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THE REACTION BETWEEN TRIPHENYLPHOSPHINE AND METHYL 2-BROMOALKANOATES

Joan Pórtulas, Francisco Sánchez-Ferrando* and José Sánchez-Pardo

Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Barcelona, Bellaterra, Barcelona, Spain.

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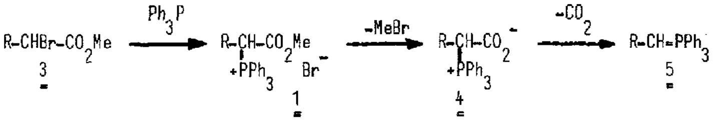
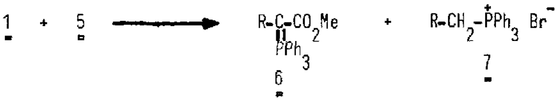
Because of the versatile applications of the Wittig reaction, the lower (1-methoxycarbonylalkyl)triphenylphosphonium bromides 1 (R = H, Me) are well characterized, useful synthetic intermediates. The higher members of the series, however, have not been isolated, with the exception of ethyl esters 1 (R = Et or *n*-Bu, ethyl esters instead of methyl esters)[1, 2]. On the other hand, the obvious preparation of salts 1, namely the reaction between triphenylphosphine 2 and a methyl 2-bromoalkanoate 3, has not been the subject of a systematic study, although it can be concluded from literature data that vigorous reaction conditions and/or long reaction times are needed for the preparation of the higher members of the series[3]. Finally, it is also known that several salts of type 1 (R = H, Ph, Ac) can decompose thermally[4, 5], giving methyl bromide, carbon dioxide, ylid 6 and salt 7 (Scheme).

In the present communication we wish to report our results on i) the reaction between 2 and 3 under several sets of experimental conditions, ii) the thermal decomposition of salts 1 in the presence of aldehydes, and iii) the straightforward Wittig reaction between 2, 3 and aldehydes in the absence of any externally added base.

The reaction between 2 and 3a (R = H), customarily carried out in benzene at room temperature, is very fast, immediate precipitation of 1a being observed upon mixing. However 1b (R = Me) is formed more slowly under similar conditions, several hours being necessary for complete precipitation according to our results. On the other hand, 2 and 3c (R = *n*-Bu) were recovered unchanged after one week at room temperature in benzene solution. Refluxing this benzene solution (or heating it at 100º under autogenous pressure, or heating the neat reactants at 100º) for 90 minutes led to the formation of pentyltriphenylphosphonium



$$\underset{3}{R\text{-}CHBr\text{-}CO_2Me} \xrightarrow{Ph_3P} \underset{1}{R\text{-}\underset{+PPh_3}{CH}\text{-}CO_2Me\ \ Br^-} \xrightarrow{-MeBr} \underset{4}{R\text{-}\underset{+PPh_3}{CH}\text{-}CO_2^-} \xrightarrow{-CO_2} \underset{5}{R\text{-}CH{=}PPh_3} \qquad (Eq.1)$$



$$1 + 5 \longrightarrow \underset{6}{R\text{-}\underset{PPh_3}{\overset{}{C}}\text{-}CO_2Me} + \underset{7}{R\text{-}CH_2\text{-}\overset{+}{P}Ph_3\ \ Br^-} \qquad (Eq.2)$$

$R\text{-}CH{=}CH\text{-}C_6H_4\text{-}NO_2$ 10

$MeO_2C\text{-}C(R){=}CH\text{-}C_6H_4\text{-}NO_2$ 11

TABLE

Thermal Wittig condensations in the absence of base

Starting compound	R	MOLAR RATIO[a] 9:1	MOLAR RATIO[a] 3:2:9	solvent	reflux time	products[b] and yields[c, d] 10	products[b] and yields[c, d] 11
1b (m.p. 160-161º)	Me	5:1		DMF	17 h	7%	7%
1c (m.p. 146-147º)	n-Bu	10:1		xylene	2 h	18%	26%
3b	Me		1:5:5	toluene	20 h	not found	41%
3c	n-Bu		1:4:4	toluene	15 h	2.3%	30%
3f	$MeO_2CCH_2CH_2$-		1:5:5	toluene	59 h	2.6%	0.7%

a) First column: aldehyde:phosphonium salt; second column: bromoester:phosphine:aldehyde.

b) All products were isolated by column chromatography or preparative tlc, and exhibited correct spectroscopic properties.

c) Calculated as per cent molar conversion of starting compound into isolated product.

d) No attempt was made to optimize yields.

bromide 7c and methyltriphenylphosphonium bromide 8, together with substantial recovery of 2 and 3c, while no 1c could be detected by NMR, although its intermediate formation can be inferred from the isolation of salts 7c and 8. Only when the reaction was conducted in dichloromethane at room temperature for more than one month could the salt 1c be isolated in crystalline form after work up, albeit in moderate (60%) yield[6]. Increasing the reaction temperature was also detrimental in this solvent, resulting in formation of 7c and 8 rather than 1c upon 2 days reflux. Similar results were obtained when 3d (R = n-C_6H_{13}) or 3e (R = n-C_8H_{17}) were used instead of 3c. The above facts allow us to conclude that reaction between 2 and the higher 3 is too slow at room temperature, while at moderate temperatures decomposition of the salts 1 is faster than their formation. These decompositions, as shown elsewhere[8], are multistage processes and involve betains 4 and ylids 5 and 6 as intermediates (Scheme).

When the decomposition of salts 1 was carried out in the presence of excess 4-nitrobenzaldehyde 9 we were able to isolate not only the Wittig adduct 10, as previously claimed,[4, 5] but also the Wittig adduct 11 (Table). Formation of products 10 shows that Wittig reaction between 9 and ylids 5 is very fast, effectively competing with the simple proton transfer involved in the transylidation[9] reaction (Eq. 2).

The same Wittig adducts could be isolated when the reaction between 2 and 3 was carried out in the presence of 9 under conditions in which salts 1 decompose (Table), thus showing the intermediate formation of ylids 5 and 6 during the reactions between 2 and 3.

1.- D.E. Clarke, P.G. Holton, R.F.K. Meredith, A.C. Richtie, T. Walker and K.D.E. Whiting: J. Chem. Soc., 1962, 2479.

2.- K. Muruyama, S. Morimura, Y. Nakamura and G. Sunagawa: Yakugaku Zasshi, 1965, 85, 757; Chem. Abst., 1965, 63, 18251a.

3.- Thus, preparation of 1 (R = Et, ethyl ester in place of methyl ester) required a 2 days reflux in benzene, while for 1 (R = n-Bu, ethyl ester in place of methyl ester) the reaction time was 20 days under reflux in ether (c.f. refs 1 and 2).

4.- N.A. Nesmeyanov, Y.S. Vasyak, V.A. Kalyavin and O.A. Reutov: Zh. Org. Khim., 1968, 4, 385; English translation, page 377.

5.- H. J. Bestmann, H. Hartung and I. Pils: Angew. Chem. Internat. Ed., 1965, 4, 957.

6.- In these dichloromethane operations the recovered haloester was actually a mixture of 3c and the corresponding chloroester, as shown by glc. This exchange between bromine and chlorine carried out by triphenylphosphine-dichloromethane has been recently described (ref. 7), although under more vigorous conditions (150º, pressure).

7.- D. Forster: JCS Chem Comms, 1975, 917 .

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9.- H.J. Bestmann: Angew. Chem. Internat. Ed., 1965, 4, 645