3,4-Bis(acetoxymethyl)-2,5-dihydroxy-2,5-dihydrofuran (10): yield, 86%; n^{27}D 1.4831; ir (neat) 3440, 1740 cm^{-1}; nmr (acetone-d_6) δ 5.60–6.15 (mm 2, HO–CH), 4.96, 4.60 (AB q, broad, 4, J = 13.0 Hz, CH_2), 2.04 (s, 6; CH_3).

Anal. Calcd for $C_{10}H_{14}O_7$: C, 48.8; H, 5.7. Found: C, 49.2; H, 5.7.

3,4-Bis[(2-tetrahydropyranyl)oxymethyl]-2,5-dihydroxy-2,5-dihydrofuran (11): yield, 77%; n^{23}D 1.4938; ir (neat) 3390 cm^{-1}; nmr ($CDCl_3$) δ 6.19, 5.84 (s, 2, HO–CH), 4.73 (s, broad, 4, =C–CH_2–O), 4.40 (t, 2, J = 7.0 Hz; CH_2O–CH–O), 3.25–4.20 (m, 4, O–CH_2), 1.20–2.20 (m, 12, pyranyl-CH_2).

Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.2; H, 7.9. Found: C, 57.9; H, 7.8.

Diethylmaleic Anhydride (13).[12] 3,4-Diethyl-2,5-dihydroxy-2,5-dihydrofuran (217 mg) in acetone (10 ml) was cooled to 0° and Jones reagent[2] (0.6 ml: 10 g CrO_3/8.5 ml concentrated H_2SO_4/30 ml H_2O) was added dropwise (magnetic stirring). After 30 min the reaction mixture was filtered, the filtrate was evaporated, and the residue was partitioned between water and ether. After extraction with ether, drying (Na_2SO_4), and evaporation, the residue was dissolved in dry methylene chloride and treated (4 hr) with molecular sieve (Linde 3 A). Filtration and distillation gave diethylmaleic anhydride (13) (150 mg, 71%): bp 102–104° (10 mm) (lit.[12] bp 115° (13 mm)); n^{21}D 1.4640; ir (neat) 1852, 1773 cm^{-1}; nmr ($CDCl_3$) δ 2.54 (q, 4, J = 7.5 Hz), 1.23 (t, 6, J = 7.5 Hz).

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Registry No.—1, 53059-82-8; 2, 14496-25-4; 3, 30614-73-4; 4, 52618-12-9; 5, 6372-18-5; *cis*-8, 53059-83-9; *trans*-8, 53059-84-0; *cis*-9, 53059-87-3; *trans*-9, 53109-80-1; *cis*-10, 53059-85-1; *trans*-10, 53059-86-2; 11, 53059-40-8; *cis*-12, 53059-41-9; *trans*-12, 53059-42-0; 13, 28843-39-2; 3,4-bis(hydroxymethyl)furan, 14496-24-3; thionyl chloride, 7719-09-7.

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Assay and Methylation of 2-Methyl-1,2-dihydroisoquinoline

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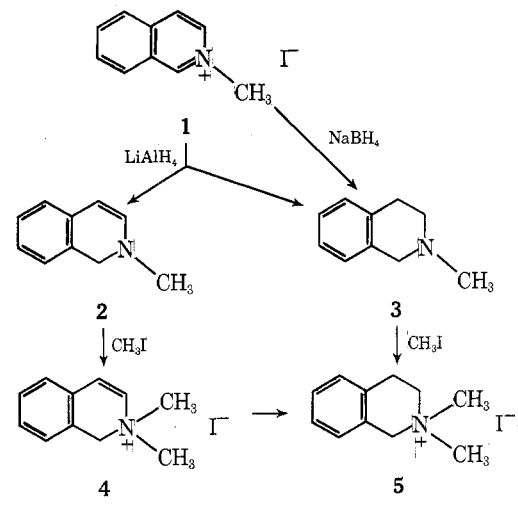
This note describes a procedure for the quantitative determination of 2-methyl-1,2-dihydroisoquinoline (2) and the course of its alkylation with methyl iodide. Dihydroisoquinoline 2 was obtained by reducing isoquinolinium methiodide (1) with lithium aluminum hydride by an optimization of the Schmid–Karrer method.[1] None of the other preparations tried were satisfactory.[2]

To determine the composition of the routinely distilled product, or more specifically the extent of overreduction to 2-methyl-1,2,3,4-tetrahydroisoquinoline (3), we developed a straightforward procedure involving dehydrogenation with excess iodine followed by iodimetric back-titration. Since the dihydroisoquinoline 2 requires 2 equiv of iodine



for aromatization while the tetrahydroisoquinoline 3 requires 4 equiv, the amount of iodine absorbed provides a reliable basis for assay. In an exploratory manner, we also investigated a spectroscopic method, which suggested that either or both of the 2-methyl-1,2-dihydroisoquinoline absorption maxima at λ_{max} (absolute C_2H_5OH) 234 and 329 nm[5] might serve as the basis for quantitative analysis. Quantitative gas–liquid chromatography was also tried but was found unreliable.

According to the iodimetric assay, the Schmid–Karrer preparation gives rise to mixtures of di- and tetrahydroisoquinoline (2 and 3), with the latter compound comprising as much as 35% of the product. One run that could not be repeated gave an exceptionally low concentration, 2%, of the tetrahydroisoquinoline. Accordingly, the tacit assumption that the Schmid–Karrer product is free of tetrahydro impurity is not warranted.[10] Whether the tetrahydroisoquinoline develops before or during the work-up was not determined. It is pertinent to note, however, that the conditions we employed, which avoided exposure to strong acid and high temperatures,[12] would not be expected to favor disproportionation of the dihydroisoquinoline.

Using starting material whose content of 2-methyl-1,2-dihydroisoquinoline (2) had been measured, we examined the reaction with methyl iodide. Only the N-alkylation product 4 was isolated. Hydrogenation of this product furnished 2,2-dimethyl-1,2,3,4-tetrahydroisoquinoline iodide (5), the same as the material obtained by methylating 2-methyl-1,2,3,4-tetrahydroisoquinoline (3).[11] Our results with the simplest alkyl group and the parent dihydroisoquinoline, therefore, agree with the tendency noted before for eneamine alkylation with alkyl halides to favor nitrogen rather than carbon.[12,13]

Experimental Section

2-Methyl-1,2-dihydroisoquinoline (2). 2-Methylisoquinolinium iodide (8.1 g; 0.030 mol) was added in one portion to a stirred suspension of lithium aluminum hydride (1.2 g; 0.030 mol) in 150 ml of ether protected with a blanket of nitrogen. The mixture was stirred at room temperature for 30 min and then quenched over 200 g of crushed ice layered with 50 ml of ether. The ether layer was separated, the solids in the aqueous phase were washed thoroughly with ether, and the combined ether layers were rinsed with portions of saturated possium chloride solution and dried. Fractional distillation gave yellow oily 2-methyl-1,2-dihydroisoquinoline (2), bp 50–60° (0.1–0.2 mm) [lit.[1,4] 60–65° bath temperature (0.03 mm); 69° (0.8 mm)], which decomposed quickly in contact with air and was stored routinely under nitrogen. The product, obtained in 70% yield, contained 65–80% dihydro- and 35–20% tetrahydroisoquinoline 3 by iodimetric analysis. Variations in these directions improved neither the yield nor the content of the desired dihydroisoquinoline.

2-Methyl-1,2,3,4-tetrahydroisoquinoline (3).[11] 2-Methylisoquinolinium iodide (5.4 g; 0.020 mol) was reduced with sodium borohydride (5.0 g; 0.13 mol) in 500 ml of methanol plus 10 ml of water essentially as described in the literature.[11] 2-Methyl-1,2,3,4-tetrahydroisoquinoline (2.5 g; 86%) was obtained as a colorless oil, bp 55–58° (0.5 mm). The hydrochloride melted at 226–228° [lit.[14] 228°].

Iodimetric Analysis for Dihydroisoquinoline. Freshly distilled material was used routinely for the assay, which was done under nitrogen. A carefully weighed sample (50–100 mg) of the reduced isoquinoline was dissolved in 10 ml of absolute alcohol and was transferred quantitatively with the help of several 2-ml volumes of solvent to 20.0 ml of a standardized solution of iodine (0.5–1.0 g) in absolute ethanol. The mixture in a stoppered flask was stirred magnetically for 40 min at room temperature. Solid potassium iodide (1.0 g) and sodium bicarbonate (0.5 g) were then introduced followed by 100 ml of water and an excess of standard 0.1 *N* sodium thiosulfate. After 10 min of stirring, the colorless solution was back-titrated with standard iodine to a pale-blue starch end point.

When pure 2-methyl-1,2,3,4-tetrahydroisoquinoline was analyzed with this procedure, it required 2.02 ± 0.01 mol of iodine per mole of substrate. Pure 2-methyl-1,2-dihydroisoquinoline, if available, would consume 1.00 mol of iodine per mole. One exceptional batch of dihydroisoquinoline required 1.02 ± 0.03 mol and so was practically homogeneous. All other samples absorbed between 1 and 2 mole of iodine per mole, from which result the composition could be directly obtained.

2,2-Dimethyl-1,2-dihydroisoquinolinium Iodide (4). Methyl iodide (3.0 g; 0.02 mol) was added slowly to a stirred solution of 2-methyl-1,2-dihydroisoquinoline (1.5 g) in 5 ml of acetonitrile. The mixture was stirred under nitrogen at room temperature for 1 day. The yellow precipitate was collected, washed with a little alcohol, and dried to give the 2,2-dimethyl compound **4** (1.0 g), mp 158.5–159.5°. Crystallization from ethanol did not change the melting point.

Anal. Calcd for $C_{11}H_{14}IN$: C, 46.01; H, 4.91; I, 44.19; N, 4.88; $(CH_3)_2N$, 10.45. Found: C, 46.00; H, 5.00; I, 44.35; N, 5.00; *N*-methyl, 10.43.

2,2-Dimethyl-1,2,3,4-tetrahydroisoquinolinium Iodide (5) from Tetrahydroisoquinolinium Iodide (3). A solution of 2-methyltetrahydroisoquinoline (0.3 g) and methyl iodide (0.35 g) in benzene (5 ml) was refluxed for 5 min. The solid deposited from the cooled mixture was crystallized from alcohol to give yellow crystals of 2,2-dimethyltetrahydroisoquinolinium iodide (**5**), mp 188–189° (sinter 183°) [lit.[15] mp 189°].

Anal. Calcd for $C_{11}H_{16}IN$: C, 45.69; H, 5.58. Found: C, 45.77; H, 5.58.

2,2-Dimethyl-1,2,3,4-tetrahydroisoquinolinium Iodide (5) from Dihydroisoquinolinium Iodide 4. A solution of dihydro compound **4** (71 mg; 0.25 mmol) in 15 ml of 1:1 water–alcohol was stirred under hydrogen at room temperature with the catalyst prereduced from 60 mg of platinum oxide. After 4 hr, 0.25 mmol of hydrogen had been absorbed; continued stirring resulted in no further uptake. Removal of catalyst and solvent left 70 mg of 2,2-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide (**5**), mp 179–180°. Crystallization from alcohol gave material with mp 186–187° (sinter 174°). The mixture melting point with the same material prepared from the tetrahydroisoquinoline was 186–187° (sinter 175°); the infrared absorption spectra of the two iodides were identical.

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Registry No.—**1**, 3947-77-1; **2**, 14990-40-0; **3**, 1612-65-3; **3 HCl**, 53112-33-7; **4**, 53112-34-8; **5**, 1637-45-2.

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Chemistry of Azoethenes and Azoethynes. I. Synthesis of Phenylazoethynylbenzene and Its Derivatives

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1-(2-Hydroxynaphthylazo)hexyne was suggested as a reaction intermediate by Robson and Tedder.[1] Later Sladkov and coworkers reported the synthesis of electron-withdrawing-group-bearing arylazoethynylbenzenes by the reaction of arenediazonium chlorides in aqueous solution with silver acetylides.[2] Their procedure gave only poor to fair yields of the azoethynes among difficult-to-separate reaction product mixtures. The simplest compound of the series, phenylazoethynylbenzene (**1**) and the electron-donating-group-bearing *p*-methoxyphenylazoethynylbenzene (**2**) cannot be obtained by their method. We have now successfully synthesized **1**, **2**, and other arylazoethynylbenzenes (**3–10**) in fair to good yields (Table I) by a new procedure.

Our method involved the reaction of purified arenediazonium salts (chlorides or bromides) with silver phenylacetylide in alcohol–chloroform (eq 1). Compounds **1–10** thus obtained were easily purified by column chromatography.

$$ArN_2^+X^- + AgC{\equiv}CPh \longrightarrow ArN{=}NC{\equiv}CPh + AgX \quad (1)$$

1–10

Compounds **1–10** exhibit ir signals in the range 2160–2165 cm^{-1} and nmr signals expected for the structures.[3] The mass spectra of these compounds all show a common fragmenation pattern (Scheme I), in agreement with the assigned structures.[3]

The uv spectra of **1–10** (Table I) show absorption in ethanol λ_{max} 360–384 nm (with log ϵ ~4) attributed to the $-N{=}NC{\equiv}C-$ group.[2] The insertion of the $-C{\equiv}C-$ group