435. *A New Synthesis of Arsonic Acids. Part I. Coupling of αβ-Unsaturated Carbonyl Compounds with Diazotised* p-*Arsanilic Acid.*

By Walter Freund.

Arsonic acids can be synthesised by treating diazotised *p*-arsanilic acid with appropriate compounds in such a way that nitrogen is split off. The arsonophenyl group reacts with the α-carbon atom of cinnamic acids and coumarin, yielding 4-arsonostilbenes and 3-*p*-arsonophenylcoumarin.

For the preparation of aromatic arsonic acids three methods are available: the Béchamp (*Compt. rend.*, 1863, **56**, 1172), the Bart (D.R.-P. 250,264/1910; *Zentr.*, 1912, II, 882), and the Rosenmund (*Ber.*, 1921, **54**, 438) process. It has now been found that diazotised arsanilic acids, *e.g.*, diazotised *p*-arsanilic acid, can under appropriate conditions be coupled with a variety of compounds in such a way that nitrogen is split off and a new arsonic acid is formed (Austral. P. 18758/1948).

It is generally assumed that by the decomposition of a diazo-compound an organic radical is formed which stabilises itself by becoming attached to another carbon atom. The reaction was first reported by Möhlau and Berger (*Ber.*, 1893, **26**, 1994), Kühling (*Ber.*, 1895, **28**, 41, 523), and Bamberger (*ibid.*, p. 403) and is usually carried out in alkaline solution.

In 1939 Meerwein, Buchner, and van Emster (*J. pr. Chem.*, **152**, 237; B.P. 480,617) described a method of arylating αβ-unsaturated carbonyl compounds by treating them with diazotised amines in weakly acidic aqueous acetone, with cupric chloride as a catalyst. This method has been adapted to introduce the phenylarsonic acid group into other molecules. As the new arsonic acid (*e.g.*, stilbene-4-arsonic acid from diazotised *p*-arsanilic acid and cinnamic acid) separates as a copper salt or copper complex salt, the cupric chloride is used up during the reaction. The formation of such salts facilitates the isolation of the arsonic acids. The yields are only moderate, approximately 30%, sometimes much smaller, but no efforts have so far been made to find out optimum conditions. The success of the reaction depends to a large extent on the particular unsaturated compound used for coupling. As observed by Meerwein *et al.* (*loc. cit.*) aromatic amines having an electronegative substituent in the *para*-position are the best arylating agents. *p*-Arsanilic acid couples well, but is somewhat inferior to *p*-nitroaniline or *p*-chloroaniline. *m*-Arsanilic acid gives lower yields, and *o*-arsanilic acid has so far failed to yield any arylation products.

Coupling of cinnamic or substituted cinnamic acid yields 4-arsonostilbenes. On the other hand, *p*-methoxycinnamic acid does not lose carbon dioxide during the reaction, the product being α-*p*-arsonophenyl-β-*p*-methoxyphenylacrylic acid. Coumarin yields 3-*p*-arsonophenylcoumarin.

A side-reaction met with in the decomposition of diazo-compounds is the formation of symmetrical azo-compounds. In the Meerwein reaction the formation of symmetrical azo-compounds has been observed only when the reaction between the diazo-compound and the αβ-unsaturated carbonyl compound is unsatisfactory (Meerwein *et al.*, *loc. cit.*). In the case of diazotised *p*-arsanilic acid, azobenzene-*pp'*-diarsonic acid is obtained if the evolution of nitrogen is slow. When the reaction is very slow, *e.g.*, when *p*-arsanilic acid reacts with 4-hydroxy-3-nitrocinnamic acid, the azobenzene-*pp'*-diarsonic acid may become the chief product.

The reaction has been extended to compounds such as furan, thiophen, furylacrylic acid, ω-2-furylheptatrienoic acid, and thienylacrylic acid; the results will be reported later.

Experimental.

Stilbene-4-arsonic Acid.—*p*-Arsanilic acid (21·7 g.), dissolved in a solution of sodium hydroxide (4·2 g.) in water (*ca.* 200 c.c.), was mixed with a solution of sodium nitrite (7·3 g.) in water (20 c.c.) and diazotised with 25% hydrochloric acid (60 g.) in the usual manner. The diazotised solution was then added to a solution of cinnamic acid (14·8 g.) in acetone (200 c.c.) in which approx. 70 g. of crystallised sodium acetate were suspended. The mixture was well shaken or stirred until the pH becomes adjusted to approx. 6. A solution of cupric chloride (20 g.) in water (45 c.c.) was added dropwise during 3—4 hours and the whole warmed gently on a water-bath to start gas evolution. The product separated as a buff-colour copper salt. When gas evolution ceased, the precipitate was allowed to settle, the supernatant liquid was decanted, and the precipitate twice agitated with 100—150 c.c. of acetone to remove unchanged cinnamic acid. These acetone washings were mixed with the first decanted mother-liquor from which by conventional methods some cinnamic acid could be recovered. The precipitate was then collected and air-dried. The dried material was digested with approx. 2N-sodium hydroxide in which the new arsonic acid was easily soluble, the copper being precipitated. After filtration, the alkaline solution was acidified with hydrochloric acid, giving the arsonic acid as a light yellowish solid which was finally dried in a desiccator. *Stilbene-4-arsonic acid* recrystallised from acetic acid, from which buff-coloured plates (30—35%) separated which did not melt at 300° (Found: C, 55·1, 55·0; H, 4·4, 4·3; As, 24·8. $C_{14}H_{13}O_3As$ requires C, 55·3; H, 4·3; As, 24·6%).

4'-Methylstilbene-4-arsonic Acid.—*p*-Arsanilic acid (10·85 g.) in N-sodium hydroxide (60 c.c.) was treated with sodium nitrite (3·65 g.) in water (10 c.c.), and the whole added with cooling to hydrochloric acid (30—32 c.c.). The clear diazo-solution was added to 4-methylcinnamic acid (8·1 g.) in acetone (approx. 220 c.c.) in which 20 g. of cryst. sodium acetate were suspended. Gas evolution set in only after some cupric chloride (altogether 10 g., in 22 c.c. of water) had been added. The gas evolution was good at 30—35° and lasted for about 0·5 hour during which the cupric chloride solution was added dropwise. A buff-coloured solid separated and was filtered off and washed with acetone (100 c.c.). The air-dried material was dissolved in 2N-sodium hydroxide. The reddish-brown solution was filtered and the filtrate treated with hydrochloric acid. The precipitate was dried in a vacuum-desiccator (yield, 4·9 g., 30%). *4'-Methylstilbene-4-arsonic acid* separated from acetic acid in slightly yellowish plates which did not melt at 300° (Found: C, 56·6, 56·5; H, 4·8, 4·8; As, 23·7. $C_{15}H_{15}O_3As$ requires C, 56·65; H, 4·7; As, 23·6%).

From the acetone–water mother-liquors 4·5 g. of 4-methylcinnamic acid were recovered.

4'-Hydroxystilbene-4-arsonic Acid.—*p*-Arsanilic acid (10·85 g.) was diazotised as above and added to a solution of *p*-hydroxycinnamic acid (8·2 g.) in acetone (120 c.c.) to which 0·3 mole of sodium chloroacetate in a little water had been added as buffer. Gas evolution set in immediately. Cupric chloride (10 g.) in water (20—22 c.c.) was added in small portions. The gas evolution lasted for approx. 40 minutes at 22°. The solid which separated was worked up in the usual way. The arsonic acid which was obtained contained nitrogenous material. It was digested with cold sodium hydrogen carbonate solution which dissolved some dark material (azobenzene-*pp'*-diarsonic acid). *4'-Hydroxystilbene-4-arsonic acid* (*ca.* 5 g.) remained undissolved in the alkaline solution. Recrystallisation from acetic acid gave slightly yellowish plates which did not melt at 300°. The material was free from nitrogen (Found: C, 52·5, 52·3; H, 4·1, 4·1; As, 23·5. $C_{14}H_{13}O_4As$ requires C, 52·5; H, 4·1; As, 23·4%). The material soluble in cold sodium hydrogen carbonate was dried on porous tile, extracted with cold alcohol, and recrystallised from acetic acid in which it is sparingly soluble with a red colour. Dark, poorly developed crystals of azobenzene-*pp'*-diarsonic acid were obtained which did not melt at 300° (Found: C, 33·4, 33·4; H, 2·9, 3·0; N, 6·5; As, 35·1. Calc. for $C_{12}H_{12}O_6N_2As_2$: C, 33·5; H, 2·8; N, 6·5; As, 34·85%) (cf. Karrer, *Ber.*, 1912, **45**, 2362; Fichter and Elkind, *Ber.*, 1916, **49**, 246).

4-Arsono-α-cyanostilbene.—Coupling of diazotised *p*-arsanilic acid with cinnamonitrile yielded *4-arsono-α-cyanostilbene* (*ca.* 20%), slightly yellowish plates and needles (from alcohol), which did not melt at 300° (Found: C, 54·6, 54·6; H, 3·5, 3·8; N, 4·1, 4·0. $C_{15}H_{12}O_3NAs$ requires C, 54·7; H, 3·65; N, 4·3; As, 22·8%).

4-Arsono-4'-methoxystilbene-α-carboxylic Acid.—Coupling of diazotised *p*-arsanilic acid with *p*-methoxycinnamic acid yielded this *acid* (*ca.* 20%) which crystallised from acetic acid in small nearly white plates which did not melt at 300° (Found: C, 51·1 51·25; H, 4·2, 4·2; As, 19·35; MeO, 7·9, 7·95. $C_{16}H_{15}O_6As$ requires C, 50·8; H, 3·9; As, 19·8; MeO, 8·2%).

*3-*p*-Arsonophenylcoumarin.*—The reaction was carried out as described in previous examples, the yield being approx. 55%. The *coumarin* crystallised from acetic acid in slightly yellowish plates which did not melt at 300° (Found: C, 51·9, 52·1; H, 3·3, 3·35; As, 21·6. $C_{15}H_{11}O_5As$ requires C, 52·0; H, 3·2; As, 21·45%).

I thank Dr. K. F. Tettweiler, formerly of the University of Melbourne, for the analyses. This work was supported in part by a grant from the National Council for Health and Medical Research, Canberra.

DEPARTMENT OF PHYSIOLOGY, THE UNIVERSITY, MELBOURNE. [*Received, January 4th, 1950.*]
