10}H_9NO_2$: C, 64.83; H, 10.34; N, 7.56. Found for *cis* isomer: C, 65.07; H, 10.42; N, 7.78; and *trans* isomer: C, 64.92; H, 10.26; N, 7.51. Analysis by gas chromatography was accomplished using a 5 ft × 1/4 in. column packed with 20% Dow Corning Silicone QF-1 on acid-washed Chromosorb W[9] at 150°.[10] Commercial acid-washed Chromosorb W caused some isomerization of the *cis* isomer. Isomerization was prevented by treating the prepared packing (20% QF-1 on acid-washed Chromosorb W) with hydrochloric acid. The packing material was stirred in 6 *N* hydrochloric acid for 5 hr., filtered, and dried at 110° for 12 hr. No isomerization resulted when Fluoropak was used as the solid support.

The long range shielding effect of the nitro group and of the *tert*-butyl group on the other hydrogen atoms of the ring is being investigated through selectively deuterated compounds.

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RECEIVED JANUARY 2, 1962

(8) W. D. Emmons and A. S. Pagano, *J. Am. Chem. Soc.*, **77**, 4557 (1955).

(9) Wilkens Instrument & Research, Inc., Walnut Creek, Calif.

(10) See Aerograph Research Notes, fall issue, 1961, published by Wilkens Instrument & Research, for example of separation of these isomers using Dow QF-1.

The Reduction of Alkyl Halides by Sodium Borohydride under Solvolytic Conditions—Evidence for the Trapping of Carbonium Ions by Borohydride

Sir:

We wish to report that the solvolysis of readily ionizable secondary and tertiary organic halides in the presence of sodium borohydride results in the formation of the corresponding hydrocarbons in excellent yields. Evidently, under these conditions the borohydride serves to trap the carbonium ions formed in the ionization of the alkyl derivatives.

$$RX \longrightarrow R^+ + X^-$$

$$R^+ + BH_4^- \longrightarrow RH + BH_3$$

The nucleophilic properties of the complex hydrides, such as lithium aluminum hydride and sodium borohydride, have long been recognized.[1-4] The reaction of alkyl halides and alkyl sulfonates exhibits typical SN2 characteristics. Thus the reaction proceeds with an inversion of configuration at the reaction center,[1,2] and the rate decreases from primary to secondary to tertiary, the tertiary halides yielding olefins predominantly.[5]

In the course of studying the reaction of sodium borohydride with alkyl halides in diglyme solution, we observed that the reaction with readily ionizable halides, such as benzhydryl chloride, is quite slow. However, the addition of water to the system markedly increases the rate of reaction and results in the formation of diphenylmethane in good yield. For example, in 100% diglyme at 45° there was realized only a 6% yield of diphenylmethane after 4 hr. from a reaction mixture which was 0.25*M* in benzhydryl chloride and 1.80*M* in sodium borohydride. On the other hand, by utilizing an aqueous medium, 20% water–80% diglyme (by volume), the reaction rate was 60-fold greater. Under these conditions, a 72% yield of diphenylmethane was realized in the same time.

In 80% aqueous diglyme, benzhydryl chloride undergoes solvolysis at 45° with a first-order rate constant of 1.34×10^{-4} sec.$^{-1}$. The rate constant for the reaction in the presence of the sodium borohydride is slightly greater, 2.1×10^{-4} sec.$^{-1}$. The slight increase is presumably due to the salt effect of the sodium borohydride. However, the similarity of the rate constants supports the conclusion that both reactions involve the same initial rate-determining step, the ionization of the benzhydryl chloride, followed by a fast reaction of the carbonium ion with the solvent to form benzhydrol, or with borohydride ion to form diphenylmethane.

The above experiments were carried out utilizing concentrations which permitted maintenance of homogeneous conditions. However, this factor is not important for reactions carried out primarily for synthetic purposes. Accordingly, the following conditions were utilized for investigating the utility of this reaction as a means of reducing readily ionizable halides and sulfonate esters: 50°, 65 vol. % diglyme, 0.5*M* in organic derivative, 4.0*M* in sodium borohydride and 1.0*M* in sodium hydroxide (to minimize hydrolysis of the borohydride).

Under these conditions benzhydryl chloride was converted into diphenylmethane in a yield of

(1) E. L. Eliel, *J. Am. Chem. Soc.*, **71**, 3970 (1949).

(2) G. K. Helmkamp and B. F. Rickborn, *J. Org. Chem.*, **22**, 479 (1957).

(3) D. J. Malter, J. H. Wotiz, and C. A. Hollingsworth, *J. Am. Chem. Soc.*, **78**, 1311 (1956).

(4) H. C. Brown and P. A. Tierney, *ibid.*, **80**, 1552 (1958).

(5) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, 1956, p. 889.

94%. Similarly, triphenylmethyl chloride formed triphenylmethane in a yield of 96%, and 2-phenyl-2-chloropropane yielded cumene in a yield of 82% (with 8% olefin and 8% of the tertiary alcohol).

The results were less favorable with 1-methyl-1-chlorocyclopentane, where a yield of 40% of methylcyclopentane was realized. The formation of 1-methylcyclopentene, 48%, represents an important side reaction. Similarly, cyclooctyl tosylate was converted into 40% cyclooctane, 49% cyclooctene, and 11% cyclooctanol.

It appears from these results that the reaction will be especially useful for those derivatives which yield relatively stable carbonium ions. However, we hope that further study will make it possible to increase the yields realized with those derivatives which provide less stable carbonium ions. The simplicity of the reaction products should also be of value in utilizing the reaction to explore the nature of carbonium ions in solvolytic media.

The following procedure is representative. In a stirred 200-ml. flask, maintained at 50°, was placed 15.1 g. (0.40 mole) of sodium borohydride, 4.0 g. (0.10 mole) of sodium hydroxide, 65 ml. of diglyme, and 35 ml. of water, followed by 7.74 g. (0.050 mole) of *t*-cumyl chloride. After 1 hr., 20 ml. of water was added, the upper layer separated, and the lower layer extracted four times with 15 ml. portions of petroleum ether (b.p. 35–37°). The combined extracts were washed with water, dried, and analyzed by gas chromatography. The analysis indicated 82% cumene, 8% of α-methylstyrene, and 8% phenyldimethylcarbinol.

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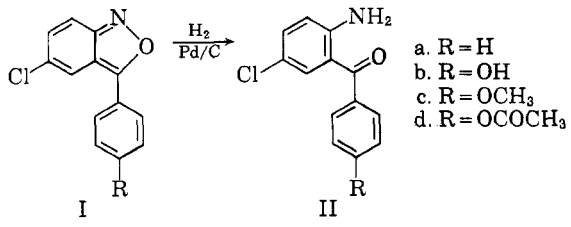
RECEIVED MARCH 12, 1962

Hydrogenation of Anthranils

Sir:

The reduction of phenylanthranils, by means of metal-acid combinations, to *o*-aminobenzophenones[1,2] has been reported, but this process is less convenient and efficient than one which has now been found useful for the same purpose, namely hydrogenation in the presence of palladium catalyst, which accomplishes the change essentially in *quantitative* yield. The improved method would appear to be significant in view of the recently increased importance of *o*-aminobenzophenones as pharmaceutical intermediates[3] and of the now greater availability of 3-phenylanthranils.[4]

At a pressure of *ca.* three atmospheres and temperatures ranging 40–60°, hydrogenations of 3-arylanthranils were carried out in the presence of 10% palladium-on-charcoal, the scale of the operation being limited only by solubility of the materials in solvent used (ethyl acetate). After uptake of approximately one molecular equivalent of hydrogen, absorption ceased or slowed abruptly, and evaporation of the filtered solutions afforded practically pure amino ketones, as follows:

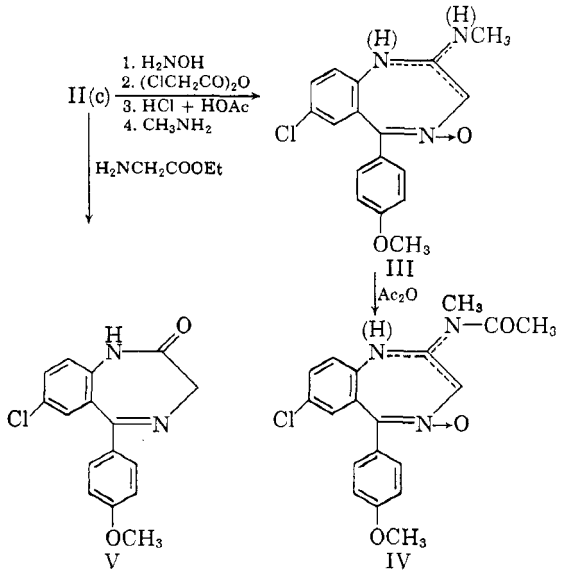


I II

3-Phenyl-5-chloroanthranil (Ia),[4] m.p. 114–116°, gave IIa,[3a,5] m.p. 98–100°, also characterized by preparation of corresponding oxime[3a] (α-form, m.p. 168–170°; β-form, m.p. *ca.* 130°), hydrazone (m.p. 134–135°; *Anal.* Found: C, 63.29; H, 4.97; N, 16.91) and by sodium borohydride reduction to corresponding aminocarbinol (m.p. 104–105.5°; *Anal.* Found: C, 67.05; H, 5.24; N, 5.90), as well as by a number of new derivatives of these, to be described later. Compound Ib,[1,2] m.p. 239° dec., λ_{max}^{Nujol} 3.05 and 3.20 (broad, bonded), 6.19 and 6.27 μ, as well as the corresponding *p*-methoxy (Ic)[2] (m.p. 144–145°) and *p*-acetoxy[1] (Id) (m.p. 172–173°) phenyl-5-chloroanthranils gave in the same way respective aminobenzophenones IIb[1] (m.p. 173–175°), IIc[2] (m.p. 100–101.5°), and IId (m.p. 127–129°; *Anal.* Found: C, 62.29; H, 4.27; N, 4.72; λ_{max}^{Nujol} 2.86, 2.95, 5.66, 6.07, 6.18, 6.23, and 6.47 μ). Both IIb and IId were converted by boiling acetic anhydride to the *N,N,O*-triacetate, m.p. 142.5–144.5°; *Anal.* Found: 61.19; H, 4.49; N, 3.72; λ_{max}^{Nujol} 5.65, 5.79, 5.88, 5.97, and 6.24 μ; $\lambda_{max}^{C_2H_5OH}$ 259 mμ (ε 12,820), apparently the same compound reported earlier[1] (incorrectly) as an *O,N*-diacetate. Compound IIc has been further characterized by similar preparation of the *N*-acetate (m.p. 151–152°; *Anal.* Found: C, 62.96; H, 4.67; N, 4.50; λ_{max}^{Nujol} 3.08, 6.06 and 6.29 μ), the *N,N*-diacetate (m.p. 120.5–122°; *Anal.* Found: C, 62.69; H, 4.89; N, 3.95; λ_{max}^{Nujol} 5.82, 6.03, 6.21, and 6.33 μ), the corresponding hydrazone (m.p. 141–142°; *Anal.* Found: C, 60.84; H, 5.18; N, 15.11) and its derivatives, the corresponding oxime (m.p. 168–169.5°; *Anal.* Found: C, 60.63; H, 4.71; N, 9.92), and by sodium borohydride reduction to the corresponding aminocarbinol (m.p. 107–109°; *Anal.* Found: C, 64.0; H, 5.37; N, 5.17); the oxime of IIc has been converted, *via* the now familiar series of steps[3b]

(1) T. Zincke and K. Siebert, *Ber.*, **39**, 1930 (1906).
(2) J. C. E. Simpson and O. Stephenson, *J. Chem. Soc.*, 353 (1942).
(3) (a) L. H. Sternbach, S. Kaiser, and E. Reeder, *J. Am. Chem. Soc.*, **82**, 475 (1960); (b) L. H. Sternbach, *et al.*, *J. Org. Chem.*, **26**, 1111, **4488**, 4936 (1961).
(4) R. B. Davis and L. C. Pizzini, *J. Org. Chem.*, **25**, 1884 (1960).
(5) F. D. Chattaway, *J. Chem. Soc.*, 340 (1904).

through the *N*-chloroacetate[6] (m.p. 142–143°) and the 2-chloromethylquinazoline 3-oxide (m.p. 151–153°; *Anal.* Found: C, 57.30; H, 3.59; N, 8.21), to compound III (m.p. 247–249°; *Anal.* Found: C, 61.69; H, 5.02; N, 12.48; λ_{max}^{Nujol} 3.12, 3.27, 6.14, 6.21, and 6.28 μ; $\lambda_{max}^{C_2H_5OH}$ 259 and 324 mμ with ϵ 40,520 and 9710, respectively), which was further *N*-monoacetylated to IV (m.p. 218.5–219.5°; *Anal.* Found: C, 61.35; H, 4.92; N,

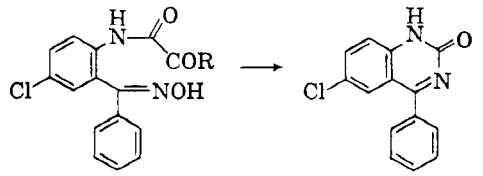


11.03) in which the presence of an infrared NH peak (λ_{max}^{Nujol} 3.05, 5.74, 6.14, and 6.23 μ) shows the seven-membered structure to be correct and excludes the nontautomeric, alternative quinazoline formulation. The amino ketone IIc was also converted by condensation with glycine ethyl ester (pyridine) to the benzdiazepinone V,[6] m.p. 216–218°.

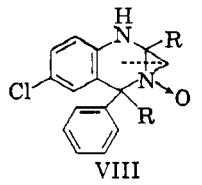
A modification in the somewhat capricious, reported procedures[4,7] for condensing substituted nitrobenzenes with arylacetonitriles, namely *isolation* of the *potassium salts* of intermediate cyanobenzylidenecyclohexadieneone oximes *before treating with water* (or aqueous acids) has led to significant improvement in the reliability[8] of, and eliminated the need for low temperatures in, preparation of arylanthranils and isonitroso compounds by this method.

The present hydrogenation method, also very useful in reduction of aromatic nitro compounds,[9] can be applied equally well in reduction of *p*-cyanobenzylidenecyclohexadienone oximes, now available in abundance,[7] to other substituted anilines, as for example, *p*-aminophenylphenylacetonitrile, m.p. 71° (*N-acetate*, m.p. 90°; *Anal.* Found: C, 76.5; H, 5.9; N, 11.4; λ_{max}^{Nujol} 2.99, 4.43, and 5.99 μ).

NOTE ADDED IN PROOF. The fact that compound VI, R = Cl (corresponding R = $NHCH_3$: m.p. 258°; *Anal.* Found: C, 58.15; H, 4.39; N, 12.4; λ_{max}^{Nujol} 2.98, 3.10, 5.96, and 6.05 μ) and congeners cyclize ($POCl_3$; decarboxylation and *N*-oxide transfer) to VII (m.p. 185°; *Anal.* Found: C, 65.45; H, 3.56; N, 10.72; λ_{max}^{Nujol} 5.97, 6.20, and



6.26 μ) and cannot be converted (acids or bases) to benzdiazepindiones, indicates that the transformation[3b,6] of 2-chloromethyl-4-aryl-6-chloroquinazoline-3-oxides to 5-aryl-7-chloro-1,3-dihydro-1,4-benzdiazepinone-4-oxides involves intermediate formation and subsequent reopening (dotted line) of the species VIII (R = OH, CH_3 or $NHCH_3$),



rather than direct opening of six-, followed by reclosure to seven-, membered ring.

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RECEIVED FEBRUARY 19, 1962

(6) S. C. Bell, T. S. Sulkowski, C. Gochman, and S. J. Childress, *J. Org. Chem.*, **27**, 562 (1962).

(7) R. B. Davis, L. C. Pizzini, and J. D. Benigni, *J. Am. Chem. Soc.*, **82**, 2913 (1960); R. B. Davis, L. C. Pizzini, and E. J. Bara, *J. Org. Chem.*, **26**, 4270 (1961).

(8) I wish to acknowledge the assistance of Miss Barbara N. Weaver in these preparations.

(9) G. N. Walker, *J. Am. Chem. Soc.*, **77**, 3844 (1955); **78**, 3698 (1956); *J. Org. Chem.*, **25**, 484 (1960); **26**, 4441 (1961).

The Structure of Isopimaric Acid

Sir:

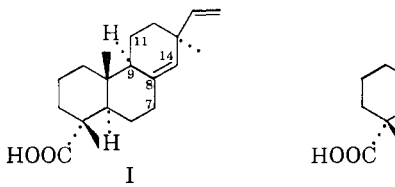
Isopimaric acid has been shown to have the same carbon skeleton, except for stereochemical differences, as pimaric acid I.[1] The nuclear double bond location had apparently been proven to be the same in the two acids,[2] and on this basis the structure and stereochemistry shown in II were assigned to isopimaric acid.[1,3] However, the

(1) (a) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959); (b) *ibid.*, *Chem. and Ind.*, 537 (1959); (c) E. Wenkert and J. W. Chamberlain, *J. Am. Chem. Soc.*, **81**, 688 (1959).

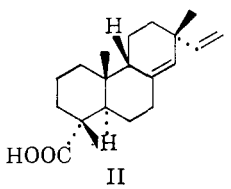
(2) G. C. Harris and T. F. Sanderson, *J. Am. Chem. Soc.*, **70**, 2081 (1948).

(3) (a) B. Green, A. Harris, and W. B. Whalley, *J. Chem. Soc.*, 4715 (1958); (b) A. K. Bose, *Chem. and Ind.*, 1105 (1960).

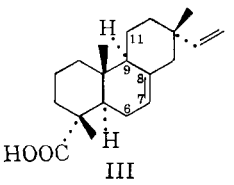
outstanding synthetic work of Church and Ireland[4] has shown that the pimaradiene prepared from isopimaric acid is different from any of the four possible pimaradienes with 8(14)-double bonds. They hence suggested that this acid had structure III. We now present proof that the double bond is in the 7(8)- position and hence that isopimaric acid is correctly represented by III.



I

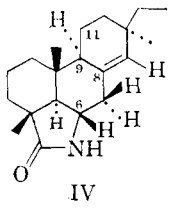


II

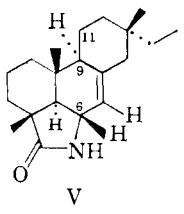


III

Hydration of the double bond of methyl dihydroisopimarate using the method of Brown and colleagues,[5] followed by oxidation with sodium dichromate in acetic acid gave a keto ester, m.p. 81° $[\alpha]_D$ +10°: C, 75.62; H, 10.16. The presence in the NMR spectrum of this ester of signals for three hydrogens α to the ketone carbonyl between τ = 7.5 and 8.2) located this function on C-7 or C-11, corresponding to original double bond locations at the 7(8) and 9(11)- positions, respectively. Choice was made between these on the basis of the NMR spectra of the two lactams IV (m.p. 210°, $[\alpha]_D$ 7°): C, 79.82; H, 10.51; and V (m.p. 198° $[\alpha]_D$ 32°): C, 79.91; H, 10.17, prepared by photolysis of the azides of dihydropimaric and dihydroisopimaric acids, respectively.[6]



IV



V

In both cases the vinyl hydrogen signal was unsplit, but in the case of V it was broadened (half-band width 6 c.p.s.) due to coupling with the adjacent tertiary hydrogen. The most significant difference between the spectra was the broadened doublet character of the signal for the 6-hydrogen of V (at τ 6.2) as contrasted with the multiplet due to this hydrogen in IV (at least 6 lines discernible at 60 Mc). Since the isomer with a 9(11)-double bond would give a 6-hydrogen pattern similar to that of IV, the double bond location is proven.

Correspondence between the plain O.R.D. curve for dihydroisopimaric acid[7] and 5-cholestene[8] is evidence for the α-orientation of the 9-hydrogen. Proof of this configuration is described by Ireland and Newbould in an accompanying communication.[9]

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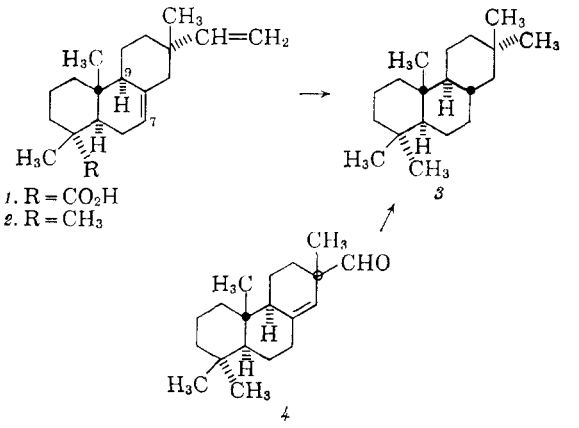
RECEIVED FEBRUARY 20, 1962

(4) R. F. Church and R. E. Ireland, *Tetrahedron Letters*, 493 (1961).
(5) H. C. Brown, *Tetrahedron*, **12**, 117 (1961).
(6) (a) J. W. ApSimon and O. E. Edwards, *Proc. Chem. Soc.*, 461 (1961); (b) *ibid.*, *Can. J. Chem.*, in press.
(7) A. K. Bose and W. A. Struck, *Chem. and Ind.*, 1628 (1959).
(8) C. Djerassi, W. Clossen, and A. E. Lipman, *J. Am. Chem. Soc.*, **78**, 3163 (1956).
(9) R. E. Ireland and J. Newbould, following communication. We are grateful to Dr. Ireland for informing us of his results prior to publication.

The Stereochemistry of Isopimaric Acid[1]

Sir:

The recently recorded[2] synthesis of the *dl*-9-isopimaradienes brought to light the earlier incorrect structural assignment[3] made for isopimaric acid. Neither of the synthetic dienes is identical with isopimaradiene, a simple degradation product of the acid that differs *only* in that the C-4 carboxyl grouping has been reduced to a methyl group. The suggestion[2] was made at that time that isopimaric acid, and hence isopimaradiene, could best be represented by the structures (1) and (2),



1. R = CO_2H
2. R = CH_3

3

4

respectively. In an accompanying communication, Edwards and co-workers[4] have elegantly established the Δ^7 double bond assignment for isopimaric acid, and we here present evidence that establishes the α-orientation for the 9-hydrogen—

(1) The support of the National Science Foundation in the form of a grant (G-19841) is gratefully acknowledged.
(2) R. F. Church and R. E. Ireland, *Tetrahedron Letters*, 493 (1961).
(3) G. C. Harris and T. F. Sanderson, *J. Am. Chem. Soc.*, **70**, 2081 (1948).
(4) W. Antkowiak, J. W. ApSimon, and O. E. Edwards, preceding communication.

the only remaining untested[2] portion of the structure (1).

Oxidation of isopimaradiene (2) with one equivalent of osmium tetroxide and then cleavage of the resulting diol (periodic acid) afforded a crude aldehyde which gave a 51% overall yield of semicarbazone (m.p. 222–223.5° dec; C, 72.37; H, 12.75; N, 10.29). On treatment of this semicarbazone with potassium hydroxide in refluxing diethylene-glycol, there resulted an 82% yield of 13,13-dimethyl-Δ^7-podocarpene (m.p. 29–31°; C, 87.51; H, 12.23). That this olefin still contained the same carbon skeletal pattern of isopimaric acid (1) was shown by the characteristic 860-, 835-, and 820- cm.$^{-1}$ infrared bands present in both compounds, as well as isopimaradiene (2).

The olefin was converted in 67% yield after chromatography on basic alumina to 13,13-dimethyl-7-podocarpanone (m.p. 151–151.5°; C, 82.43; H, 11.77) by hydrobroration and then oxidation.[5] The hydrocarbon (3) (m.p. 53.5–54°; C, 86.77; H, 12.82) was then available in a 78% overall yield by Raney nickel desulfurization of the crude dithioketals obtained with ethanedithiol.[6]

An authentic sample of the racemate of this hydrocarbon was available from the epimeric mixture of aldehydes (4) previously related to sandaracopimaradiene and pimaradiene in these laboratories.[7] Thus, 13,13-dimethyl-$\Delta^{8(14)}$-podocarpene (evap. dist. at 90° (0.02 mm.); C, 87.48; H, 12.41), obtained in 88% yield from the mixture of aldehydes by Wolff-Kishner reduction,[8] was transformed to 13,13-dimethyl-14-podocarpanone (m.p. 58–60°; C, 82.45; H, 11.70) in 70% yield by the hydroboration-oxidation sequence.[5] Ketalization[6] of this ketone with ethanedithiol and then Raney nickel disulfurization of the resulting dithioketal (m.p. 210–212°; C, 71.43; H, 10.11) afforded a 74% over-all yield of the racemic modification of the hydrocarbon (3) (evap. dist. at 75° (0.02 mm.); C, 87.15; H, 12.74). That this racemic hydrocarbon was identical with that obtained above from isopimaric acid (1) was demonstrated by comparison of their infrared spectra. In view of the known stereochemistry[7] of the synthetic hydrocarbon, this evidence confirms the suggested α-orientation of the 9-hydrogen in isopimaric acid (1).

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(5) H. C. Brown, *Tetrahedron*, **12**, 117 (1961).
(6) L. F. Fieser, *J. Am. Chem. Soc.*, **76**, 1945 (1954).
(7) R. E. Ireland and P. W. Schiess, *Tetrahedron Letters*, No. 2., 37 (1960).
(8) Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1948).