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A WITTIG REACTION ON MUCOCHLORIC AND MUCOBROMIC ACIDS. PREPARATION OF ETHYL (2E,4Z)-4,5-DIHALO-2,4-PENTADIENOATES AND ALKYL (2E)-5-BROMO-2-PENTEN-4-YNOATES

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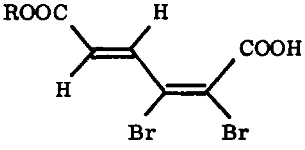
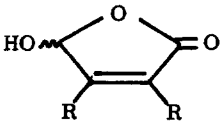
Abstract. Reaction of mucochloric and mucobromic acid with (ethoxycarbonylmethylene) triphenylphosphorane affords the ethyl ester of (2E,4Z)-4,5-dichloro- and (2E,4Z)-4,5-dibromo-2,4-pentadienoic acid respectively; in the latter case ethyl (2E)-5-bromo-2-penten-4-ynoate is formed concomittantly.

In an attempt to prepare (2Z,4E)-2,3-dibromo-5-ethoxycarbonyl-2,4-pentadienoic acid (1, R=Et), mucobromic acid (2, R=Br) was treated with 1.2-molar equivalents of (ethoxycarbonylmethylene) triphenylphosphorane (3) in 1,2-dimethoxyethane at ambient temperature. A precipitate, shown to be $Ph_3\overset{+}{P}CH_2COOEt\ \overset{-}{Br}$, formed quickly.[1] Although t.l.c. in several solvents revealed only one mobile component in the reaction mixture, the ^1H n.m.r. spectrum of this product, isolated by absorption chromatography, suggested two compounds were present, and i.r. spectroscopy indicated the presence of an acetylene. Crystallisation from petroleum ether gave one of these products, ethyl (2E,4Z)-4,5-dibromo-2,4-pentadienoate (4, R^1=Et, R^2=Br),[2] m.p. 54-56°, $\delta_H(CDCl_3)$ 1.30 (t, J = 8 Hz, CH_3), 4.24 (q, CH_2), 6.33 (d, J = 15 Hz, =CH-), 7.38 (d, =CH-), and 7.46 (s, =CHBr); $\delta_C(CDCl_3)$ 14.2 (CH_3), 60.8 (CH_2), 120.2 (=CHBr), 124.5 (=CH-), 128.6 (=CBr-), 140.4 (=CH-), and 165.8 (C=O).



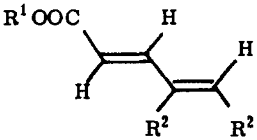
(1)



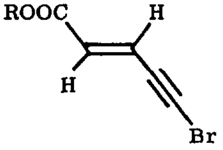
(2)

$Ph_3\overset{+}{P}\overset{-}{C}HCO_2Et$

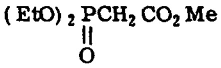
(3)



(4)

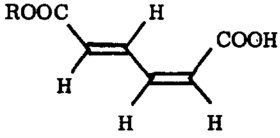


(5)



$(EtO)_2\overset{\displaystyle O}{\underset{\|}{P}}CH_2CO_2Me$

(6)

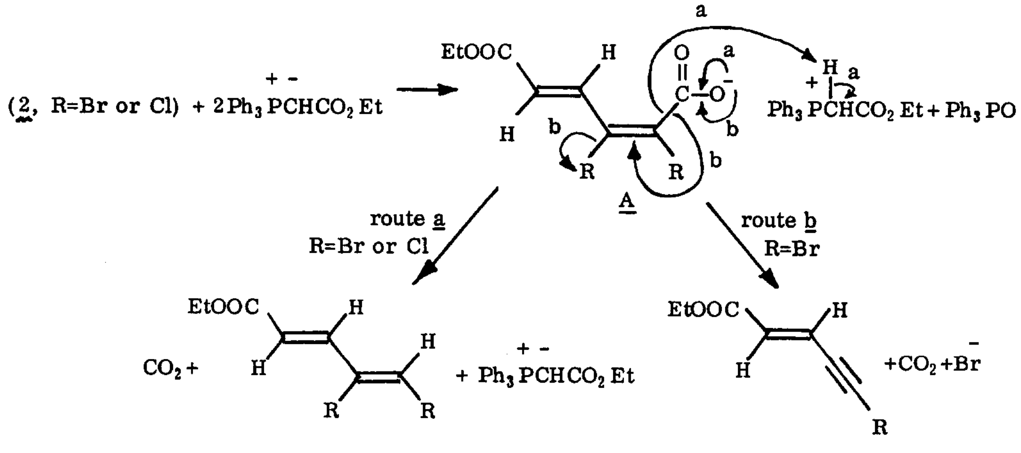


(7)

From the mother liquors of the crystallisation of (4) was isolated by distillation a liquid [b.p. 95° (bath) /20 mm with some decomposition[3]] which on the basis of its spectral data was identified as ethyl (2E)-5-bromo-2-penten-4-ynoate (5, R=Et); ν_{max}^{film} 2200 and 2160 cm^{-1} (C≡C), 1720 cm^{-1} (C=O), no absorption near 3300 (C≡C-H); $\delta_H(\mathrm{CDCl_3})$ 1.29 (t, J = 7 Hz, $\mathrm{CH_3}$), 4.24 (q, $\mathrm{CH_2}$), 6.31 (d, J = 15 Hz, =CH-), and 6.75 (d, =CH-); $\delta_C[(\mathrm{CD_3})_2\mathrm{CO}]$ 14.5 ($\mathrm{CH_3}$), 60.8 ($\mathrm{C{\equiv}\underline{C}Br}$), 61.4 ($\mathrm{CH_2}$), 77.9 ($\mathrm{\underline{C}{\equiv}C\text{-}Br}$), 124.6 (=CH-), 133.2 (=CH-), and 165.6 (C=O). Integration of the ^{1}H n.m.r. spectrum of the mixture of (4) and (5) initially obtained, showed them to be present in approximately equimolar amounts, and each to be formed in ~39% yield.

Treatment of mucochloric acid (2, R=Cl) with two[4] molar equivalents of phosphorane (3) gave, in 60% yield, ethyl (2E, 4Z)-4,5-dichloro-2,4-pentadienoate (4, R^1=Et, R^2=Cl), m.p. 47-49°, $\delta_H(\mathrm{CDCl_3})$ 1.32 (t, J = 7 Hz, $\mathrm{CH_3}$), 4.25 (q, $\mathrm{CH_2}$), 6.35 (d, J = 16 Hz, =CH-), 6.84 (s, =CHCl-), and 7.36 (d, =CH-); $\delta_C(\mathrm{CDCl_3})$ 14.2 ($\mathrm{CH_3}$), 60.9 ($\mathrm{CH_2}$), 122.4 (=CH-), 126.1 (=CHCl), 133.5 (=CCl-), 138.1 (=CH-), and 165.9 (C=O). From this reaction we were not able to isolate a chloroacetylene corresponding to (5), and the i.r. spectrum of the crude product gave no indication of its presence.

A possible rationalization for these reactions is shown in the Scheme, and involves a carboxylate intermediate, A.



Scheme

That compound (4, R^1=Et, R^2=Br) is not the precursor of the bromo-acetylene (5, R=Et) was demonstrated in a separate experiment which showed that the former compound was unaffected by treatment with phosphorane (3) under the reaction conditions.

In the light of these results it was surprising that treatment of (2, R=Br) with one molar equivalent of methyl diethylphosphonoacetate (6) in a Horner-Emmons reaction[5] afforded in 55% yield, predominantly,[6] the (2Z, 4E) isomer of 2,3-dibromo-5-methoxycarbonyl-2,4-pentadienoic acid (1, R=Me), m.p. 135-142°, $\delta_H[(\mathrm{CD_3})_2\mathrm{CO}]$ 3.94 ($\mathrm{CH_3}$), 6.76 (d, J = 16 Hz, =CH-), 8.37 (d, =CH-), and 12.3 (br.s, COOH); $\delta_C[(\mathrm{CD_3})_2\mathrm{CO}]$ 52.3 ($\mathrm{CH_3}$), 126.0 (=CBr-), 129.2 (=CH-), 133.6 (=CBr-), 138.7 (=CH-), and 163.5, 166.4 (2 × C=O).[7] However, it should be noted that similar treatment of 5-hydroxy-

2(5H) furanone (2, R=H) is known[8] to give (2Z, 4E)-5-methoxycarbonyl-2,4-pentadienoic acid (7, R=Me). We have reacted 5-hydroxy-2(5H) furanone (2, R=H) with phosphorane (3) and obtained in 30% yield (2Z, 4E)-5-ethoxycarbonyl-2,4-pentadienoic acid (7, R=Et) m.p. 90-92°, δ_H($CDCl_3$) 1.35 (t, J = 7 Hz, CH_3), 4.30 (q, CH_2), 6.05 (d, $J_{2,3}$ = 11 Hz, H-2), 6.22 (d, $J_{4,5}$ = 15 Hz, H-5), 6.83 (dd, $J_{2,3}$ = $J_{3,4}$ = 11 Hz, H-3), 8.41 (dd, H-4), and 11.34 (br. s, COOH)[9]; δ_C ($CDCl_3$) 14.3 (CH_3), 61.0 (CH_2), 123.8, 130.0, 138.2, 142.8 (4 × =CH-), and 166.2, 170.6 (2 × C=O).

It seems that the halogen substituents in mucochloric and mucobromic acids (2, R=Cl and Br, respectively) are responsible for the different outcome of their reaction with phosphorane (3), compared to that between 5-hydroxy-2(5H) furanone (2, R=H) and (3), probably by stabilizing an incipient carbanion at C-2 in the intermediate A shown in the Scheme. The reason for the different outcome of the reaction of mucobromic acid with phosphorane (3) and with the phosphonate anion from (6) is not clear to us, but the extent of protonation of the carboxylate group in A in the different reaction media might be an important factor.

Further evidence for the possible involvement of the carboxylate species A (Scheme) in the formation of the acetylene (5, R=Et) was obtained by treatment of (1, R=Me) with one molar equivalent of phosphorane (3), which gave, after chromatography, the crystalline methyl (2E)-5-bromo-2-penten-4-ynoate (5, R=Me), m.p. 53-54°, ν_{max}^{Nujol} 2200, 2160 cm^{-1} (C≡C), 1720 cm^{-1} (C=O), no absorption near 3300 (C≡C-H); δ_H($CDCl_3$) 3.93 (s, CH_3), 6.59 (d, J = 17 Hz, =CH-), and 7.05 (d, =CH-); δ_C[$(CD_3)_2CO$] 52.1 (CH_3), 60.8 (C≡CBr), 77.7 (C≡C-Br), 124.8 (=CH-), 132.6 (=CH-), and 166.0 (C=O). However, the fact that little of the alkene (4, R^1=Me, R^2=Br) was produced in this reaction suggests that if the species A is a central intermediate, as shown in the Scheme, then its mode of decomposition (route a or route b) is strongly dependent on the reaction conditions as well as on the type of halogen substituent it contains.

The reaction of mucochloric and mucobromic acid with phosphoranes such as (3) provides convenient syntheses of the alkyl esters of (2E, 4Z)-4,5-dihalo-2,4-pentadienoic acids.[10] In addition the decarboxylative route[12] to the conjugated bromo-acetylenes of the type (5) affords a useful synthesis of this interesting class of compounds.

Notes and References

1. Triphenylphosphine oxide is reasonably soluble in 1,2-dimethyoxyethane and it did not precipitate in these reactions.

2. Compounds (1, R=Me), (4, R=Et, R^2=Br), (4, R^1=Et, R^2=Cl), (5, R=Me), and (7, R=Et) gave satisfactory elemental analyses, and mass spectra were in accordance with their structures. Partial decomposition of bromo-acetylene (5, R=Et) on distillation led to unsatisfactory elemental analysis of this compound.

3. The instability of conjugated bromo-acetylenes towards distillation has been noted previously; see L. Brandsma, 'Preparative Acetylenic Chemistry', Elsevier, Amsterdam, 1971, p. 99.

4. Treatment of (2, R=Cl) with one molar equivalent of (3) gave (4, R^1=Et, R^2=Cl) in only 20% yield.

5. For reviews see A. V. Dombrovskii and V. A. Dombrovskii, Russ. Chem. Rev. (Engl. Transl.), 1966, 35, 733; J. Boutagy and R. Thomas, Chem. Rev., 1974, 74, 87.

6. From its ^1H n.m.r. spectrum, the compound appeared to contain a very small proportion of the (2*E*, 4*E*)-isomer, although this was not apparent in the ^{13}C n.m.r. spectrum. Repeated recrystallisation did not remove this isomer.

7. The broad m.p. range for (**1**, R=Me) may be partly due to its thermal lability. After heating (**1**, R=Me) at its m.p. for approx. 2 min., t.l.c. (CH_2Cl_2=MeOH, 9:1 v/v) showed that it was partially, but cleanly converted into a faster running compound, indicated by n.m.r. spectroscopy to be the lactone resulting from Michael-type addition of the carboxyl group to the α,β-unsaturated ester moiety.

8. G. Pattenden and B. C. L. Weedon, *J. Chem. Soc. (C)*, 1968, 1984.

9. This ^1H n.m.r. spectrum shows the expected similarities to the spectrum reported[8] for the corresponding methyl ester (**7**, R=Me).

10. Surprisingly, it appears that of this class of compounds, only methyl (2*E*, 4*Z*)-4,5-dichloro-2,4-pentadienoate (**4**, R^1=Me, R^2=Cl) has been described previously,[11] prepared by a normal Wittig reaction between (*Z*)-2,3-dichloro-acrylaldehyde and (methoxycarbonylmethylene)-triphenylphosphorane.

11. A. Roedig, H. Göpfert, and D. Scheutzow, *Justus Liebigs Ann. Chem.*, 1979, 194.

12. V. Jäger, in Houben-Weyl Methoden der Organischen Chemie, ed. E. Müller, G. Thieme Verlag, Stuttgart, 1977, vol. V/2a, p. 239-246.

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