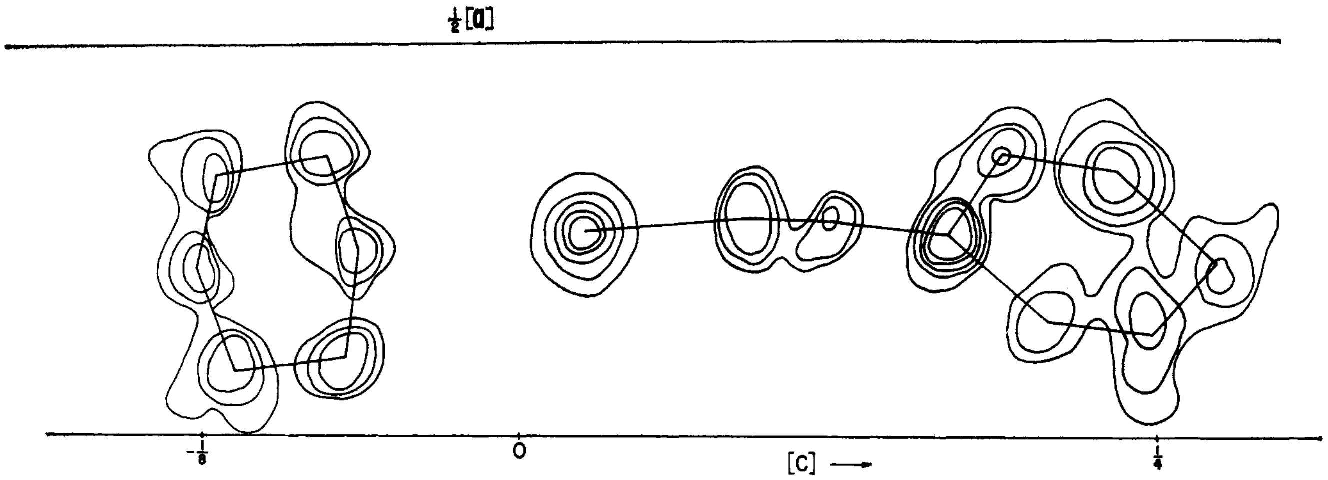

Fig. 1.—Electron density projection of the $C_{12}H_{14}ONI$ complex; contour levels 1/Å.^{2} starting at three, for C, N, O; contour levels 20e/Å.^{2} for I, starting at ten.

atomic coordinates calculated from the Fourier projection, there was one significant phase change and a better agreement factor of $R = 0.18$ was obtained. The slight apparent departure from linearity of the side-chain portion of iodophenylacetylene which is indicated in Fig. 1 may represent experimental error.

Southwick and Kirchner proposed structures I, II, or III for the compound $C_{12}H_{14}ONI$. After considering the results of hydrogenation or reduction with lithium aluminum hydride, and the infrared, ultraviolet, and nuclear magnetic resonance spectra, they concluded that I is most probably the correct structure. However, owing to the instability of the compound, they regarded their structure determination as inconclusive and suggested this X-ray structure determination.

The exclusion of formulas II and III is unambiguous on the basis of the Fourier projection shown in Fig. 1. The only alternatives to formula I which remain would be others of the same geometry as I but having the iodine atom adjacent not to the nitrogen of the morpholine structure, but to a different atom, such as the oxygen.

The existence of other charge transfer complexes in which a basic nitrogen is coordinated with the iodine of an organic iodide[2] suggests that formula I is indeed the correct representation of the substance. Bjornvatten and Hassel[2] found the length of the iodine–nitrogen bond in the quinoline–iodoform complex to be 2.99 Å. The iodine to nitrogen distance in the Fourier *projection*, shown in Fig. 1, is 2.51 Å., which is compatible with an *actual* distance of about 2.9 Å.

An isotropic temperature factor of 2.5 Å.$^{-2}$ was assumed for the iodine and one of 4.0 Å.$^{-2}$ for the light atoms.

Experimental

Owing to the instability of the compound and the frequency of twinning, much difficulty was experienced in obtaining a crystal suitable for X-ray diffraction intensity measurements. A small untwinned crystal, grown by slow evaporation of a normal hexane solution, was sealed in a 0.3-mm. glass capillary. Upon exposure to X-rays for about 80 hr., some decomposition was indicated by a color and shape change of the crystal and by a spread of the diffraction spectra.

The intensity measurements were made visually from CuKα multifilm Weissenberg photographs. For many high angle reflections the CuKα_1 and CuKα_2 spectra were completely resolved. For these reflections the intensity of the CuKα_1 reflection was measured and multipled by a factor of 1.5. For partially resolved reflections a linear interpolation method due to Sakurai[3] was used. After interfilm scaling and averaging of resulting intensity values, the 292 observed ($h0l$) intensities were reduced to structure factor amplitudes by the standard Lorentz and polarization corrections. About 36 reflections were observed to have intensities too small to be measured and these were arbitrarily assigned a value of one-third of the weakest intensity measureable. No absorption corrections were applied to the data. The computations were carried out on an IBM 1620 computer using the programs of Shiono, Hall, and Chu,[4] and of Beurskens.[5]

Acknowledgment.—The author would like to thank Professor P. L. Southwick for suggesting the problem and for providing the crystals; Dr. R. McMullan and Professor G. A. Jeffrey for their valuable help and criticism; and the U. S. Public Health Service for the financial support of this undergraduate summer work.

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The Cuprous Chloride-Catalyzed Reaction of Diazomethane with Norbornene Derivatives

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The cuprous ion-catalyzed reaction of diazomethane with olefins recently has been applied in syntheses of cyclopropyl compounds from a number of cyclic hydrocarbons.[1] The intermediate in this catalyzed reaction is also reactive enough to form cyclopropyl derivatives or homologs directly from aromatic compounds.[1,2] We should like to report the stereochemistry of this reaction with regard to formation of cyclopropyl compounds

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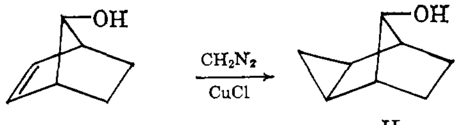
from derivatives of norbornene and report the utility of this reaction in a case where the widely used Simmons–Smith synthesis[3] (involving reaction of olefin with methylene iodide–zinc copper couple) has given poor results.

Passage of a stream of nitrogen gas containing diazomethane through a solution of *anti*-7-norbornenol (I) in ether at 0° in the presence of cuprous chloride resulted in formation of *anti*-8-tricyclo[3.2.1.0^{2,4}]octanol (II), m.p. 75–76°, in 40% yield after recrystallization. The presence of a cyclopropyl ring in II is indicated by an infrared absorption band at 1040 cm.$^{-1}$.[4] More specifically, this group was indicated by two complex n.m.r. multiplets centered at τ 9.4 and 10.04 and corresponding to three hydrogens and one hydrogen, respectively.[5]



I

II

The formation of *exo* product in the addition of a methylene unit to norbornene by the Simmons–Smith procedure has been inferred[3,6,7] on the basis of preferred direction of approach to norbornene.[8] The *exo* configuration of the cyclopropyl methylene group in II has been established by an X-ray crystallographic analysis[9] on the *p*-bromobenzenesulfonate of II. No *endo* isomer was isolated from the reaction although an unknown substance was present in the crude product to the extent of 9% (gas–liquid phase chromatographic analysis).

The Simmons–Smith reaction intermediate does not react with aromatic systems, and it is stereoselective in its reaction with norbornene.[1,3,6] The formation of predominate *exo* product (II) in the cuprous ion–diazomethane reaction indicates that, although the intermediate is active enough to react with aromatic systems, it still is selective in its approach to the norbornene double bond. Catalyzed reaction of diazomethane with 7-norbornadienyl acetate resulted in a methylene addition product which is a mixture of isomers as indicated by distinct sets of n.m.r. absorption for different olefinic and acetate hydrogens. Like copper-catalyzed reactions of other diazo compounds, the intermediate from cuprous ion and diazomethane appears to be discriminate in its direction of approach to olefins, but it has low discriminating ability between two olefinic bonds.[10]

All of our earlier attempts to prepare II by the Simmons–Smith procedure failed; however, it recently has been obtained by this method in quantities too small to be fully characterized.[7] Although the Simmons–Smith reaction is subject to directive[11] and accelerative[12] influences of hydroxyl groups close to the double bond of olefinic alcohols, the configuration of alcohol I is *anti* and the hydroxyl group is prevented sterically from lending aid to the formation of a cyclopropyl ring. Instead, the iodomethylzinc iodide apparently is destroyed by the alcohol in a side reaction.[11] In contrast, the cuprous chloride-catalyzed reaction of diazomethane I readily occurs.

The possibility of "forcing" this catalyzed reaction to completion by continued addition of diazomethane, while monitoring the result by gas–liquid phase chromatography of samples taken during the reaction, leads to easy isolation of relatively pure product. This feature of the reaction and its simplicity suggests that it may be generally useful, especially in cases where the Simmons–Smith reaction fails or occurs only in low yields.

The solvolytic reactivity of the *p*-bromobenzenesulfonate ester of alcohol II is being studied as a measure of participation of the cyclopropyl group in carbonium ion formation at the 7-position of the bicyclo[2.2.1]-heptane ring structure.

Experimental

General Procedure.[13]—The diazomethane generator[14] consisted of a 250-ml. three-necked flask, in an ice bath, containing 45 ml. of a magnetically stirred 50% potassium hydroxide solution. Diethyl ether (100 ml.) formed an upper layer in the flask. Addition of N-methyl-N-nitrosurea, in approximately 1-g. lots, generated diazomethane which dissolved in the ether layer. This addition was carried out over several hours during the reaction so that at no time was there a very high concentration of diazomethane in the ether; the yellow color of the solution acted as a guide to concentration. A continuous stream of nitrogen was bubbled through the ether layer. This carried the diazomethane through a drying tube (KOH pellets) and through an inlet tube to the bottom of a solution of olefin in ethyl ether. This solution, containing *ca.* 0.3 g. of suspended cuprous chloride (B.D.H.,[15] A.R. grade) was in a 50-ml. flask fitted with a magnetic stirrer and a water condenser. This reaction flask was cooled also in an ice bath. No attempt was made to retain high concentrations of diazomethane in the reaction flask by condensing the leaving vapors at Dry Ice temperature. Although this is wasteful of diazomethane, the danger of explosions is, in our experience, eliminated. Ether was replenished in the generator flask and in the reaction flask as it was swept out by the nitrogen stream. The progress of the reaction was monitored by gas–liquid chromatography of the ether solution and the generation of diazomethane continued until the olefin was consumed. Initial experiments with norbornene as substrate yielded the known[3] tricyclo[3.2.1.0^{2,4}]octane, however 2-norbornanol was formed in one run where water was present in the reaction flask.

Preparation of *anti*-8-Tricyclo[3.2.1.0^{2,4}]octanol (II).—Diazomethane generated from 8.87 g. of N-methyl-N-nitrosurea reacted with 3.3 g. of *anti*-7-norbornenol[15b] in 40 ml. of ether containing 0.3 g. of cuprous chloride. After 6 hr., the olefin was completely consumed and two major products (ratio of 10:1) were indicated by g.l.p.c. After filtration to remove cuprous chloride and evaporation of the ether, crystallization from petroleum ether (b.p. 65–110°) yielded 1.49 g. (40% based on olefin, 14% based on diazomethane generated) of alcohol II, m.p. 75–76°. More product II was contained in the mother liquor and could be obtained pure by g.l.p.c. on an Apiazon J column at 140°.

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(13) See ref. 1 for similar procedures.

(14) F. Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y. 1943, p. 165.

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Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.25; H, 9.71.

The n.m.r. spectrum[16] of this compound in CCl_4 showed absorption at τ 6.47, 7.13, and 7.97 in ratios 1:1:2, corresponding to bridge hydrogen, hydroxyl hydrogen, and two bridgehead hydrogens. In addition, there were four complex bands centered at *ca.* τ 8.3 and 8.7 (total of four hydrogens), *ca.* 9.3 (three hydrogens), and 10.04 (one hydrogen). These correspond, respectively, to the four *exo*/*endo* hydrogens, three hydrogens of the cyclopropyl ring, and a fourth cyclopropyl hydrogen at highest field.[5]

The *p*-bromobenzenesulfonate ester of II, recrystallized from petroleum ether, melted at 83–83.5°.

Anal. Calcd. for $C_{14}H_{15}BrO_3S$: C, 48.98; H, 4.40. Found: C, 49.17; H, 4.50.

Reaction of CH_2N_2–CuCl with 7-Norbornadienyl Acetate.[15]—Reaction of diazomethane generated from 23.3 g. of N-methyl-N-nitrosurea with 9.0 g. of 7-norbornadienyl acetate over 8 hr. gave a product, separated by g.l.p.c. on a 5-ft. Ucon polar column at 110°, with analysis agreeing with addition of one methylene unit to the diolefin.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.40; H, 7.25.

The n.m.r. spectrum of this sample showed it to be *ca.* a 3:1 mixture of two compounds arising from addition to either of the double bonds of the diolefin. That is, there were triplets at τ 3.65 and 4.32 (area ratio 3:1) for olefinic hydrogens, singlets at 5.55 and 6.02 (ratio 1:3) for bridge hydrogens, multiplets centered at 7.10 and 7.65 (ratio *ca.* 3:1), peaks at 8.08 and 8.12 (ratio *ca.* 1:3) for acetate hydrogens, and a broad multiplex at *ca.* 9.0 for cyclopropyl hydrogens.

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[16] N.m.r. spectra were determined on a Varian A-60 spectrometer.

Trisarylmethanes. Synthesis of Diarylcarbinol Precursors by Controlled Catalytic Hydrogenation

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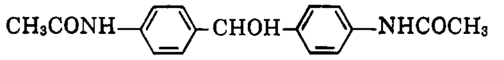
Previous studies in these laboratories[1] have demonstrated that pararosaniline pamoate and certain closely related compounds are effective in experimental schistosomiasis and paragonimiasis. Simple trisarylmethanes also have been reported to be effective against intestinal helminths, filariae, trichomonads, and trypanosomes.[2] It was, therefore, of interest to prepare various trisarylmethanes, including basically substituted compounds of structure II, for biological evaluation and for use as synthetic intermediates. The present communication describes a novel method for the preparation of selected diarylcarbinols, namely the controlled catalytic hydrogenation of the corresponding diaryl ketones, and their conversion to various trisarylmethanes.

The most attractive route to trisarylmethanes of structure II appeared to be condensation[3] of the corresponding aromatic amine[4,5] with 4,4′-diaminobenzhydrol. Wichelhaus[6] describes the conversion of 4,4′-diaminobenzophenone to the benzhydrol with sodium amalgam. This technique, however, is unattractive for large scale work. The erratic nature of this benzophenone–benzhydrol conversion with other reagents is evident from the literature. Treatment of 4,4′-diaminobenzophenone with tin and hydrochloric acid[7] or of 4-butyroylamino-4′-nitrobenzophenone with palladium and hydrogen[8] leaves the ketone function intact. Reduction of 4,4′-diaminobenzophenone with excess lithium aluminum hydride gives the hydrogenolysis product, 4,4′-methylenedianiline.[9] Numerous attempts in these laboratories to effect the reduction to the benzhydrol utilizing a variety of standard chemical and catalytic methods failed.

Efforts to convert 4′,4‴-carbonylbisacetanilide[10] to 4′,4‴-(hydroxymethylene)bisacetanilide (I) were more successful. Chemical reduction gave positive but still unsatisfactory results, whereas catalytic hydrogenation under standard conditions gave primarily the hydrogenolysis product, 4′,4‴-methylenebisacetanilide. Fortunately, application of Kindler's procedure,[11] involving the use of a palladium catalyst, poisoned with nicotinamide or N,N-diethylnicotinamide, afforded I in 63% yield. Although the carbinol exhibited a variable melting point which was an unsatisfactory criterion of purity, the ultraviolet spectrum[12] (λ 254 mμ, E_1^1 1120, no absorption over 300 mμ) afforded an excellent method for detecting residual ketone (λ 231 mμ, E_1^1 614; λ 306 mμ, E_1^1 1060) during purification. The controlled catalytic hydrogenation technique also was used successfully for the preparation of 4′,4‴-(hydroxymethylene)bistrifluoroacetanilide (61%), 4-methylbenzhydrol[13] (80%), 4-chlorobenzhydrol[14] (35%), and 4-aminobenzhydrol[9] (59%), but failed with 4-bromobenzophenone, 4-hydroxybenzophenone, 4-(dimethylamino)benzophenone, 4-hydroxybenzophenone acetate ester, 2-benzoylbenzoic acid, and 4,4′-bis(dimethylamino)benzophenone. The moderate success achieved with 4-chlorobenzophenone is noteworthy in view of the known susceptibility of



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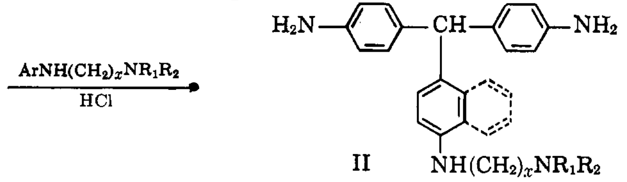

II

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