

are not so apparent. The results of careful tests for the physiological properties which are being made on these substances will be reported in a subsequent communication.

### Summary

1. Several alkamine alcohols of the type  $\text{HO}-(\text{CH}_2)_n\text{N}_y^x$  and secondary and tertiary amines are described.
2. Esters of these alcohols are recorded and described.
3. These esters are reported to possess anesthetic properties.

OXFORD, OHIO

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

## SYNTHESES WITH TRIARYLVINYLMAGNESIUM BROMIDES. TRIARYLACRYLIC ACIDS AND THE INDONES DERIVED FROM THEM

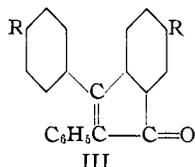
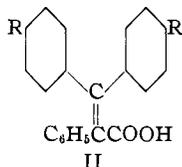
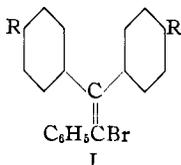
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It has been shown recently<sup>2</sup> that triphenylvinyl bromide reacts with magnesium to form a Grignard reagent which can be carbonated to give triphenylacrylic acid. The present paper describes the results obtained in similar reactions where certain substituted triphenylvinyl bromides were used

Two disubstituted triphenylvinyl bromides were studied:  $\alpha$ -phenyl- $\beta$ , $\beta$ -di-*p*-tolylvinyl bromide (I, R = CH<sub>3</sub>) and  $\alpha$ -phenyl- $\beta$ , $\beta$ -di-*p*-anisylvinyl bromide (I, R = OCH<sub>3</sub>). Both of these compounds reacted with magnesium to form Grignard reagents which on carbonation yielded the correspondingly substituted acrylic acids (II). The elimination of water from these acids led to the formation of 6-methyl-2-phenyl-3-*p*-tolylindone (III, R = CH<sub>3</sub>) and of 3-*p*-anisyl-6-methoxy-2-phenylindone (III, R = OCH<sub>3</sub>)

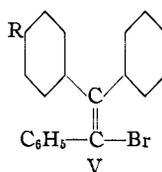
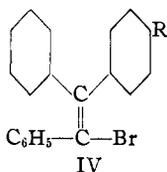


While all monosubstituted triphenylvinyl bromides having the substituent in one of the  $\beta$ -phenyl groups should exist in two stereoisomeric forms, the isolation of both of these forms was accomplished in only one of three cases studied.  $\alpha$ , $\beta$ -Diphenyl- $\beta$ -*p*-chlorophenylvinyl bromide was obtained in the *cis* form (IV, R = Cl) and in the *trans* form (V, R = Cl); only the *cis* form of  $\alpha$ , $\beta$ -diphenyl- $\beta$ -*p*-tolylvinyl bromide (IV, R = CH<sub>3</sub>),

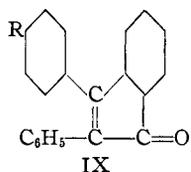
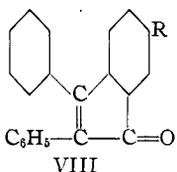
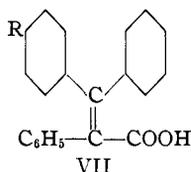
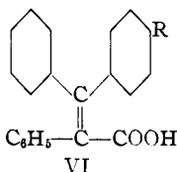
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<sup>2</sup> Koelsch, *THIS JOURNAL*, **54**, 2045 (1932).

and only the *trans* form of  $\alpha,\beta$ -diphenyl- $\beta$ -*p*-anisylvinyl bromide (V, R = OCH<sub>3</sub>) could be isolated.



These bromides all reacted readily with magnesium to form Grignard reagents whose subsequent carbonation gave triarylacrylic acids.  $\alpha,\beta$ -Diphenyl- $\beta$ -*p*-tolylvinylmagnesium bromide gave one acid, *cis*- $\alpha,\beta$ -diphenyl- $\beta$ -*p*-tolylacrylic acid (VI, R = CH<sub>3</sub>).  $\alpha,\beta$ -Diphenyl- $\beta$ -*p*-anisylvinylmagnesium bromide gave a mixture of *cis*- $\alpha,\beta$ -diphenyl- $\beta$ -*p*-anisylacrylic acid (VI, R = OCH<sub>3</sub>) and the corresponding *trans* acid (VII, R = OCH<sub>3</sub>) in the ratio of about one part of the *cis* to seven parts of the *trans* compound. The Grignard reagent from *cis*- $\alpha,\beta$ -diphenyl- $\beta$ -*p*-chlorophenylvinyl bromide gave a mixture of *cis* and *trans*  $\alpha,\beta$ -diphenyl- $\beta$ -*p*-chlorophenylacrylic acids in which the *cis* acid (VI, R = Cl) greatly predominated; the Grignard reagent from the isomeric *trans* bromide gave a similar mixture of which *trans*- $\alpha,\beta$ -diphenyl- $\beta$ -*p*-chlorophenylacrylic acid (VII, R = Cl) was the more abundant constituent.



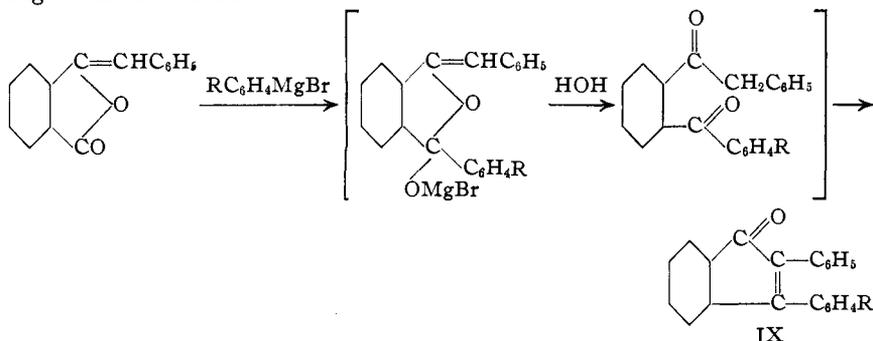
In determining the steric relationship of the phenyl groups in these triarylacrylic acids, *i. e.*, in assigning them to the *cis* or *trans* series, use was made of their ring closure to indones. It is apparent from an inspection of their formulas that a *cis* acid (VI) will give a  $\beta$ -substituted-2,3-diphenylindone (VIII), while a *trans* acid (VII) will give a 3-*p*-substituted-phenyl-2-phenylindone (IX).

Thionyl chloride in carbon tetrachloride was found to be an ideal reagent for bringing about this ring closure, in that by its use the high temperature (200°) necessary when zinc chloride is employed<sup>3</sup> was avoided. Such a high temperature has been shown to bring about isomerization of

<sup>3</sup> Meyer and Weil, *Ber.*, 30, 1284 (1897).

certain substituted cinnamic acids.<sup>4</sup> Sulfuric acid, which has been used for the preparation of 2,3-diphenylindone from triphenylacrylic acid,<sup>5</sup> was found to be unusable because of its destructive action toward the methoxylated acids. Under the conditions developed for carrying out the reaction with thionyl chloride, a pure triarylacrylic acid gave practically the theoretical yield of a pure indone, pointing to the absence of rearrangement.

One of each pair of structurally isomeric indones corresponding to one of each pair of stereoisomeric triarylacrylic acids was synthesized according to the reactions<sup>6</sup>

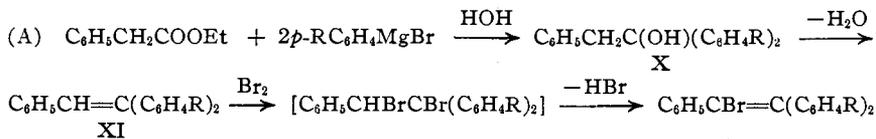


After the structure of one of the isomeric indones had been determined by this synthesis, that of the other was assigned by elimination.

The assignment of *cis* and *trans* structures to the triarylvinyl bromides rests on grounds less secure than those underlying the assignment of these structures to the triarylacrylic acids. To give structures to the bromides, it was necessary to assume that no "inversion" had taken place during two reactions, each of which involved the replacement of an atom or group whose presence was responsible for the isomerism. Such an assumption appears to be little warranted, especially since it is here shown that *some* "inversion" at least occurred in the synthesis of  $\alpha,\beta$ -diphenyl- $\beta$ -*p*-chlorophenylacrylic acid and of  $\alpha,\beta$ -diphenyl- $\beta$ -*p*-anisylacrylic acid. In the present paper, the prefixes *cis* and *trans* have been applied to the bromides mainly for convenience in nomenclature.

### Experimental

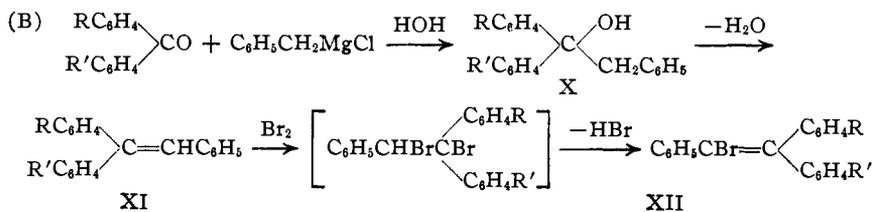
Two methods are available for the preparation of triarylvinyl bromides



<sup>4</sup> Stoermer and Voht, *Ann.*, **409**, 40, 53 (1915).

<sup>5</sup> Weitz and Scheffer, *Ber.*, **54**, 2341 (1921).

<sup>6</sup> Löwenbein and Ulich, *ibid.*, **58**, 2662 (1925); Weiss and Sauer mann, *ibid.*, p. 2736.



While method (A) is applicable to the synthesis of only disubstituted compounds and was used to prepare only  $\alpha$ -phenyl- $\beta,\beta$ -di-*p*-anisylvinyl bromide, method (B) is of general application and was used for the preparation of the other bromides described in this paper (XII, R = R' = CH<sub>3</sub>; or R' = H and R = CH<sub>3</sub>, OCH<sub>3</sub>, or Cl). The yields in all reactions involved in either method were usually over 90%.

**The Carbinols (X).** Table I.—In order to isolate the carbinols, it was necessary to decompose the intermediate ROMgX compounds with ammonium chloride solution and to exclude mineral acids, which readily effect the elimination of water. The carbinols may be converted directly into the bromides by treating their 30% solutions in acetic acid with a slight excess of a 40–50% solution of bromine in acetic acid. They were recrystallized from ethanol containing a little ammonia.

TABLE I  
THE CARBINOLS

( )-ethanol	M. p., °C.	Formula	Analyses			
			Calcd. C	H	Found C	H
$\alpha,\alpha$ -Di- <i>p</i> -tolyl- $\beta$ -phenyl-	(Not isolated)					
$\alpha,\alpha$ -Di- <i>p</i> -anisyl- $\beta$ -phenyl-	140	C <sub>22</sub> H <sub>22</sub> O <sub>3</sub>	<sup>a</sup>			
$\alpha,\beta$ -Diphenyl- $\alpha$ - <i>p</i> -tolyl-	89	C <sub>21</sub> H <sub>20</sub> O	87.5	6.94	87.3	6.5
$\alpha$ - <i>p</i> -Anisyl- $\alpha,\beta$ -diphenyl-	112	C <sub>21</sub> H <sub>20</sub> O <sub>2</sub>	<sup>b</sup>			
$\alpha$ - <i>p</i> -Chlorophenyl- $\alpha,\beta$ -diphenyl-	83	C <sub>20</sub> H <sub>17</sub> OCl	77.7	5.51	77.7	5.61

<sup>a</sup> Roca, *Anales soc. españ. fis. quim.*, 15, 29 (1917); *Chem. Abstracts*, 12, 475 (1918).

<sup>b</sup> Ley and Kirchner, *Z. anorg. allgem. Chem.*, 173, 395 (1928).

**The Ethylenes (XI).** Table II.—The ethylenes were prepared by distilling the carbinols under reduced pressure in the presence of a trace of sulfuric acid.

TABLE II  
THE ETHYLENES

( )-ethylene	B. p., °C. (mm.)	Formula	Analyses			
			Calcd. C	H	Found C	H
$\alpha,\alpha$ -Di- <i>p</i> -tolyl- $\beta$ -phenyl-	258–259 (24)	C <sub>22</sub> H <sub>20</sub>	92.9	7.1	91.5	7.1
$\alpha,\alpha$ -Di- <i>p</i> -anisyl- $\beta$ -phenyl-	283–285 (18)	C <sub>22</sub> H <sub>20</sub> O <sub>2</sub>	(Ref. a, Table I)			
$\alpha,\beta$ -Diphenyl- $\alpha$ - <i>p</i> -tolyl-	245–250 (27)	C <sub>21</sub> H <sub>18</sub>	93.2	6.7	93.2	6.5
$\alpha$ - <i>p</i> -Anisyl- $\alpha,\beta$ -diphenyl-	260–270 (25)	C <sub>21</sub> H <sub>18</sub> O	(Ref. b, Table I)			
$\alpha$ - <i>p</i> -Chlorophenyl- $\alpha,\beta$ -diphenyl-	(Not isolated)					

**The Triarylvinyl Bromides (XII).** Table III.—Bromination of the carbinols or of the ethylenes in acetic acid according to the procedure which has been described for the preparation of triphenylvinyl bromide<sup>2</sup> gave the substituted triphenylvinyl bromides. In general, they were purified by crystallization from alcohol.

TABLE III  
THE BROMIDES

( )-vinyl bromide	M. p., °C.	Formula	Analyses			
			Calcd. C	H	Found C	H
$\beta,\beta$ -Di- <i>p</i> -tolyl- $\alpha$ -phenyl-	132-133	$C_{22}H_{19}Br$	72.7	5.23	72.8	5.19
$\beta,\beta$ -Di- <i>p</i> -anisyl- $\alpha$ -phenyl-	109-111	$C_{22}H_{19}O_2Br$	66.8	4.82	66.7	4.82
$\alpha,\beta$ -Diphenyl- $\beta$ - <i>p</i> -tolyl-	114-116	$C_{21}H_{17}Br$	72.2	4.87	72.2	4.76
$\beta$ - <i>p</i> -Anisyl- $\alpha,\beta$ -diphenyl-	118-120	$C_{21}H_{17}OBr$	69.1	4.66	68.8	4.66
<i>cis</i> - $\beta$ - <i>p</i> -Chlorophenyl- $\alpha,\beta$ -diphenyl-	156-158	$C_{20}H_{14}ClBr$	65.0	3.79	65.0	4.2
<i>trans</i> - $\beta$ - <i>p</i> -Chlorophenyl- $\alpha,\beta$ -diphenyl-	103-105	$C_{20}H_{14}ClBr$	65.0	3.79	64.6	3.54

Extended fractional crystallization of  $\alpha,\beta$ -diphenyl- $\beta$ -*p*-anisylvinyl bromide and of  $\alpha,\beta$ -diphenyl- $\beta$ -*p*-tolylvinyl bromide from benzene, carbon tetrachloride or acetic acid did not effect a separation of either compound into two forms. In both cases a small amount of low melting substance was obtained from the first mother liquors, but no pure substance could be isolated from this.

**Separation of  $\alpha,\beta$ -Diphenyl- $\beta$ -*p*-chlorophenylvinyl Bromide into *Cis* and *Trans* Forms.**—Water was added to the acetic acid solution in which the bromide had been prepared and the crude bromide thus obtained, which slowly solidified, was crystallized from ethanol, in which it is quite difficultly soluble, to remove a small amount of oily impurities. The crystalline mixture (60 g.) was dissolved in 50 ml. of hot benzene, and 50 ml. of methanol was added. On cooling the solution, 27 g. of bromide melting at 155-157° crystallized. This, redissolved in 30 ml. of hot benzene and reprecipitated by the addition of 30 ml. of methanol, gave 25 g. of pure *cis* bromide, m. p. 156-158°. The oily residue left after the removal of the solvents from the combined mother liquors by distillation under reduced pressure was dissolved in 200 ml. of hot ethanol. Cooling this solution gave 27.5 g. of practically pure *trans* bromide, m. p. 100-105°.

**Carbonation of the Triarylvinylmagnesium Bromides. The Triarylacrylic Acids.** Table IV.—The Grignard reagents were prepared from 10 g. of a bromide, 0.05 ml. of ethyl bromide, a small crystal of iodine, 1.1 equivalents of magnesium and 100 ml. of ether.

The Grignard reagents were carbonated by leading in dry carbon dioxide as long as it was absorbed. Decomposition of the magnesium compounds with dilute sulfuric acid and extraction of the resulting ethereal solutions with dilute sodium carbonate gave aqueous solutions of the sodium salts

of the triarylacrylic acids. From these the organic acids were precipitated with dilute hydrochloric acid. They were recrystallized from acetic acid.

TABLE IV  
THE ACIDS

No.	( )-acrylic acid	M. p., °C.	Color with concd. H <sub>2</sub> SO <sub>4</sub>	
			Cold	Hot
1	$\alpha$ -Phenyl- $\beta$ , $\beta$ -di- <i>p</i> -tolyl-	205-206	Brown-yellow	Scarlet
2	$\alpha$ -Phenyl- $\beta$ , $\beta$ -di- <i>p</i> -anisyl-	169-170	Red-violet	Orange-red
3	<i>cis</i> - $\alpha$ , $\beta$ -Diphenyl- $\beta$ - <i>p</i> -tolyl-	185-195	Emerald green	Dark red
4	<i>cis</i> - $\alpha$ , $\beta$ -Diphenyl- $\beta$ - <i>p</i> -anisyl-	179-180	Brown-orange	Red
5	<i>trans</i> - $\alpha$ , $\beta$ -Diphenyl- $\beta$ - <i>p</i> -anisyl-	153-155	Brown-orange	Red
6	<i>cis</i> - $\alpha$ , $\beta$ -Diphenyl- $\beta$ - <i>p</i> -chlorophenyl-	203-205	Emerald green	Red-violet
7	<i>trans</i> - $\alpha$ , $\beta$ -Diphenyl- $\beta$ - <i>p</i> -chlorophenyl-	205-211	Emerald green	Red-violet

No.	Formula	Neut. equiv.		Analyses			
		Calcd.	Found	Calcd.		Found	
				C	H	C	H
1	C <sub>22</sub> H <sub>20</sub> O <sub>2</sub>	328	327	84.0	6.1	84.2	6.05
2	C <sub>22</sub> H <sub>20</sub> O <sub>4</sub>	360	354	76.6	5.56	76.5	5.67
3	C <sub>22</sub> H <sub>18</sub> O <sub>2</sub>	314	308	84.0	5.73	83.2	5.77
4	C <sub>22</sub> H <sub>18</sub> O <sub>3</sub>	330	333	80.0	5.45	80.0	5.6
5	C <sub>22</sub> H <sub>18</sub> O <sub>3</sub> + 1/2H <sub>2</sub> O	339	338	77.8	5.6	77.5, 77.4	5.4, 5.6
6	C <sub>21</sub> H <sub>18</sub> O <sub>2</sub> Cl	335	328	75.2	4.48	75.6	4.45
7	C <sub>21</sub> H <sub>18</sub> O <sub>2</sub> Cl	335	324	75.2	4.48	75.4	4.48

**Separation of  $\alpha$ , $\beta$ -Diphenyl- $\beta$ -*p*-anisylacrylic Acid into *Cis* and *Trans* Forms.**—Fractional solution in ether followed by crystallization from acetic acid gave the two forms of this acid. The higher melting *cis* acid is nearly insoluble in ether, while the *trans* acid is readily soluble.

**$\alpha$ , $\beta$ -Diphenyl- $\beta$ -*p*-chlorophenylacrylic Acids.**—The mixture of *cis* and *trans* acids obtained from 10 g. of the pure *cis* (or *trans*) bromide was separated by repeated fractional crystallization from carbon tetrachloride into 3-3.5 g. of *cis* (or *trans*) acid and an approximately equal weight of a mixture of *cis* and *trans* acids (neut. equiv., calcd.: 335; found: 327) which melted at 178-195° and which gave a separable mixture of isomeric chlorodiphenylindones on treatment with thionyl chloride.

**$\alpha$ , $\beta$ -Diphenyl- $\beta$ -*p*-tolylacrylic Acid.**—Despite the unsharp melting point of this acid, the presence of isomers in it could not be demonstrated by repeated fractional crystallizations. Furthermore, the indone obtained from it was homogeneous.

**The Indones. Table V.**—To a solution of 0.5 g. of a triarylacrylic acid in 2 ml. of dry carbon tetrachloride was added 0.5 ml. of thionyl chloride. The solution was refluxed for four hours, cooled and poured into water. The carbon tetrachloride was expelled by boiling, leaving the indone crystalline and melting only a few degrees lower than the pure compound. Recrystallization from acetic acid gave the pure ketone in a yield of 0.35-0.45 g.

TABLE V  
 THE INDONES

No.	( )-indone	M. p., °C.	Form	Color <sup>a</sup>
1	2-Phenyl-3- <i>p</i> -anisyl-6-methoxy-	153-154	Needles	Dark red
2	2-Phenyl-3- <i>p</i> -tolyl-6-methyl-	161-161.5	Needles	Bright red
3	2,3-Diphenyl-6-methyl-	175-177	Flat needles	Bright red
4	2-Phenyl-3- <i>p</i> -tolyl <sup>b</sup>	133-134	Prisms	Maroon
5	2,3-Diphenyl-6-methoxy-	167-168	Prisms	Garnet red
6	2-Phenyl-3- <i>p</i> -anisyl <sup>c</sup>	114-115	Needles	Scarlet
7	2,3-Diphenyl-6-chloro-	186-188	Plates	Orange
8	2-Phenyl-3- <i>p</i> -chlorophenyl <sup>c</sup>	162-164	Prisms	Orange

<sup>a</sup> The indones give color reactions with sulfuric acid identical with those given by the acrylic acids from which they are prepared. <sup>b</sup> Obtained from benzalphthalide. <sup>c</sup> Same compound obtained from benzalphthalide and from the appropriate acrylic acid.

No.	Formula	Analyses			
		Calcd.		Found	
		C	H	C	H
1	C <sub>23</sub> H <sub>18</sub> O <sub>3</sub>	80.6	5.26	80.6	5.39
2	C <sub>23</sub> H <sub>18</sub> O	89.0	5.8	89.2	5.65
3	C <sub>22</sub> H <sub>16</sub> O	89.1	5.4	89.0	5.56
4	C <sub>22</sub> H <sub>16</sub> O	89.1	5.4	88.5	5.32
5	C <sub>22</sub> H <sub>16</sub> O <sub>2</sub>	84.5	5.13	84.4	5.45
6	C <sub>22</sub> H <sub>16</sub> O <sub>2</sub>	84.5	5.13	84.4	4.98
7	C <sub>21</sub> H <sub>13</sub> OCl	79.5	4.11	79.6	4.22
8	C <sub>21</sub> H <sub>13</sub> OCl	79.5	4.11	79.2	4.28

The preparation of 2-phenyl-3-*p*-substituted-phenylindones from benzalphthalide was carried out according to the procedure described in the literature.<sup>6</sup> Mixed melting points proved the identity of the compounds thus prepared with the appropriate ones obtained from the triarylacrylic acids.

### Summary

It has been shown that the formation of Grignard reagents from triarylvinyl bromides is a quite general reaction.

A number of triarylacrylic acids have been prepared from triarylvinylmagnesium bromides, and in the cases where these acids exist in stereoisomeric forms it has been possible to assign structures to the isomers isolated.

The triarylacrylic acids have been found to undergo ring closure to form indones when they are treated with thionyl chloride.

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