2. *Optical Rotatory Power and Molecular Structure. Part I. The Synthesis and Optical Resolution of* As-*Spirobis*-1,2,3,4-*tetrahydroarsinolinium Iodide.*

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The spirocyclic salt, (±)-*As*-spirobis-1,2,3,4-tetrahydroarsinolinium iodide (III; E = As, X = I), has been synthesised and resolved into the (+)- and the (−)-iodide, $[M]_D$ +133°, −131·5° in chloroform. The rotatory dispersion of a solution of the (+)-iodide has been investigated and the results have enabled a comparison with the molecular rotations of similar optically active arsonium and phosphonium salts to be made.

Before the work now described, individual members of only two eutropic series * of compounds had been resolved into optically active forms. These are the 2-*p*-chlorophenacyl-thio-, -seleno-, and -telluro-isochromanium picrates (I; E = S, Se, and Te) resolved by Holliman and Mann,[1] and 9-*p*-carboxyphenyl-2-methoxy-9-arsafluorene (II; E = As) and its antimony analogue (II; E = Sb) resolved by Campbell and Poller [2] and Campbell and Morrill [3] respectively.

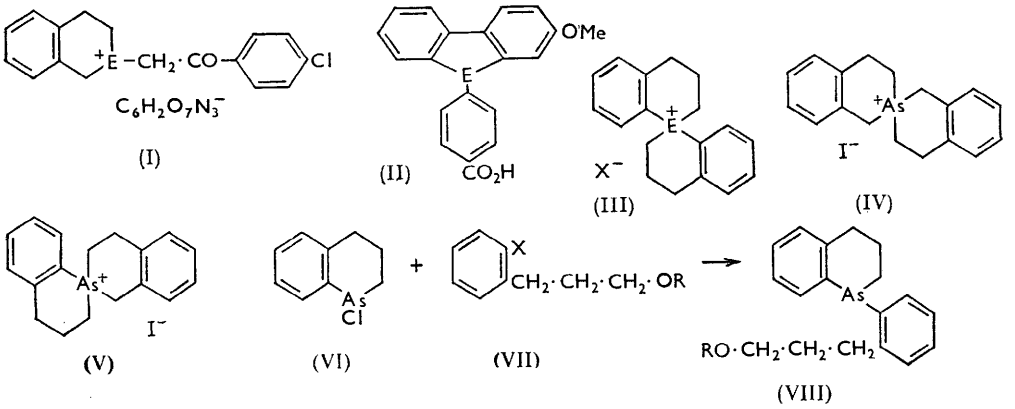
The sulphonium and selenonium picrates (I; E = S, Se) had $[M]_D$ +250° and +504° respectively in acetone solution, and although the (−)-picrate of the tellurium compound (I; E = Te) underwent slow racemisation, evidence was adduced that the optically pure picrate would have $[M]_D$ *ca.* −750°. The arsa- and stibia-fluorene compounds (II) had $[M]_D$ +609° and +650° respectively in pyridine. It is significant that in both of these eutropic series there is an increase in optical rotatory power with increase in atomic weight of the hetero-atom. In order to determine if this relation holds in other eutropic series we have synthesised and resolved the spirocyclic arsonium salt (III; E = As, X = I), the analogous phosphonium salt (III; E = P, X = I) having recently been resolved by Hart and Mann.[4]

This spirocyclic arsonium salt is isomeric with *As-spiro*bis-1,2,3,4-tetrahydroisoarsinolinium iodide (IV) synthesised and resolved by Holliman and Mann,[5] differing from

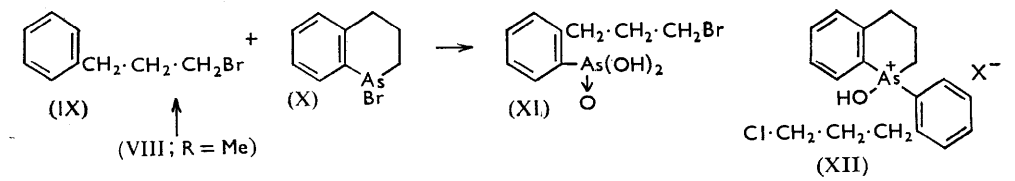
* The term " eutropic series of compounds " is defined [1] as a series of compounds consecutive members of which differ only in that they contain consecutive elements of any one sub-group of the Periodic classification; *e.g.*, PCl_3, $AsCl_3$, $SbCl_3$, $BiCl_3$.

[1] Holliman and Mann, *J.*, 1945, 37.
[2] Campbell and Poller, *J.*, 1956, 1195.
[3] Campbell and Morrill, *J.*, 1955, 1662.
[4] Hart and Mann, *J.*, 1955, 4107.
[5] Holliman and Mann, *J.*, 1945, 45.

the latter compound only in the positions of the arsenic atom in both of the heterocyclic rings. A comparison of the optical rotatory power of these two compounds together with that of the third isomeric spirocyclic salt (V) would be of considerable interest.



The synthesis of the salt (III; E = As, X = I) was attended by greater difficulties than had been experienced with other spirocyclic salts containing phosphorus or arsenic as the centre atoms, whose preparations have previously been described.[4,5,6] In our first attempts, the substituted arsinoline (VIII; R = Me) was prepared by the interaction of 1-chloro-1,2,3,4-tetrahydroarsinoline [7] (VI) and the Grignard or lithio-derivative of 3-*o*-bromophenylpropyl methyl ether (VII; R = Me, X = MgBr or Li); in the early stages of this work, lack of ethylene oxide required in the synthesis [8] of the methyl ether (VII) necessitated the development of an alternative route employing ethyl malonate. It was hoped that the arsinoline (VIII; R = Me) would yield the desired spiro-bromide on treatment with hydrobromic acid. This reagent, when applied under a variety of conditions, did not give the desired product; in only the following two cases were the products identified. When the arsinoline was heated with a mixture of constant-boiling hydrobromic acid and glacial acetic acid in a stream of gaseous hydrogen bromide, 3-phenylpropyl bromide (IX) was formed. Repetition of this experiment using a 50% (w/v) solution of hydrogen bromide in acetic acid gave a product which was not purified but appeared to consist chiefly of 1-bromo-1,2,3,4-tetrahydroarsinoline (X). Oxidation of this product with nitric acid gave a colourless crystalline compound, the analysis of which indicated that it was the arsonic acid (XI) formed by ring-opening of the arsinoline (X) during oxidation.



Instead of the action of the hydrobromic acid being confined to fission of the ether group (with the formation of a 3-bromopropyl group which should then rapidly cyclise), it became clear that the reaction also involved cleavage of the exocyclic bond to the arsenic atom, the substituted phenyl group attached thereto being replaced by a bromine

[6] Lyon and Mann, *J.*, 1945, 30; Lyon, Mann, and G. H. Cookson, *J.*, 1947, 662.
[7] Roberts, Turner, and Bury, *J.*, 1926, 1443.
[8] Beeby and Mann, *J.*, 1951, 411.

atom. Similar replacement of phenyl groups attached to arsenic in heterocyclic systems has been found previously [9,10] and it is therefore not surprising that a substituted phenyl group should exhibit a similar tendency. It is noteworthy that phenyl groups attached to a phosphorus atom are not normally removed in this manner.[11]

Because of the labile character of the exocyclic bond to the arsenic atom, a route to the required spiro-salt was sought in which the conditions would be sufficiently mild for this bond to remain unaffected. In order to retain the valuable protective properties of the ether group in a Grignard reaction and yet gain the advantage of greater acid-sensitivity than that displayed by the methoxy-group, we prepared 3-*o*-bromophenylpropyl trityl ether (VII; R = CPh_3, X = Br) from the corresponding alcohol (VII; R = H, X = Br). The Grignard derivative of the ether with 1-bromo-1,2,3,4-tetrahydroarsinoline readily yielded the arsinoline (VIII; R = CPh_3): the product was however a gum from which no crystalline material could be isolated; vacuum-distillation caused oxidation and partial decomposition, since, after hydrolysis with dilute acetic acid and treatment with thionyl chloride, the only product isolated was the unstable hydroxy-chloride (XII; X = Cl), which furnished the stable crystalline hydroxy-nitrate (XII; X = NO_3) on treatment with dilute nitric acid. However, reduction of the hydroxy-chloride with sulphur dioxide readily afforded the highly soluble spirocyclic chloride (III; E = As, X = Cl) which was therefore converted directly into the less soluble iodide (III; E = As, X = I). In subsequent preparations of the spiro-salt, the tertiary arsine (VIII; R = CPh_3), without purification, was treated with dilute acetic acid for conversion into the corresponding alcohol (VIII; R = H). A chloroform solution of this crude product was treated with sulphur dioxide to reduce any arsine oxide, and the dried product (obtained as a gum) was then treated directly with excess of phosphorus tribromide to produce the crystalline spiro-bromide (III; E = As, X = Br). The optimum overall yield of the bromide starting from cinnamyl alcohol for the preparation of the ether (VIII; R = CPh_3) was only 0·01%.

For resolution, the spiro-bromide was converted into the (+)-bromocamphorsulphonate but fractional crystallisation afforded no evidence of resolution. Treatment of the bromide with silver (−)-menthyloxyacetate readily afforded the crystalline (−)-menthyloxyacetate, which after five recrystallisations from diethyl ketone had attained a constant rotation; treatment of this salt with sodium iodide furnished the optically pure (−)-iodide, $[M]_D$ −131·5° in chloroform. The (−)-iodide was much more soluble in ethanol than the racemic compound, and use was made of this property to isolate the (+)-iodide. The mother-liquors from the first recrystallisation of the (−)-menthyloxyacetate, containing an excess of the (+)-arsonium (−)-menthyloxyacetate, were evaporated, and the residue was treated in ethanolic solution with sodium iodide, whereupon a crop of the racemic iodide was deposited. The filtrate was taken to dryness and the residue, after recrystallisation from water, afforded the optically pure (+)-spiroarsonium iodide, $[M]_D$ +133° in chloroform. Both iodides were optically stable in chloroform solution during 24 hours in the dark.

The rotatory dispersion of a 0·655% solution of the (+)-iodide in " AnalaR " chloroform was investigated over the wavelength range 5893—3650 Å (Table 1). Rotations have been calculated from the simple Drude equation $\alpha = k/(\lambda^2 - \lambda_0^2)$, reference values being the observed rotations for 5893 and 4358 Å. Solution of the simultaneous equations gives the rotation constant, $k = 0{\cdot}2134$, and the dispersion constant, $\lambda_0^2 = 0{\cdot}07907$; hence $\lambda_0 = 2812$ Å. The data indicate that the dispersion of the (+)-arsonium iodide is not simple; the departure from the simple Drude equation becomes particularly marked in the ultraviolet region, indicating the approach of an absorption band. Examination of the ultraviolet absorption spectrum showed that there was no appreciable absorption between

[9] Beeby, G. H. Cookson, and Mann, *J.*, 1950, 1921.
[10] Jones and Mann, *J.*, 1955, 401.
[11] Mann and Millar, *J.*, 1952, 3045.

4000 and 2900 Å, but an intense band was found to occur at 2595 Å (log ε 4·95) which was preceded by a shoulder at 2670 Å (log ε 4·93).

The molecular rotations of the new iodide (III; E = As, X = I) at various wavelengths are compared with those of the eutropic spirocyclic phosphonium iodide (III; E = P, X = I) and the isomeric spirocyclic arsonium iodide (IV) in Table 2. The pair of

TABLE 1. *Rotatory dispersion of* (+)-As-*spirobis*-1,2,3,4-*tetrahydroarsinolinium iodide.*

	Na	Hg	Hg	Cd	Hg	Hg	Hg
λ (Å)	5893	5780	5461	5086	4358	4047	3650
λ^2 (Å^2) × 10^{-2}	0·3472	0·3341	0·2982	0·2587	0·1900	0·1639	0·1332
α (obs.)	0·796°	0·861°	0·995°	1·185°	1·924°	2·758°	3·145°
[α]	30·38°	32·86°	37·97°	45·24°	73·43°	105·3°	120·0°
α (calc.)	0·796°	0·837°	0·974°	1·189°	1·924°	2·516°	3·945°
α (obs.) − α (calc.)...	0·000°	+0·024°	+0·021°	−0·004°	0·000°	+0·242°	−0·800°

TABLE 2. *Molecular rotations,* [*M*].

Wavelength (Å)	6708	6438	6104	5893	5780	5461	5219
(III; E = As; X = I) *	—	—	—	133·1°	144°	166·4°	—
(III; E = P; X = I)[4] †	—	−59·5°	—	−66	—	−75	—
(IV) [5] ‡	−256°	—	−310°	−344	−363	−413	−455°
Wavelength (Å)	5105	5086	4811	4358	4047	3650	
(III; E = As; X = I) *	—	198·3°	—	321·8°	461·3°	526°	
(III; E = P; X = I)[4] †	—	−83	—	−136	—	—	
(IV) [5] ‡	−487°	—	−575°	−740	—	—	

All solutions in chloroform: * 0·655%; † 0·520%; ‡ 0·385%.

eutropic salts (III; E = P, As; X = I) show the same relation between optical rotatory power and the atomic weight of the hetero-atom as has been observed in the other two known examples of eutropic series of optically active compounds (I and II), *viz.*, an increase in rotation with an increase in atomic weight of the hetero atom.

Rotatory dispersion measurements could not be made on the compounds of the series (I) since salts with colourless anions could not be isolated,[1] and Campbell *et al.*[2,3] have not recorded dispersion measurements on the two members of series (II). With the salts (III; E = P and As, X = I), that containing arsenic has the higher rotation throughout the range of wavelengths over which measurements were made by a factor of 2—2·4, but there appears to be no simple relation between the rotatory powers of these two compounds. Although the range of wavelengths employed for the measurements on the iodide (III; E = P, X = I) was too short to provide decisive evidence, the data were considered to indicate that the dispersion was not simple.[4] Thus the phosphorus and arsenic compounds are similar in this respect.

The spiro-iodide (IV) has a higher rotation than has the salt (III; E = As, X = I). Unfortunately, although the rotatory powers of these salts were measured at nine and seven wavelengths respectively, only four wavelengths were common to both series. For these wavelengths, however, there is a linear relation between the rotatory powers of the two salts: $X = 2{\cdot}1Y + 65$, where X and Y are the molecular rotations of the iodides (IV) and (III; E = As, X = I) respectively. Holliman and Mann [5] have stated that the rotatory dispersion of the iodide (IV) is simple, but their measurements were not carried into the ultraviolet region. It is thus not possible to distinguish between the iodides (IV) and (III; E = As, X = I) on this basis, since the marked departure from the simple Drude equation is apparent for the salt (III; E = As, X = I) only below 4358 Å.

Further discussion of the optical rotatory powers of these and other related optically active compounds is postponed.

EXPERIMENTAL

Preparations and manipulations of arsenic compounds (except quaternary salts) were carried out under nitrogen. Rotations were measured in a 4 dm. tube on chloroform solutions, with

Na_D light (λ 5893 Å) unless otherwise stated. Observed rotations quoted to three places of decimals were taken on a Rudolph photoelectric polarimeter; in other cases, a visual instrument was used. All compounds were colourless unless otherwise described.

Diethyl 2-Bromobenzylmalonate.—Diethyl malonate (192·5 g.) was added with stirring, to a solution of sodium (25·5 g., 0·92 equiv.) in absolute ethanol (2 l.). After the addition of 2-bromobenzyl bromide (250 g., 0·83 mol.) the mixture was boiled under reflux on a water-bath for 3 hr. and set aside overnight. Most of the ethanol was removed by distillation, water was added, and the lower oily layer separated. This, together with two ethereal extracts of the aqueous layer, was dried ($CaCl_2$), the ether removed, and the residue fractionated. The main fraction, b. p. 124—134°/0·006 mm., on redistillation gave *diethyl 2-bromobenzylmalonate* (204 g., 67%), b. p. 115—120°/0·004 mm. (Found: C, 50·7; H, 5·3. $C_{14}H_{17}O_4Br$ requires C, 51·2; H, 5·2%).

β-o-*Bromophenylpropionic Acid.*—Diethyl 2-bromobenzylmalonate (204 g.) was heated, with frequent shaking, with a solution of potassium hydroxide (200 g.) in water (200 c.c.) on a boiling-water bath for 6 hr. The yellow solution was diluted with an equal volume of water, evaporated to half bulk, and diluted again with water. After being cooled and filtered, the mixture was acidified with concentrated hydrochloric acid (500 c.c.). The precipitated acid was collected and dried (155 g.; m. p. 139—140° with effervescence and preliminary softening).

The 2-bromobenzylmalonic acid was heated rapidly to 165° in a wax-bath and maintained at that temperature until effervescence ceased (15 min.). The cooled crystalline product was recrystallised from light petroleum (b. p. 80—100°; 1 l.) (charcoal), giving β-o-*bromophenylpropionic acid* (131 g., 91·5%), m. p. 97—98·5° (Found: C, 47·5; H, 4·1. $C_9H_9O_2Br$ requires C, 47·2; H, 3·9%).

3-o-*Bromophenylpropan-1-ol* (VII; R = H, X = Br).—β-*o*-Bromophenylpropionic acid (130 g.) in absolute ether (1 l.) was added to a stirred suspension of lithium aluminium hydride (22 g.) in absolute ether (1 l.) at such a rate that gentle refluxing was maintained. The complete mixture was boiled under reflux for 6 hr., set aside overnight, and then boiled for a further 2 hr. Ether (1 l.) was removed by distillation, and the residual mixture cooled and hydrolysed with water (250 c.c.), followed by 10% v/v sulphuric acid (1 l.). After filtration, the ethereal layer was separated and washed with 5% sodium hydroxide solution (300 c.c.) and then with water. The dried (K_2CO_3) ethereal solution was distilled, and the residue fractionated to yield the alcohol (65 g.), b. p. 88—91°/0·015 mm. (lit.,[8] b. p. 106—108°/0·5 mm.). Acidification of the alkaline washings precipitated the original acid (46·5 g.), m. p. and mixed m. p. 97—97·5°. After allowance for the recovered acid, the yield of the alcohol was 84%.

The alcohol was characterised as the *phenylurethane*, needles, m. p. 77—77·5° [from light petroleum (b. p. 80—100°)] (Found: C, 56·9; H, 4·8. $C_{16}H_{16}O_2NBr$ requires C, 57·5; H, 4·8%), and the p-*nitrobenzoate*, prisms, m. p. 58—59° (from light petroleum) (Found: C, 52·9; H, 4·0. $C_{16}H_{14}O_4NBr$ requires C, 52·8; H, 3·85%).

1,2,3,4-*Tetrahydro*-1-(o-3-*methoxypropylphenyl*)*arsinoline* (VIII; R = Me).—n-Butyllithium (1 mol.) in ether was slowly added with stirring to a solution of 3-*o*-bromophenylpropyl methyl ether (20 g.) in dry ether (90 c.c.), the temperature being kept between 5° and 10° by external cooling. Dry ether (20 c.c.) was added, and the mixture boiled under reflux with stirring for 1·5 hr. After cooling, dry ether (85 c.c.) was added followed by the slow addition, with stirring, of a solution of 1-chloro-1,2,3,4-tetrahydroarsinoline [7] (17·5 g., 1 mol.) in dry ether (85 c.c.). The mixture was boiled for 1 hr., cooled, and then hydrolysed with 10% v/v sulphuric acid (350 c.c.) and crushed ice (250 g.). The ethereal layer, combined with three successive ethereal extracts of the aqueous layer, was washed in turn with 10% aqueous sodium carbonate and water, dried ($CaCl_2$), and distilled. The main fraction of the *arsinoline* (14·4 g., 55%) had b. p. 192—194°/1 mm. (Found: C, 66·5; H, 6·95. $C_{19}H_{23}OAs$ requires C, 66·7; H, 6·8%).

The arsinoline was also prepared in similar yield by the interaction of the Grignard derivative of 3-*o*-bromophenylpropyl methyl ether (formed by the " entrainment " method using ethyl bromide and activated magnesium powder [12]). The *methiodide*, obtained by interaction of the arsine with boiling methyl iodide, formed needles, m. p. 122·5—123·5°, from acetone (Found: C, 48·8; H, 5·5. $C_{20}H_{26}OIAs$ requires C, 49·6; H, 5·4%).

Reaction of the Arsinoline (VIII; R = Me) *with Hydrobromic Acid.*—(*A*) The arsinoline (7·4 g.), mixed with 48% w/v aqueous hydrobromic acid (150 c.c.) and acetic acid (150 c.c.), was heated at 120° for 5·5 hr., a stream of hydrogen bromide being passed through the mixture.

[12] Holliman and Mann, *J.*, 1942, 739.

The lower, insoluble layer which had formed was extracted with chloroform, the extract being washed in turn with water (twice), aqueous sodium carbonate, and water, and then dried ($CaCl_2$). After removal of the chloroform, the residue was distilled: the main fraction (2·3 g.; b. p. 52—62°/0·25 mm.) was warmed with a solution of ammonium dithiocarbamate in aqueous ethanol on the water-bath for 0·5 hr. Dilution of the mixture with water gave an oil which readily solidified. Recrystallisation (once from light petroleum–ether and once from cyclohexane) gave 3-phenylpropyl dithiocarbamate, m. p. and mixed m. p. 70—71°.

(*B*) The arsinoline (4 g.) in a 50% w/v solution (20 c.c.) of hydrogen bromide in acetic acid was heated at 120° under reflux for 3·5 hr. with a stream of hydrogen bromide as before. The mobile liquid residue remaining after removal of the solvent was heated under reduced pressure at 150° for 1·5 hr., giving a product almost completely soluble in ether. The filtered ethereal solution, after removal of the solvent, was distilled, 1·84 g. of the total distillate (2·88 g.) having b. p. 118—120°/0·19 mm. This fraction contained bromine and arsenic but failed to yield a methiodide. An aqueous suspension of this product was oxidised with concentrated nitric acid; the resulting dark brown solution, on cooling, deposited crystals, m. p. 134—135° after three recrystallisations from dilute nitric acid, almost certainly of *o*-3-bromopropylphenylarsonic acid (Found: C, 33·6; H, 3·6; Br, 22·7. $C_9H_{12}O_3BrAs$ requires C, 33·4; H, 3·7; Br, 24·7%). The properties of the compound confirm this identification. It did not contain nitrogen, was insoluble in ether, and crystallised from hot water. Its aqueous solution had pH 6, gave no precipitate with silver nitrate solution, and did not decolorise potassium permanganate. The acid was soluble in both aqueous sodium hydroxide and sodium carbonate (CO_2 evolution), and was reprecipitated on acidification. It did not decolorise bromine in chloroform solution.

3-o-*Bromophenylpropyl Triphenylmethyl Ether* (VII; R = CPh_3, X = Br).—3-*o*-Bromophenylpropan-1-ol (46 g.) was slowly added to a warm solution of triphenylmethyl chloride (60 g., 1 mol.) in dry pyridine (100 c.c.) with stirring. The ether began to separate when about half the alcohol had been added. The mixture was heated for 2 hr. on the boiling-water bath and whilst still warm was poured into water (400 c.c.). The precipitated oil solidified and was collected, washed with water, and recrystallised (ethanol), giving the *ether* (80 g., 82%), m. p. 84—86°, raised by five recrystallisations to 89—91° (Found: C, 73·35; H, 5·7. $C_{28}H_{25}OBr$ requires C, 73·5; H, 5·5%).

1-*Bromo*-1,2,3,4-*tetrahydroarsinoline* (X).—1,2,3,4-Tetrahydro-1-methylarsinoline [13] (15 g.) in dry carbon tetrachloride (25 c.c.) was treated with bromine (1 mol.) in carbon tetrachloride, a white precipitate of the arsinoline dibromide separating. After 2 hr. at 0°, the mixture was stirred whilst being heated at 130° to remove the solvent. Some decomposition occurred during this operation and was completed by heating under reduced pressure, effervescence becoming vigorous above 60°. The pale yellow liquid, on distillation, gave 1-*bromo*-1,2,3,4-*tetrahydroarsinoline* (13·4 g., 68%), b. p. 174—180°/11 mm., which readily crystallised (Found: C, 41·1; H, 4·0. $C_9H_{10}BrAs$ requires C, 39·6; H, 3·7%).

The bromoarsinoline, treated with piperidine *NN*-pentamethylenedithiocarbamate (1 mol.) in dry benzene, gave S-(1,2,3,4-*tetrahydroarsinolin*-1-*yl*)-NN-*pentamethyleneurethane*, m. p. 159—160° (from acetone) (Found: C, 51·0; H, 5·75. $C_{15}H_{20}NS_2As$ requires C, 51·0; H, 5·7%).

1,2,3,4-*Tetrahydro*-1-(o-3-*triphenylmethoxypropylphenyl*)*arsinoline* (VIII; R = CPh_3).—3-o-Bromophenylpropyl triphenylmethyl ether (21·8 g.) and ethyl bromide (2·6 g., 0·5 mol.) in ether (200 c.c.) were added to activated magnesium powder [12] (1·8 g., 1·58 equiv.) under ether (10 c.c.) and conversion into the Grignard derivative was completed by boiling under reflux for 2·75 hr. 1-Bromo-1,2,3,4-tetrahydroarsinoline (14·4 g., 1·1 mol.) in ether (50 c.c.) was added at room temperature, and the mixture boiled for 2 hr. The chilled mixture was hydrolysed with saturated ammonium chloride solution (250 c.c.), and the ethereal layer was separated, washed with water twice, and dried (Na_2SO_4). Attempted distillation at 10^{-3} mm. of the residue remaining after removal of the solvent caused decomposition.

A portion of the residue (3 g.) was treated at 0° with thionyl chloride (3·4 c.c.), the mixture then being heated on the boiling-water bath for 3 hr. The residue remaining after removal of the excess of thionyl chloride *in vacuo* at 100° crystallised on trituration with ethyl acetate, giving the unstable cream-coloured 1-(o-3-*chloropropylphenyl*)-1,2,3,4-*tetrahydro*-1-*hydroxyarsinolinium chloride* (XII; X = Cl) (1·2 g.), m. p. 158—161° (from ethyl acetate) (Found: C, 55·9; H, 4·5. $C_{18}H_{21}OCl_2As$ requires C, 54·2; H, 5·3%). An aqueous solution of this salt,

[13] Burrows and Turner, *J.*, 1921, **119**, 426.

treated with dilute nitric acid, gave the *hydroxy-nitrate* (XII; X = NO_3), m. p. 128·5—129° (from dilute nitric acid) (Found: C, 50·6; H, 5·1. $C_{18}H_{21}O_4NClAs$ requires C, 50·8; H, 5·0%).

1,2,3,4-*Tetrahydro*-1-(o-3-*hydroxypropylphenyl*)*arsinoline* (VIII; R = H).—The crude trityl ether (VIII; R = CPh_3) (13·3 g.) was boiled under reflux with aqueous acetic acid (50 c.c.; 35 vols. of acid : 65 vols. of water) for 50 min. The aqueous layer was decanted from the residual gum, which was extracted with chloroform. The extract, washed once with water, was covered with 5N-hydrochloric acid (100 c.c.) containing potassium iodide (0·2 g.), and chilled in ice whilst a stream of sulphur dioxide was passed through for 2·5 hr. The chloroform layer was washed with water and dried (Na_2SO_4), and the chloroform removed. The residue (12·7 g.) was used for the preparation of the spirocyclic salts without further purification.

(±)-As-*Spirobis*-1,2,3,4-*tetrahydroarsinolinium Bromide, Iodide, and Picrate* (III; E = As).—The crude residue (24 g.) from the previous preparation containing triphenylmethanol was treated with phosphorus tribromide (4·5 c.c.) at 0°. After being heated on the water-bath for 1 hr., the mixture was triturated with ether and then dissolved in hot ethanol. On slow cooling, the *spiro-bromide* separated (4·32 g.); three recrystallisations from ethanol gave the *dihydrate*, m. p. 253—254° (Found: C, 50·1; H, 5·0. $C_{18}H_{20}BrAs,2H_2O$ requires C, 50·6; H, 5·7%). Drying at 80°/0·1 mm. produced the anhydrous *salt*, m. p. 270—271° (Found: C, 54·8; H, 5·5. $C_{18}H_{20}BrAs$ requires C, 55·3; H, 5·15%). The *iodide*, prepared by double decomposition in aqueous ethanol, gave cream-coloured plates, m. p. 277—278°, from ethanol [Found: C, 48·9; H, 4·7; I(ionic), 28·8. $C_{18}H_{20}IAs$ requires C, 49·3; H, 4·6; I, 29·0%]. The yellow *picrate*, prepared similarly, had m. p. 102—103° after four recrystallisations from ethanol (Found: C, 53·4; H, 4·4; N, 8·0. $C_{24}H_{22}O_7N_3As$ requires C, 53·4; H, 4·1; N, 7·8%).

Resolution of the Spiro-bromide (III; E = As, X = Br).—The bromide dihydrate (5 g.) and silver (−)-menthyloxyacetate [14] (3·76 g., 1 mol.) in acetone (125 c.c.) were boiled under reflux for 30 min. The hot mixture was filtered, the insoluble residue extracted twice with hot acetone (20 c.c.), and the solvent removed from the combined filtrates under reduced pressure. Trituration of the residual gum in ether caused crystallisation. The (−)-menthyloxyacetate, when recrystallised four times from diethyl ketone, afforded the (−)-*arsonium* (−)-*menthyloxyacetate dihydrate*, m. p. 87—89° (Found: C, 63·95; H, 7·8. $C_{30}H_{41}O_3As,2H_2O$ requires C, 64·3; H, 8·1%); drying at 40° *in vacuo* gave the highly hygroscopic anhydrous *salt*, m. p. 88·5—90° (Found: C, 68·4; H, 8·3. $C_{30}H_{41}O_3As$ requires C, 68·7; H, 7·9%). A 0·484% solution of the dihydrate had α^{20} −0·941°, $[M]^{20}$ −288°. After a fifth recrystallisation the m. p. was unaltered and a 0·480% solution of the dihydrate had α^{20} −0·921°, $[M]^{20}$ −286°.

The (−)-*arsonium picrate*, obtained from the (−)-arsonium (−)-menthyloxyacetate with aqueous-alcoholic sodium picrate, formed yellow crystals, m. p. 95—97°, from aqueous ethanol (Found: C, 53·7; H, 4·2. $C_{22}H_{24}O_7N_3As$ requires C, 53·4; H, 4·1%). A 0·757% solution had α^{20} −0·74°, $[M]^{20}$ −131·8°.

When the (−)-arsonium (−)-menthyloxyacetate was treated with sodium iodide in aqueous-ethanolic solution, only a small quantity of solid was deposited. The residue remaining on evaporation of the solution was dissolved in boiling water, and the solution, when filtered and cooled, deposited the (−)-*iodide* as needles, m. p. 223—223·5° (Found: C, 49·5; H, 4·9. $C_{18}H_{20}IAs$ requires C, 49·3; H, 4·6%). A 0·593% solution had $\alpha^{22·5}$ −0·712°, $[M]^{22·5}$ −131·5°. These values were unchanged after the solution had been set aside in the dark for 24 hr.

The diethyl ketone mother-liquors from the first recrystallisation of the (−)-menthyloxyacetate were evaporated under reduced pressure. An ethanolic solution of the residual gum was boiled (charcoal) and filtered, the warm filtrate then being treated with ethanolic sodium iodide containing a trace of water. On cooling, the (±)-iodide was deposited, m. p. (after three recrystallisations from ethanol) 276—277° alone, and 274—278° when mixed with the authentic (±)-iodide of m. p. 277—278° (Found: C, 49·4; H, 4·8%). The solution from which this racemic iodide had separated was now rich in the (+)-iodide. The residue obtained by evaporation was taken up in boiling water, and the solution filtered. Cooling caused separation of some crystals together with a gum. The crystals were filtered off (leaving the gum on the walls of the tube) and, after two recrystallisations from water (charcoal), gave the (+)-*iodide*, m. p. 223—223·5° (Found: C, 48·75; H, 4·9. $C_{18}H_{20}IAs$ requires C, 49·3; H, 4·6%); a 0·655% solution had α^{21} +0·796°, $[M]^{21}$ +133·1°. A mixture of the (+)- and the (−)-iodide, containing only approximately equal amounts, had m. p. 220—274°.

The (±)-*arsonium* (+)-*bromocamphorsulphonate* was prepared by mixing ethanolic solutions

[14] Mann and Watson, *J.*, 1947, 511.

of equimolecular quantities of the spiro-iodide and of silver (+)-bromocamphorsulphonate, filtering, and evaporating the filtrate under reduced pressure. The residual gum crystallised when rubbed with ethyl acetate, giving the *sulphonate*, m. p. 191—192° and 191·5—193° after the first and the third recrystallisation, respectively, from diethyl carbonate (Found: C, 53·8; H, 5·8. $C_{28}H_{34}O_4BrSAs$ requires C, 54·1; H, 5·5%); a 0·487% solution in methanol had $[M]^{19}$ +284°. The iodide and picrate prepared therefrom in the usual way were both optically inactive. Recrystallisation of the bromocamphorsulphonate from diethyl ketone and from ethyl methyl ketone similarly gave no evidence of resolution.

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