3,5-dinitro-2-ethylindole (0.33 g., 0.00140 mole) in aqueous 1% sodium hydroxide solution (20 ml.) and ethanol (15 ml.). After 1 hr. the resulting precipitate was filtered off and recrystallized twice, once with charcoal, giving a mixture as pale yellow needles (0.15 g.), m.p. 188–210°. Extraction of the mixture with aqueous 40% sodium hydroxide solution, and two recrystallizations from acetone–ethanol yielded pale yellow needles (0.09 g., 26%), m.p. 227–229°.

2-Methyl-3,5,7-trinitroindole (37).—The compound[16] crystallized from ethanol–water as cream-colored crystals: m.p. 213–215°; lit.[16] m.p. 205–206° (anhydrous form[57]); λ_{max}, mμ (log ε, calculated as the anhydrous form, which is the only form we observed), in 95% ethanol (does not obey Beer's law) at c 1.528 × 10^{-4} M, intense maximum between 233 and 309, 344 (3.37); at c 3.056 × 10^{-5} M, 284 (4.24), 350 (3.98); ν_{NH} 3380 (m) and 3330 (m), ν_{NO_2} 1537 (s), 1355 (s) cm.$^{-1}$ in Nujol; pK_a = 7.3.

1,2,3-Trimethylindole (with Norman W. Gill and Frederic J. Baude, 1962).—The compound (which according to previous work[58] should contain 13% 2,3,3-trimethyl-3H-indole) was obtained in 89% yield, n^{25}D 1.5950, free of NH bands in the infrared spectrum, by methylation of 2,3-dimethylindole[29c,59] with a 15% excess of sodium and methyl iodide in liquid ammonia, according to the procedure used for preparation of 1-methylindole[60] and 1,2-dimethylindole.[50] Redistillation gave a center cut: b.p. 89° (0.75 mm.); n^{27}D 1.5930; λ_{max}, mμ (log ε), in 95% ethanol 231 (4.52), 287 (3.83), 293 infl. (3.81).

5-Nitro-1,2,3-trimethylindole (41).[2b] **A. From 1,2,3-Trimethylindole.**—A solution of sodium nitrate (1.60 g., 0.0188 mole) in concentrated sulfuric acid (50 ml.) was added dropwise, with stirring, to a solution of 1,2,3-trimethylindole (3.00 g., 0.0188 mole) in concentrated sulfuric acid (50 ml.) at 5°. The solution was stirred for 5 min. more and then poured onto crushed ice. The resulting dark yellow precipitate was filtered off, dried, dissolved in the minimum amount of benzene, and placed on a column of alumina (100 g.) which had been packed wet with petroleum ether. Elution with 1:1 benzene–petroleum ether removed bright yellow needles (1.54 g., 40%), m.p. 138.5–140.5°. There was no depression in mixture melting point, 139–141.5°, with the sample prepared from 2,3-dimethyl-5-nitroindole, and the infrared spectra in Nujol were identical.

Attempted nitration of 1,2,3-trimethylindole with nitric acid in acetic acid at ice-bath temperature gave an unstable, greenish solid, which decomposed upon attempted recrystallization.

B. From 2,3-Dimethyl-5-nitroindole (40).—A solution of 2,3-dimethyl-5-nitroindole[29] (1.00 g., 0.00525 mole) in anhydrous ether (50 ml.) was added dropwise, with stirring, to a solution of sodamide (from sodium, 0.60 g., 0.0261 g.-atom, and ferric nitrate nonahydrate, 0.10 g.) in liquid ammonia (200 ml.). After the solution had been stirred for 15 min., methyl iodide (1.00 g., 0.00704 mole) was added slowly, and then stirring was continued for 15 min. The ammonia was allowed to evaporate, water was added to the residue, and the resulting mixture was extracted with methylene chloride. The methylene chloride extracts were dried and concentrated, and petroleum ether was added, causing formation of a dark orange precipitate. The precipitate was dissolved in a minimum of benzene and placed on a column of alumina (25 g.) which had been packed wet with petroleum ether. Elution with 1:1 benzene–petroleum ether removed bright yellow needles (0.64 g., 60%): m.p. 140–141.5°[41]; lit.[30a] m.p. 138–139°; λ_{max}, mμ (log ε), in 95% ethanol 214 (4.30), 264 infl. (4.12), 282 (4.32), 340 (3.92); ν_{NO_2} 1505 (ms), 1326 (s) cm.$^{-1}$ in Nujol.

5-Nitro-2,3,3-trimethyl-3H-indole (43).[2b]—A solution of sodium nitrate (1.70 g., 0.0200 mole) in concentrated sulfuric acid (50 ml.) was added dropwise, with stirring, over a period of 1 hr. to a solution of 2,3,3-trimethyl-3H-indole[61] (3.18 g., 0.0200 mole) in concentrated sulfuric acid (25 ml.) cooled to 5° in an ice bath. The resulting solution was poured into ice–water (1 l.), producing a clear yellow solution. Basification to pH 10 with aqueous sodium hydroxide solution caused separation of a crystalline product, which was recrystallized from methylene chloride–petroleum ether, with charcoal, yielding blunt straw-colored needles (3.32 g., 81%): m.p. 130–131.5°[41]; lit. 88% yield,[31] m.p. 124–125°,[30a] 127°,[31] 128°[30b]; λ_{max}, mμ (log ε), in 95% ethanol 222 infl. (4.01), 302 (4.08); $\nu_{C=N}$ 1565 (s), ν_{NO_2} 1517 (s), 1339 (s) cm.$^{-1}$ in Nujol. There was no depression in mixture melting point, 130–131.5°, with a sample[30] prepared by polyphosphoric acid catalyzed[30b] cyclization of 3-methyl-2-butanone p-nitrophenylhydrazone.[62]

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(58) M. Nakazaki, *Bull. Chem. Soc. Japan*, **32**, 838 (1959).
(59) H. R. Snyder and C. W. Smith, *J. Am. Chem. Soc.*, **65**, 2452 (1943).
(60) K. T. Potts and J. E. Saxton, *Org. Syn.*, **40**, 68 (1960).
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(62) H. D. Dakin, *J. Biol. Chem.*, **4**, 235 (1908); *Chem. Zentr.*, **79**, I, 1260 (1908).

The Action of Triphenylphosphine Dibromide on Sterol and Bile Acid Derivatives[1]

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By the action of triphenylphosphine dibromide, cholesterol and cholestanol give 3β-bromocholest-5-ene and 3α-bromocholestane, respectively; cholest-1-en-3-one and 4-bromocholest-4-en-3-one are similarly obtained from cholestanone. The order of reactivity of the hydroxyl groups of cholic acid toward this reagent is 3 > 7 > 12.

The conversion of alcohols to alkyl halides by the use of tertiary phosphine dihalides has been described by Horner and co-workers[2]; furthermore, attention has recently been drawn to the advantages of these reagents over phosphorus pentahalides in effecting substitution without elimination or molecular rearrangement. Other reactions which have been reported[2,3] for these reagents include the conversion of carboxylic acids to acid chlorides, aldehydes and ketones to *gem*-dihalogen products, amides and oximes to nitriles, and phenols to aryl halides. The use of triphenylphosphine dibromide as a reagent for the cleavage of ethers under mild conditions has also been recently described.[4] The mechanism of the formation of alkyl halides from alcohols is under study by Wiley[5] and a preliminary account of the gross features has been given. With regard to the stereochemical consequences of this displacement, an inversion of configuration

(1) The award of a research grant (AM-3439) from the National Institute of Arthritis and Metabolic Diseases, U.S. Public Health Service (to R. S.), is gratefully acknowledged.
(2) L. Horner, H. Oediger, and H. Hoffmann, *Ann.*, **626**, 26 (1959).
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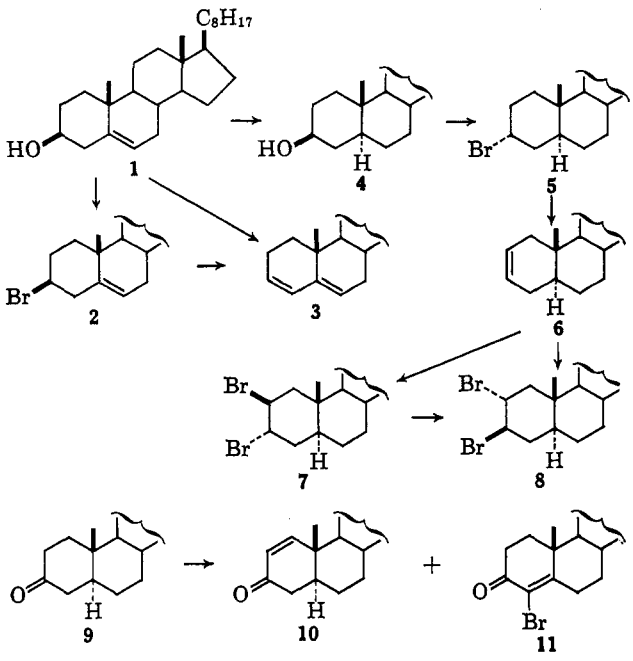
CHART I



occurred in the two examples reported for optically active alcohols.[2,5]

Since there frequently exists a need, particularly in degradative studies, for selective dehydroxylation (>C–OH → >C–H), we sought to examine the utility of triphenylphosphine dibromide as a reagent in the first stage of the sequence >C–OH → >C–Br → >C–H in polyfunctional molecules, particularly in the presence of double bonds, carbonyl groups, and less reactive hydroxyl groups. Some readily available steroids were satisfactory for this purpose and our results, some of which have appeared in a preliminary communication,[6] are now described.

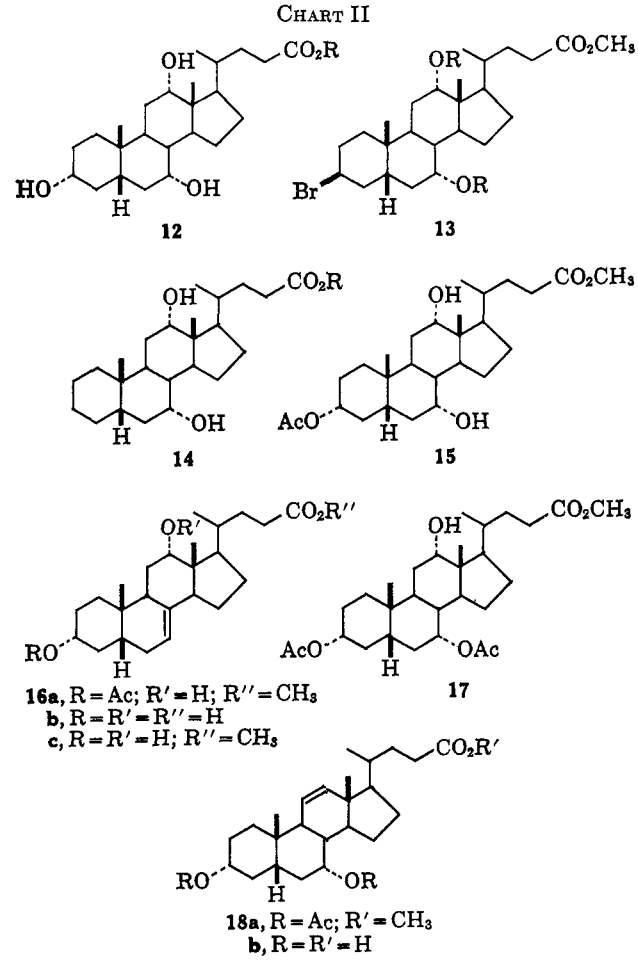
Treatment of cholesterol (**1**) with 10 molar equiv. of triphenylphosphine dibromide at 90° readily gave 3β-bromocholest-5-ene (**2**) isolated in 80% yield after chromatography on basic grade II (Spence H) alumina (see Chart I). The retention of configuration in the homoallylic system is in accordance with the behavior previously noted in the use of phosphorus penta- or trihalides[7] and triphenylphosphite dihalides.[8] When the reaction product was isolated by chromatography on grade I neutral or basic alumina, there was obtained, instead, cholesta-3,5-diene (**3**) in high yield and purity. This provides an excellent one-step method of preparation for this hydrocarbon; prior methods have recently been listed.[9] The halide (**2**) was quantitatively converted to the hydrocarbon (**3**) by the same chromatographic treatment.

When cholestan-3β-ol (**4**) was treated with an excess of triphenylphosphine dibromide under the same conditions, displacement occurred as expected with inversion of configuration, and 3α-bromocholestane (**5**) was isolated in excellent yield. We have noted that **5** also undergoes dehydrobromination in contact with neutral alumina to give cholest-2-ene (**6**), which was characterized by formation of its dibromides as previously described.[10,11] The dibromides were readily separated by chromatography on basic alumina, the 2β,3α- (diaxial) dibromide (**7**) predominating over the 2α,3β- (diequatorial) dibromide (**8**) by a 5:1 ratio. When the mixture was chromatographed on neutral alumina, however, equilibration occurred and only the more stable diequatorial isomer (**8**) was isolated.

Cholestan-3-one (**9**) is also appreciably attacked by triphenylphosphine dibromide under the conditions used for the alcohols **1** and **4**. Although about 25% of the ketone was recovered unchanged, there were also isolated two unsaturated ketones, identified as cholest-1-en-3-one (**10**) and 4-bromocholest-4-en-3-one (**11**). This suggests that side reactions involving the carbonyl group might be expected in an attempted halogen displacement of a hydroxyl group in a hydroxy ketone. It also indicates that this reaction may have synthetic utility in converting cyclohexanones to conjugated cyclohexenones, particularly for substrates in which the presence of other isolated double bonds interfere in the standard procedures.

In order to test the selectivity of triphenylphosphine dibromide toward hydroxyl groups of varying reactivity, we have studied its action on derivatives of cholic acid (**12**, R = H), in which it is well established that the reactivity of the three hydroxyl groups toward acylation is 3α > 7α > 12α (see Chart II).

CHART II



(6) D. Levy and R. Stevenson, *Tetrahedron Letters*, 341 (1965).

(7) C. W. Shoppee ["Chemistry of the Steroids," 2nd Ed., Butterworth and Co. (Publishers) Ltd., London, 1964, pp. 50–51] gives leading references.

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Treatment of methyl cholate (**12**, R = CH_3) with an equimolar quantity of the reagent gave in excellent yield a bromodiol ester (**13**, R = H), characterized by acetylation to the bromodiacetate (**13**, R = Ac). The structure of the bromodiol was established by debromination with Raney nickel to give the known methyl 7α,12α-dihydroxycholanate (**14**, R = CH_3), and after base hydrolysis, 7α,12α-dihydroxycholanic acid (isodesoxycholic acid, **14**, R = H), previously obtained from methyl cholate by preferential oxidation[12-14] at C-3 followed by Wolff–Kishner reduction.[12]

As anticipated, methyl cholate 3-acetate (**15**) was recovered unchanged under the conditions used successfully for the 3-hydroxyl displacement in methyl cholate. When subjected to the conditions (10:1 molar ratio of reagent, 20 hr., 90°) under which cholesterol and cholestanol reacted, however, elimination of the 7α-hydroxyl group from **15** occurred, and methyl 3α-acetoxy-12α-hydroxychol-7-enate (**16a**) was isolated in about 70% yield; it was further identified as the unsaturated diol acid (**16b**) and the diol methyl ester (**16c**). This elimination has previously been reported, although in less satisfactory yield, using *p*-toluenesulfonyl chloride[15] and phosphorus oxychloride.[16]

Under still more forcing conditions (25:1 molar ratio of reagent, 50 hr.), the 12α-hydroxyl group could be eliminated. Thus, the methyl ester 3,7-diacetate (**17**) yielded methyl 3α,7α-diacetoxychol-11-enate (**18a**) with constants in good agreement with those reported recently for this compound[17] prepared by the action of excess phosphorus oxychloride[18] on **17**. The product was further characterized by hydrolysis to the diol acid (**18b**). Thus, with regard to the reactivity of the three hydroxyl groups of cholic acid, the same order holds for the reaction with triphenylphosphine dibromide as for acylation. The 3α-hydroxyl group undergoes selective replacement with the bromo group in the presence of 7α- and 12α-hydroxyl groups, whereas the 7α-hydroxyl group is selectively eliminated in the presence of a 12α-hydroxyl group.

Experimental Section

Specific rotations were determined in chloroform solution. Melting points were determined using a Gallenkamp melting point apparatus. Petroleum ether refers to the fraction, b.p. 38–54°. Woelm grade I neutral alumina had pH 7.3, and Spence Type H alumina was grade II and had pH 9.8.

Triphenylphosphine dibromide was prepared and used as a solution in dimethylformamide which had been distilled from calcium hydride and stored over molecular sieves. Triphenylphosphine was added to the dry solvent, in a flask which had been flushed with nitrogen and protected from moisture, followed by an equimolar quantity of bromine.

Action of Triphenylphosphine Dibromide on Cholesterol. A.—To a solution of triphenylphosphine dibromide (2.3 g.) in dry dimethylformamide (25 ml.) was added cholesterol (192 mg.) in the same solvent (*ca.* 2 ml.) and the mixture was stirred for 20 hr. at bath temperature of 90° under a nitrogen atmosphere. The mixture was then diluted with water and extracted with ether, and the extract was washed with sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Removal of the ether gave a semisolid residue, which was triturated with petroleum ether, the insoluble solid triphenylphosphine oxide was removed by filtration, and the filtrate was chromatographed on alumina (Spence Type H). Evaporation of the eluate (50 ml.) gave a product (180 mg.) which on one crystallization from acetone or ether–methanol gave **3β-bromocholest-5-ene** (**2**) as needles (168 mg.), m.p. 96–98°, $[\alpha]_D$ −25° (*c* 1.0) (lit.[19] m.p. 98°, $[\alpha]_D$ −21°).

B.—The reaction mixture obtained as above from cholesterol (250 mg.) was chromatographed on Woelm alumina (neutral, grade I). The eluate obtained with petroleum ether (50 ml.) on evaporation gave a product (210 mg.) which on crystallization from ether–methanol yielded **cholesta-3,5-diene** (**3**) as needles (195 mg.): m.p. 77–79°; $[\alpha]_D$ −117°; λ_{max}^{EtOH} 228 mμ (ϵ 18,300), 235 (18,700), and 245 (13,400); lit.[9] m.p. 78–80°, $[\alpha]_D$ −121°.

Dehydrobromination of 3β-Bromocholest-5-ene. A.—A solution of the bromocholestene (30 mg.) in petroleum ether was added to a column of Woelm alumina (neutral, grade I). Crystallization of the eluted product from ether–methanol gave cholesta-3,5-diene (24 mg.), m.p. 77–79°, $[\alpha]_D$ −114°.

B.—Similar treatment of the bromocholestene (25 mg.) on Spence Type H alumina (grade I, activated by heating for 10 hr. at 110° and 0.5 mm.) gave cholesta-3,5-diene (15 mg.), m.p. 77–79°.

Action of Triphenylphosphine Dibromide on Cholestan-3β-ol (**4**).—A solution of cholestan-3β-ol (470 mg.) in dimethylformamide was added to triphenylphosphine dibromide (5.2 g.) in dimethylformamide (25 ml.); the mixture was heated with stirring at 90° for 20 hr. under a nitrogen atmosphere, then worked up in the usual way. Elution of the product with petroleum ether from a column of alumina (Spence Type H) gave, after one crystallization from ether–methanol, **3α-bromocholestane** (**5**) as needles (435 mg.), m.p. 100–102°, $[\alpha]_D$ +26° (*c* 1.2) (lit.[20] m.p. 103–104°, $[\alpha]_D$ +29°).

Cholest-2-ene.—A solution of 3α-bromocholestane (24.6 mg.) in petroleum ether (0.5 ml.) was chromatographed on alumina (Woelm, neutral, grade I). Evaporation of the petroleum ether eluate gave an oil (20.1 mg.) which crystallized on standing. Two recrystallizations from ether–methanol gave cholest-2-ene (**6**) as long needles (15.2 mg.), m.p. 73–75°, $[\alpha]_D$ +64° (*c* 1.6) (lit.[10] m.p. 74–75°, $[\alpha]_D$ +66°).

Addition of Bromine to Cholest-2-ene. A.—A solution of bromine (0.015 g.) in acetic acid (0.5 ml.) was added to a solution of cholest-2-ene (17 mg.) in ether (5 ml.). The mixture was allowed to stand at room temperature for 2 hr., concentrated under reduced pressure, and extracted with ether, and the extract washed with water and dilute sodium hydrogen carbonate solution and dried ($MgSO_4$). The residue (25 mg.), obtained by removal of the ether, was dissolved in a minimum volume of petroleum ether and chromatographed on alumina (Spence Type H). Elution with the same solvent (15 ml.) yielded a solid which on one crystallization from methanol gave **2β,3α-dibromocholestane** (**7**) (15 mg.), m.p. 123–125°, $[\alpha]_D$ +74° (*c*, 1.5) (lit.[10] m.p. 123–124°, $[\alpha]_D$ +76°). The product from the second eluate (20 ml.) on crystallization from methanol gave **2α,3β-dibromocholestane** (**8**) (3 mg.) as needles, m.p. 142–144°, $[\alpha]_D$ −26° (*c* 1.3) (lit.[10] m.p. 144–145°, $[\alpha]_D$ −30°).

B.—In an experiment performed as in A above, except that the reaction product was chromatographed on Woelm alumina (neutral, grade I), there was obtained from cholest-2-ene (28 mg.) on elution only 2α,3β-dibromocholestane (26 mg.), m.p. 143–144°, $[\alpha]_D$ −27° (*c* 1.1).

Isomerization of 2β,3α-Dibromocholestane.—A solution of 2β,3α-dibromocholestane (15 mg.) in petroleum ether was added to a column of alumina (Woelm, neutral, grade I), and eluted with the same solvent. One crystallization of the product from ether–methanol yielded 2α,3β-dibromocholestane (12 mg.), m.p. 142–144°, $[\alpha]_D$ −23° (*c* 1.2).

Action of Triphenylphosphine Dibromide on Cholestan-3-one.—To a solution of triphenylphosphine dibromide (4.0 g.) in dimethylformamide (25 ml.) was added cholestanone (400 mg.) and the mixture was heated with stirring at 90° for 20 hr. under a nitrogen atmosphere. The crude reaction mixture, isolated in the usual way, was examined by thin layer chromatography and five constituents, including unchanged ketone and triphenylphosphine oxide, detected. The mixture was dissolved in

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petroleum ether and chromatographed on alumina (Spence Type H). The first fraction eluted by petroleum ether gave an unidentified oil (47 mg.) which rapidly darkened in color on standing at room temperature. A second fraction (100 mg.) eluted by the same solvent (50 ml.) was unchanged cholestanone (m.p. 129°, identical infrared spectrum). The third fraction, eluted with the same solvent (35 ml.), was an oil which crystallized on standing. One recrystallization from ether–methanol gave **cholest-1-en-3-one (10)** as small needles (98 mg.): m.p. 97–98°, $[\alpha]_D$ +53° (*c* 1.3), λ^{EtOH} 232 mμ (ε 10,500); lit.[21] m.p. 98–100°, $[\alpha]_D$ +57.5°, λ 231 mμ (log ε 3.99).

The last fraction eluted by petroleum ether (35 ml.) gave an oil, which crystallized from ether–methanol to give **4-bromocholest-4-en-3-one (11)** as needles (84 mg.): m.p. 112–114°, $[\alpha]_D$ +104° (*c* 1.1), λ^{EtOH} 261 mμ (ε 10,500); lit.[22] m.p. 114–115°, $[\alpha]_D$ +107°.

Action of Triphenylphosphine Dibromide on Methyl Cholate (12, R = H).—Methyl cholate (250 mg.) was added to a solution of triphenylphosphine dibromide (253 mg.) in dimethylformamide (10 ml.) and the mixture was heated with stirring at 90° for 2 hr. under a nitrogen atmosphere. The crude product, isolated in the usual way, gave a positive Beilstein test and thin layer chromatography indicated the presence of one major product in addition to triphenylphosphine oxide and a small amount of starting material. The product was dissolved in benzene and chromatographed on silica gel. The benzene eluate (60 ml.) on evaporation gave a colorless oil, which yielded an amorphous solid (300 mg.) on attempted crystallization from ether–petroleum ether. This solid was dissolved in pyridine (10 ml.), acetic anhydride (1 ml.) was added, and the mixture was left overnight at room temperature, diluted with water, and extracted with ether. The washed and dried extract was evaporated and the residue was crystallized from aqueous methanol to give **methyl 3β-bromo-7α,12α-diacetoxycholanate (13, R = Ac)** as long needles (290 mg.), m.p. 176–177°, $[\alpha]_D$ +45° (*c* 0.9).

Anal. Calcd. for $C_{29}H_{45}BrO_6$: C, 61.15; H, 7.96; Br, 14.03. Found: C, 61.01; H, 8.13; Br, 13.97.

Methyl 7α,12α-Dihydroxycholanate (14, R = CH_3).—Amorphous methyl 3β-bromo-7α,12α-dihydroxycholanate (40 mg.) was dissolved in 95% ethanol (25 ml.) and Raney nickel (*ca.* 2 ml. of suspension) was added. The mixture was stirred vigorously for 24 hr. in a hydrogen atmosphere, filtered, and evaporated. Crystallization of the residue from aqueous methanol gave methyl 7α,12α-dihydroxycholanate as very small needles (30 mg.), m.p. 148–150°, $[\alpha]_D$ +22° (lit.[23] m.p. 151°).

7α,12α-Dihydroxycholanic Acid (14, R = H).—The methyl ester (15 mg.) was dissolved in 5% methanolic potassium hydroxide solution (5 ml.), left at room temperature overnight, acidified with 10% aqueous hydrochloric acid, diluted with water, and extracted with ether. Evaporation of the washed and dried extract gave an oil (10 mg.) which on crystallization from aqueous methanol gave 7α,12α-dihydroxycholanic acid as prisms, m.p. 206–208°, $[\alpha]_D$ +28° (lit.[23] m.p. 206–208°, $[\alpha]_D$ +27°).

Methyl 3α-Acetoxy-12α-hydroxychol-7-enate (16a).—Methyl 3α-acetoxy-7α,12α-dihydroxycholanate (15, 250 mg.) was added to a solution of triphenylphosphine dibromide (2.5 g.) in dimethylformamide (10 ml.) and the mixture was heated with stirring at 90° for 20 hr. It was worked up in the usual way, and a solution of the neutral product in benzene was chromatographed on silica gel. Crystallization of the benzene-eluted fraction from aqueous methanol gave methyl 3α-acetoxy-12α-hydroxychol-7-enate as needles (163 mg.), m.p. 172–173°, $[\alpha]_D$ +104° (*c* 1.1) (lit.[16] m.p. 172–174°, $[\alpha]_D$ +101°).

Hydrolysis of the ester with 5% ethanolic potassium hydroxide solution gave 3α,12α-dihydroxychol-7-enic acid (16b) as prisms, m.p. 208–210°, $[\alpha]_D$ +86° (*c* 1.3) (lit.[16] m.p. 210–212°, $[\alpha]_D$ +93°, dioxane).

Esterification of the acid with diazomethane gave methyl 3α,12α-dihydroxychol-7-enate (16c) as small needles, m.p. 64–66°, $[\alpha]_D$ +82° (*c* 1.2) (lit.[16] m.p. 64–67°, $[\alpha]_D$ +78°).

Methyl 3α,7α-Diacetoxychol-11-enate (18a).—Methyl 3α,7α-diacetoxy-12α-hydroxycholanate (260 mg.) was added to a solution of triphenylphosphine dibromide (5.5 g.) in dimethylformamide (15 ml.); the mixture was heated at 90° for 50 hr. with constant stirring, then worked up in the usual way. Purification of the product by silica gel chromatography and elution with benzene gave methyl 3α,7α-diacetoxy-chol-11-enate as needles (130 mg.), m.p. 138–139°, $[\alpha]_D$ +4° (*c* 1.3), after crystallization from aqueous methanol (lit.[17] m.p. 139–141°, $[\alpha]_D$ +9°).

Hydrolysis of the ester with 5% ethanolic potassium hydroxide solution gave 3α,7α-dihydroxychol-11-enic acid (18b) as small flat needles, m.p. 203–205°, $[\alpha]_D$ +5° (*c* 0.9) (lit.[17] m.p. 204–206°, $[\alpha]_D$ +9°, dioxane).

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(22) J. I. Shaw and R. Stevenson, *J. Chem. Soc.*, 3549 (1955).

(23) S. Kuwada and S. Morimoto, *Bull. Chem. Soc. Japan*, **17**, 147 (1942).

Proton Magnetic Resonance Spectra of Certain Methyltetrazoles

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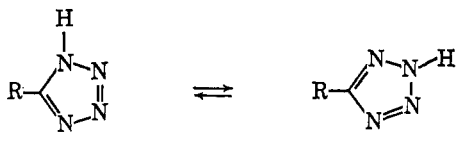
Proton n.m.r. spectra were used to study the tautomeric equilibrium of a 5-substituted tetrazole. The chemical shifts of the C-methyl resonances of the isomeric dimethyltetrazoles were insufficiently different to assign the composition of 5-methyltetrazole. From temperature and concentration dependence studies of the N–H resonance, it was concluded that in SO_2 solution 5-methyltetrazole exists in a dimeric, hydrogen-bonded species. A convenient synthesis of 5-methyltetrazole, its conversion to 2,5-dimethyltetrazole, and the characterization of the latter compound are also reported.

That a tautomeric equilibrium can exist for tetrazoles is well recognized. It has been difficult, however, to determine the relative amounts of tautomers or even to demonstrate their interconvertibility prior to nuclear magnetic resonance spectroscopy. The classical approach to such a problem, deriving the assignment of tautomeric structure from product composition, is inadequate.[2]



Ia Ib

(1) (a) Based in part on the Honors Thesis of W. T. B. (1962).

(2) For a discussion of the pitfalls inherent in such procedures, see A. R. Katritzky and J. M. Lagowski, "Advances in Heterocyclic Chemistry," Vol. 1, A. R. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1963, pp. 321–324.