Tetrahedron Letters No. 6, pp 373 - 376, 1975. Pergamon Press. Printed in Great Britain.

A NEW BROMINATING REAGENT: 2-CARBOXYETHYLTRIPHENYLPHOSPHONIUM PERBROMIDE

Victor W. Armstrong, Najmul H. Chishti and Robert Ramage.
(The Robert Robinson Laboratories, University of Liverpool).

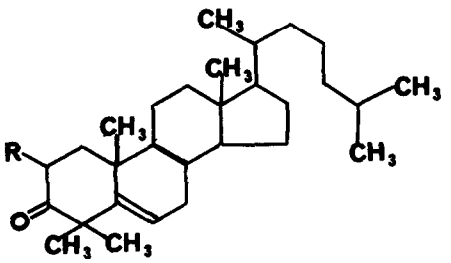
(Received in UK 5 December 1974; accepted for publication 23 December 1974)

Selective bromination of C-H α to a ketonic carbonyl function can be effected by pyridinium hydrobromide perbromide[1], phenyltrimethylammonium perbromide[2,3] and pyrrolidone-2-hydrotribromide[4] with varying degrees of selectivity in the presence of other functional groups reactive towards bromine. We have found that 2-carboxyethyltriphenylphosphonium perbromide (2) is a more stable crystalline salt which can be added with advantage to this class of selective brominating reagents.

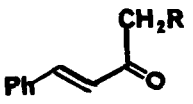
$$(Ph)_3\overset{+}{P}CH_2CH_2COOH \quad X^-$$

1 X = Br
2 X = Br_3

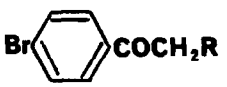
The perbromide (2) can be conveniently prepared by reacting PH_3P, acrylic acid and 49% aqueous HBr at 100°C for 10 min. to produce the bromide (1)[5,6] which, on treatment with Br_2/HOAc affords the orange perbromide; m.p.139° (MeCN). Although there is no need to isolated the intermediate salt (1) in this preparation, it is also useful to regenerate the perbromide (2) from the bromide (1) which is a by-product from bromination reactions involving (2). This means, in effect, that the salt (1) can be considered to be a Br_2 transfer agent.



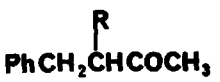
3 R=H
4 R=Br



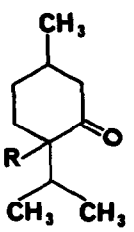
5 R= H
6 R= Br



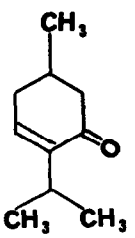
7 R=H
8 R=Br



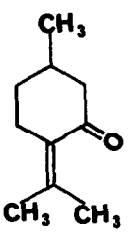
9 R=H
10 R=Br



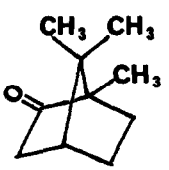
11 R=H
12 R=Br



13



14



15

On addition of the reagent (2) in THF to solutions of the ketones (3), (5) and (7) in THF at room temperature the initial orange-yellow solution was decolourised in 0.25-2.00h. After filtration of the insoluble bromide (1) the monobromo derivatives[7] (4), (6) and (8) were isolated in yields of 60-80%. These examples illustrate the selectivity of the reagent for bromination α to a ketonic carbonyl function in the present of an olefinic double bond. In the case of the unsymmetrically substituted ketones (9) and (11) α-bromination occurred predominantly at the positions indicated leading to (10) and (12) due to preferred enolisation in that direction. The position of bromination in (11) was confirmed by conversion of the bromo-compound (12) into the 2,4-dinitrophenylhydrazone derivative (m.p.140-141^{0}C) of $\Delta^{2,3}$ menthenone (13) which could be differentiated clearly by NMR from the 2,4-dinitrophenylhydrazone of pulegone (14). No reaction was observed in the case of the bicyclic ketone, camphor (15) or with esters under the above conditions.

EXPERIMENTAL

2-Carboxyethyltriphenylphosphonium Perbromide (2).

Method (a): Ph_3P (26.2g, 0.1 mole), acrylic acid (7.2g, 0.1 mole) and 49% HBr (50ml) were stirred at room temperature until solution attained then heated at 95-100^0 for 10 min. whereupon the mixture was cooled and glacial HOAc (240ml) added. Bromine (9.8ml) was added slowly with stirring to this mixture at 0^{0}C. After 0.5h the product was filtered and crystallised from acetonitrile to give 2-carboxyethyltriphenylphosphonium perbromide (52.5g, 91%) m.p. 139-141^0 (C, 44.13; H, 3.70; Br, 41.92%. $C_{21}H_{20}Br_3O_2P$ requires C, 43.87; H, 3.47; Br, 41.70%).

Method (b): via (1): 2-Carboxyethyltriphenylphosphonium bromide (1)[5,6] (15g, 0.36 mole) in glacial HOAc (95ml) was cooled to 5-10^{0}C and bromine (3.68ml) was added slowly to the stirred mixture. After a further 0.5h the perbromide (2) (18.0g, 87%) was isolated as before.

Acknowledgement. We thank S.R.C. - Eli Lilly for a C.A.S.E. award to V.W.A. and S.R.C. for an award to N.H.C.

REFERENCES

[1] C. Djerassi and C.R. Scholz, J.Amer.Chem.Soc., 70, 417 (1948).

[2] A. Marquet and J. Jacques, Bull.Soc.Chim.France, 90 (1962).

[3] W.S. Johnson, J.D. Bass and K.L. Williamson, Tetrahedron, 19, 861 (1963).

[4] D.V. Awang and S. Wolfe, Canad.J.Chem. 47, 706 (1969).

[5] H. Hoffman, Ber., 94, 1331 (1961).

[6] The salt (1) was obtained crystalline, m.p. 196-198°.

[7] The monobromo derivatives were identical with authentic materials. NMR clearly supported the bromine substitution at the positions indicated.