RETENTION TIME RELATIONSHIPS FOR STEROIDAL AMINES[a]

Compound[b]	C-22 Config.[b]	C-25 Config.[c]		Time[d]
Tomatidine (I)		25 normal(L)	C5α	4.26
5α-Solasodan-3β-ol (II)		25 iso(D)	C5α	4.10
Solasodine (III)		25 iso(D)	Δ^5	3.95
Dihydrotomatidine A (IV)	22α	25L	C5α	7.33
Dihydrotomatidine B (V)	22β	25L	C5α	7.65
Dihydrosolasodine A (VI)	22α	25D	Δ^5	7.20
Dihydrosolasodine B (VII)	22β	25D	Δ^5	7.85
Tetrahydrosolasodine A (VIII)	22α	25D	C5α	7.27
Tetrahydrosolasodine B (IX)	22β	25D	C5α	7.95
C-25L,22-isosolanidan-3-one (X)	22α	25α(L)	R,=O	3.32
C-25D,22-isosolanidan-3-one (XI)	22α	25β(D)	R,=O	3.37
C-25D,solanidan-3-one (XII)	22β	25β(D)	R,=O	2.33
Solanidan-3-one (XIII)	22β	25α(L)	R,=O	2.41
C-25L,22-isosolanidan-3β-ol (XIV)	22α	25α(L)	R,—OH	3.05
C-25D,22-isosolanidan-3β-ol (XV)	22α	25β(D)	R,—OH	3.09
C-25D,solanidan-3β-ol (XVI)	22β	25β(D)	R,—OH	2.13
Solanidan-3β-ol (XVII)	22β	25α(L)	R,—OH	2.24
Cholestane[e]				1.00[d]

[a] Argon ionization detector, 6 ft. × 4 mm. i.d. column, pressure 20 p.s.i., temperature 222°, 0.75% SE-30 phase on Chromosorb W, 80–100 mesh. [b] The notation follows Sato *et al.* [c] The normal configuration corresponds to an axial 25-methyl; the iso configuration to an equatorial 25-methyl. [d] Relative retention time, with cholestane as reference compound. [e] Time, 3.9 min.

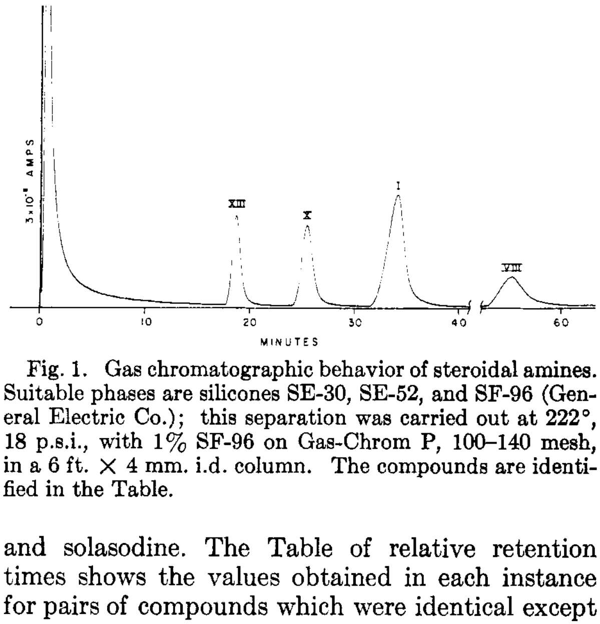

Fig. 1. Gas chromatographic behavior of steroidal amines. Suitable phases are silicones SE-30, SE-52, and SF-96 (General Electric Co.); this separation was carried out at 222°, 18 p.s.i., with 1% SF-96 on Gas-Chrom P, 100–140 mesh, in a 6 ft. × 4 mm. i.d. column. The compounds are identified in the Table.

and solasodine. The Table of relative retention times shows the values obtained in each instance for pairs of compounds which were identical except for the configuration of substituents at C-22 and C-25 carbon atoms. In compounds IV–IX, those having the 22a configuration (Diol A series of Sato and Latham[7]) had a uniformly lower retention time than that observed for the corresponding compounds having the 22β configuration (Diol B series).

For solanidane derivatives, the E,F ring relationship was found to be of major importance in determining the relative retention times. Compounds of the 22β-H series had uniformly much lower retention times than compounds of the 22α-H series. The configuration of the methyl group at C-25 had a smaller effect on the retention time; for each pair of compounds the lower retention time was found when the 22-H and 25-methyl had a *cis*-relationship.

The fact that these compounds may be separated readily by gas chromatographic techniques at 222° is a further illustration of the value of these methods for studying compounds and reactions in the steroid and alkaloid fields. In this instance the stereochemical assignments were made on the basis of relationships established by classical chemical procedures (footnote or references), but it is evident that for groups of compounds correlations may be made between structural features and retention times.

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[7] Y. Sato and H. G. Latham, *J. Am. Chem. Soc.*, **78**, 3150, 3146 (1956); Y. Sato and N. Ikekawa, *J. Org. Chem.*, in press.

Reaction of Benzyne with Organophosphorus Esters[1]

Sir:

Extensive investigations of the reactions of benzyne with nucleophiles have been conducted in recent years[2]; a number of these reactions have employed heteroatom nucleophiles leading to the

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[1] Phosphonic Acids and Esters V. Part IV, C. E. Griffin, *Chem. & Ind.*, 1058 (1960).

[2] For a recent review of the chemistry of benzyne, see R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960).

establishment of phenyl-nitrogen, -oxygen and -sulfur bonds. In an extension of studies involving amines as nucleophiles, Wittig and Benz[3] have shown that triarylphosphines react with benzyne; thus, phenyl biphenylene phosphine can be isolated in low yield from the reaction of benzyne with triphenyl phosphine. We now report the phenylation of the organophosphorous nucleophiles, sodium dialkylphosphonates, and trialkyl phosphites, via a benzyne intermediate; the reaction leads to the formation of phenyl phosphonates and constitutes a new synthetic method for this class of compounds.

Sodium diethylphosphonate (0.05 mole) and *o*-fluorobromobenzene (0.05 mole) were treated with magnesium (0.062 mole) in anhydrous tetrahydrofuran. After the spontaneous reaction had ceased, the mixture was refluxed for 1 hr. and hydrolyzed by established procedures.[3,4] The organic residue was distilled to yield diethyl phenylphosphonate (I) (41%), b.p. 103–104° (0.5 mm.) [lit.[5] b.p. 104–105° (0.5 mm.)]. The infrared spectrum of the product was identical in all respects with that of an authentic sample. Triphenylene (*ca.* 5%), a normal byproduct of benzyne reactions,[4] was isolated from a lower boiling fraction. In a similar experiment, sodium dimethylphosphonate was phenylated to yield dimethyl phosphonate (II) (37%), b.p. 103–104° (4 mm.), 243–245° (760 mm.), (lit.[6] b.p. 247°).

Triethyl phosphite (0.30 mole), *o*-fluorobromobenzene (0.06 mole) and magnesium (0.06 mole) in anhydrous tetrahydrofuran reacted vigorously with the evolution of a gaseous product which was identified as uncontaminated ethyl bromide by its infrared spectrum. From the reaction mixture, the sole isolable product was I (21%); variation in reactant ratios gave no appreciable increase in yield.[7] When triethyl phosphite was employed as solvent, initiation of the reaction was difficult and a lower yield of I was obtained.[8] The ester (I) was identified by a comparison of its infrared spectrum with that of an authentic sample and, in one experiment, by acidic hydrolysis to the known acid, phenylphosphonic acid. Trimethyl phosphite was similarly phenylated to form II in low yield. Benzyne phenylation is not restricted to phosphites but may be extended to other trivalent esters, *e.g.* ethyl diphenylphosphinite was phenylated to yield triphenyl phosphine oxide in 17% yield.

While the phenylation of sodium dialkylphosphonates probably follows the conventional course for reaction of benzyne with anions,[2] the phenylation of the trivalent esters differs mechanistically from previously demonstrated courses.[3,8] Further studies directed toward an elucidation of the mechanism of the latter reactions and a determination of the scope of the synthetic method are in progress.

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[3] G. Wittig and E. Benz, *Chem. Ber.*, 92, 1999 (1959).

[4] E. M. Arnett, *J. Org. Chem.*, 25, 324 (1960).

[5] G. M. Kosolapoff, *J. Am. Chem. Soc.*, 70, 3465 (1948).

[6] A. Michaelis and E. Benzinger, *Ber.*, 8, 1310 (1875).

[7] The yields obtained are probably minimal since no rigorous efforts were made to establish optimum conditions. Additionally, in a blank experiment, only a 60% recovery of I was obtained with the isolation technique employed.

[8] These results are probably a reflection of the lower solvating power of triethyl phosphite as compared with tetrahydrofuran. Solvation has been postulated as a dominant factor in the formation and reactions of benzyne, *cf.* ref. 2 and F. Scardiglia and J. D. Roberts, *Tetrahedron*, 3, 197 (1958).

[8] G. Wittig and W. Merkle, *Ber.*, 76, 109 (1943).

Hydration of Steroidal 1,2-Disubstituted Ethylenes

Sir:

The hydration of certain steroidal trisubstituted ethylenes to the corresponding secondary alcohols through successive hydroboration and hydrogen peroxide oxidation has recently been described,[1] the hydroboration being carried out by means of lithium aluminum hydride and boron trifluoride in ether (method a)[1b,2] or by passing diborane into a solution of the steroid in an ether (method b).[3]

We have found that steroidal 1,2-disubstituted ethylenes on similar hydration give rise to comparable amounts of both possible positionally isomeric alcohols. Thus Δ^1-cholestene (I) by method a[4] followed by chromatography on alumina yielded 35%[5] of cholestan-1α-ol (II) (m.p. 103–104°, $[\alpha]_D$ +36°[6]; ketone: m.p. 86–88°, $[\alpha]_D$ +114°) and 40% of cholestan-2α-ol (III) (m.p. 181–182°, $[\alpha]_D$ +28°; acetate: m.p. 89–91°, $[\alpha]_D$ 0°; ketone: m.p. 129–130°, $[\alpha]_D$ +50°). Δ^2-Cholestene (IV) either by method a[4] or by method b (in tetrahydrofuran solu-

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[1] (a) W. J. Wechter, *Chem. & Ind.* (*London*), 294 (1959); (b) S. Wolfe, M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, 24, 1034 (1959); (c) M. Nussim and F. Sondheimer, *Chem. & Ind.* (*London*), 400 (1960); (d) F. S. Alvarez and M. Arreguin, *Chem. & Ind.* (*London*), 720 (1960).

[2] F. Sondheimer and S. Wolfe, *Can. J. Chem.*, 37, 1870 (1959).

[3] H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, 81, 6428 (1959).

[4] Experimental details as for cholesterol,[1b] except that the peroxide oxidation was carried out as described in the experimental example given below.

[5] Yields are given to the nearest 5%.

[6] All rotations in chloroform unless otherwise stated.