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Facile dibromoolefination of lactones using bromomethylenetriphenylphosphorane†

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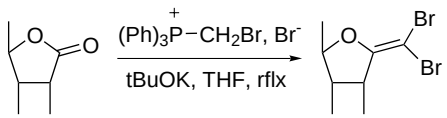
Abstract—Dibromoolefination of lactones was achieved in high yields using bromomethylenetriphenylphosphorane in refluxing tetrahydrofuran. This reaction is believed to proceed via bromination of the monobromophosphorane from the corresponding bromomethyltriphenylphosphonium bromide with concomitant formation of methylenetriphenylphosphorane as shown by ^{31}P NMR. Transylidation should occur to afford the reactive dibromomethylenetriphenylphosphorane.

Halogenated olefins proved interesting intermediates for the synthesis of elaborated compounds. Acetylenics can be formed easily from dibromo compounds using the well known Corey–Fuchs method.[1,2] A one-step variant has also been proposed.[3] Recently, uses of dibromoolefins as substrates in the Suzuki[4] or Stille reaction[5] have been described. Numerous methods are available for the synthesis of dichloro or dibromo vinylic compounds among which Wittig-type methodologies occupy a prominent place.[6] Esters and lactones are, in principle, poorly reactive in Wittig olefination.[7] However, in the last decade we were able to establish the usefulness of phosphorus-based reagents for the olefination of the carbonyl group of esters and lactones.[8] The dichloroolefins obtained this way underwent facile epoxidation with *m*-chloroperbenzoic acid followed by immediate transposition to afford the corresponding acylchloride. Further transformation of the latter gave an easy access to anomeric azido esters.[9] Unexpectedly, the rather hindered and poorly reactive dichloroolefinic bond undergo facile electrophilic addition of chlorine to provide the corresponding tetrachlorocompounds.[10] Transformation of these dichloroolefins to acetylenic open-chain alcohols has been also described.[11] Given the observed peculiar reactivity of these oxygen-substituted dichloroolefinic bonds, we attempted to widen the scope of these transformations by examining the reactivity of the corresponding dibromo compounds. Formation of the latter was thus investigated. A direct route to dibromoolefins seemed the reaction of the lactone with triphenylphosphine and carbon tetrabromide.[6,12] Although this reaction is well documented with carbonyl groups it seemed that the reactivity of ester carbonyl groups was too poor to ensure clean transformation. In sharp contrast with our previously reported results,[8] heating lactone **1** with triphenylphosphine and carbon tetrabromide in refluxing THF, gave only minute amounts of the expected dibromoolefin. In order to obtain the less hindered monobromoolefins which should also present interesting properties, we investigated the reaction of bromomethylenetriphenylphosphorane with lactones.



Bromomethyltriphenylphosphonium bromide[13] **17** was treated with potassium *tert*-butoxide giving the corresponding phosphorane **18**,[2] which reacted with lactone **1** in refluxing tetrahydrofuran to provide a single compound. Mass spectrometry undoubtedly established the structure of this compound which was clearly the dibromoolefin **2**. Good yields of this compound were obtained using a fourfold excess of phosphonium salt **17**. A series of dibromoolefins was obtained using an optimized procedure according to the results shown in Table 1. The results shown here deserve a few com-

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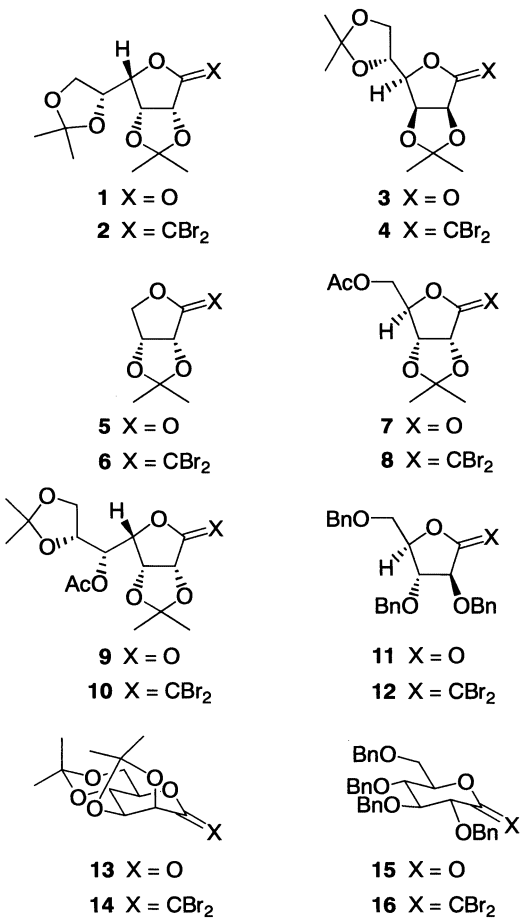
Table 1. Results of dibromoolefinations[a]

Entry	Substrate	Product	Reaction time (h)	Yield (%)
1	**1**	**2**	0.5	87
2	**3**	**4**	0.5	69
3	**5**	**6**	1	83
4	**7**	**8**	2	60
5	**9**	**10**	2	52
6	**11**	**12**	2	35
7	**13**	**14**	1	60
8	**15**	**16**	2	32

[a] Four molar equivalents of the phosphonium salt **17** and *t*BuOK were used.

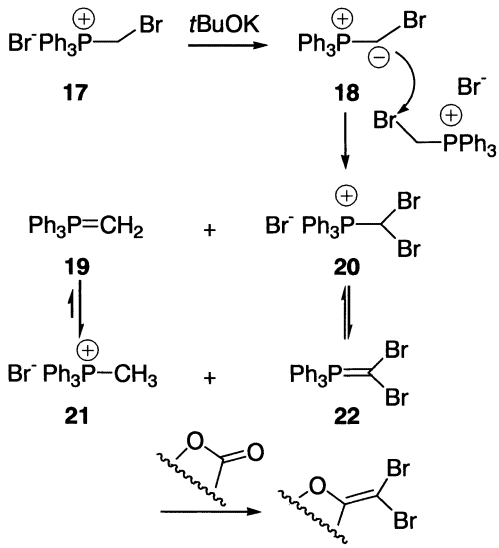
ments. The yields were excellent with lactones **1**, **3** and **5**, where only one face of the lactone ring is hindered. The yields were slightly lower with lactones **7** and **9** and it should be noted that the acetate group present on these substrates did not react under these conditions.[8] The δ-lactone **13** gave also excellent results. This was not the case with the two lactones **11** and **15** which are protected with benzyl groups. One may assume that given the basic conditions, the well-established β-elimination of a benzyloxy group should take place.[14]



The most intriguing feature of these results is obviously the unexpected formation of a dibromoolefin starting from a monobromophosphonium salt. The formation of vinylic bromides from ketone and aldehyde carbonyl groups via Wittig olefination with phosphorane **18** is well documented. Typically this reaction is performed at low temperature and gives an excellent yield of monobromolefins. It seems clear that the reaction observed with lactones is due to reaction conditions, especially the high temperature used as compared with the olefination of ketones and aldehydes. Only a few examples report on the formation of such dihaloolefins as by-products,[15] in the Wittig olefination with monohalomethylenetriphenylphosphorane, but to the best of our knowledge no preparative use of this reaction has been reported.

The observed dibromoolefination can obviously be explained by two different mechanisms. On the one hand, dibromomethylenetriphenylphosphorane **22** should be formed from **18** under the reaction conditions and reacts with the lactone. Thus, according to Scheme 1, deprotonation of **17** with *t*BuOK leads to phosphorane **18** in equilibrium with **17** as shown by NMR. Thus, ylide **18** could react with the phosphonium salt **17** to give the dibromomethylenephosphonium bromide **20** and the phosphorane **19**. Subsequent transylidation between **19** and **20** or deprotonation of the latter by *t*BuOK, would afford the phosphorane **22** and then the dibromoolefin.[16] On the other hand, the expected monobromoolefin would be formed and undergo electrophilic bromination and subsequent elimination to afford the dibromoolefin.

Attempts were made to shed light on the reaction mechanism by following the course of the reaction of bromomethyltriphenylphosphonium bromide **17** with *t*BuOK. The experiments were thus carried out in THF although the different species are poorly soluble.[17] The reaction of **17** with *t*BuOK in the absence of lactone was followed by NMR and showed the pattern A in Fig. 1 after 2 h.



Scheme 1. Possible mechanism for dibromethylenation.

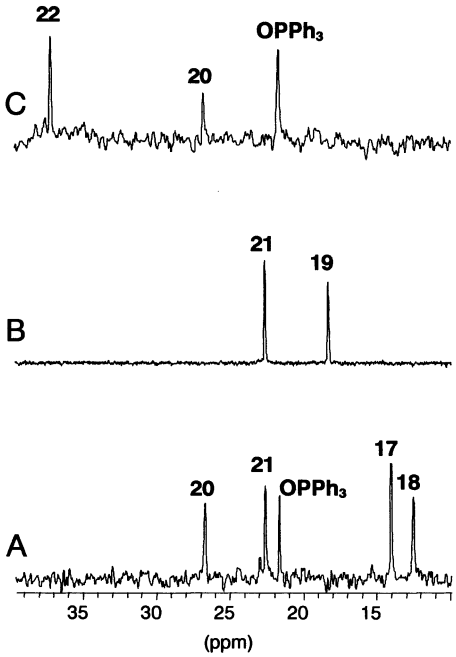


Figure 1. ^{31}P NMR spectra in THF of: (A) **17**+*t*BuOK; (B) **21**+*t*BuOK; (C) PPh_3–CBr_4.

Five main phosphorylated species were detected. The starting salt **17** was still present, in equilibrium with the corresponding phosphorane **18** (12.5 ppm) (Table 2). Evidence for the formation of methyltriphenylphosphonium salt **21** (22.5 ppm) was obtained by examining the reaction of this species with *t*BuOK (B, Fig. 1). It is clear that the phosphorane **19** (18 ppm) is in equilibrium with **21**. No traces of phosphorane **19** was detected in the first experiment (A) confirming a rapid ylide exchange which favor the formation of brominated phosphorane at the expense of methylenephosphorane **19**. The presence of triphenylphosphine oxide (21.6 ppm) in the reaction (A) was established by adding pure material. In order to identify the fifth signal (26.6 ppm) the reaction of triphenylphosphine and carbon tetrabromide was next examined. Previous studies by Appel showed the complexity of the reaction of triphenylphosphine and carbon tetrahalide.[18] The reaction of triphenylphosphine with carbon tetrabromide allowed the isolation of a solid which is believed to contain the dibromo-olefinating species.[1] However, the NMR spectrum of this solid (C, Fig. 1) exhibited three peaks (37, 26.6 and 21.6 ppm). Two peaks were attributed, respectively, to triphenylphosphine oxide (21.6 ppm) and to the dibromomethylphosphonium salt **20** on the basis of its ^{13}C NMR spectrum.[3] The third peak (37 ppm) disappeared upon addition of *t*BuOK in the NMR sample C leading to rapid formation of triphenylphosphine oxide,[19] and was attributed to the phosphorane **22**. Although no spectral evidence of the presence of **22** in this reaction was obtained, the existence of phosphonium salt **20** could be considered as an indirect proof of the formation of phosphorane **22** in the reaction medium, which explain the observed dibromoolefination of lactone.

Table 2. ^{31}P chemical shifts of phosphorylated species in THF[a]

Substrate	Chemical shift (δ)
17	14
18	12.5
19	18
20	26.7
21	22.5
22	37

[a] ^{31}P NMR chemical shifts were measured in ppm relative to external 85% H_3PO_4.

In conclusion the reaction of monobromomethyltriphenylphosphorane with lactone gave only the corresponding dibromoolefins. NMR studies provided strong evidence for the formation of dibromomethylphosphonium salt suggesting the transient formation of dibromomethylenephosphorane. This unusual reaction opens the way to a novel series of *C*-glycosylidene compounds which cannot be prepared using the triphenylphosphine/carbon tetrabromide reagent.

Acknowledgements

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References

1. Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett*. **1972**, 3769–3772.
2. Matsumoto, M.; Kuroda, K. *Tetrahedron Lett*. **1980**, *21*, 4021–4024.
3. (a) Michel, P.; Gennet, D.; Rassat, A. *Tetrahedron Lett*. **1999**, *40*, 8575–8578; (b) For a review, see: Eymery, F.; Iorga, B.; Savignac, P. *Synthesis* **2000**, 185–213.
4. (a) Roush, W. R.; Moriarty, K. J.; Brown, B. B. *Tetrahedron Lett*. **1990**, *31*, 6509–6512; (b) Shen, W. *Synlett* **2000**, 737–739; (c) Bauer, A.; Miller, M. W.; Vice, S. F.; McCombie, S. W. *Synlett* **2001**, 254–256.
5. Shen, W.; Wang, L. *J. Org. Chem*. **1999**, *64*, 8873–8879.
6. (a) Ramirez, F.; Desai, N. B.; McKelvie, N. *J. Am. Chem. Soc*. **1962**, *84*, 1745; (b) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev*. **1989**, *89*, 863; (c) Bestmann, H. J.; Zimmerman, R. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, p. 171.
7. (a) Suda, M.; Fukushima, A. *Tetrahedron Lett*. **1981**, *22*, 759–762; (b) Murphy, P. J.; Brennan, J. *Chem. Soc. Rev*. **1988**, *17*, 1–30; (c) Murphy, P. J.; Lee, S. E. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3049–3066.
8. (a) Lakhrissi, M.; Chapleur, Y. *Synlett* **1991**, 583–587; (b) Lakhrissi, M.; Chapleur, Y. *J. Org. Chem*. **1994**, *59*, 5752–5757; (c) Lakhrissi, M.; Chapleur, Y. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 750–752.

9. Lakhrissi, M.; Chapleur, Y. *Tetrahedron Lett*. **1998**, *39*, 4659–4662.
10. Lakhrissi, M.; Taillefumier, C.; Chaouch, A.; Didierjean, C.; Aubry, A.; Chapleur, Y. *Tetrahedron Lett*. **1998**, *39*, 6457–6460.
11. Yadav, J. S.; Prahlad, V.; Chander, M. C. *J. Chem. Soc., Chem. Commun*. **1993**, 137–138.
12. For a review see: Appel, R. *Angew. Chem., Int. Ed. Engl*. **1975**, *14*, 801.
13. Wolinski, J.; Erikson, K. L. *J. Org. Chem*. **1965**, *30*, 2208–2210.
14. (a) Hall, R. H.; Bischofberger, K.; Eitelman, S. J.; Jordaan, A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2236–2241; (b) Rosenblum, S. B.; Bihovsky, R. *J. Am. Chem. Soc*. **1990**, *112*, 2746–2748; (c) Czernecki, S.; Perlat, M.-P. *J. Org. Chem*. **1991**, *56*, 6289–6292.
15. (a) Fischer, H.; Fischer, H. *Chem. Ber*. **1966**, *99*, 658–667; (b) Bestmann, H. J.; Rippel, H. C.; Dostalek, R. *Tetrahedron Lett*. **1989**, *30*, 5261–5262.
16. This type of ylide dismutation has been already described by Bestmann in the 1960s: Bestmann, H. J. *Chem. Ber*. **1962**, *95*, 58–63. Olefination of lactone **1** with phosphorane **19** gave only 20% of the corresponding olefin.
17. Preliminary experiments were run in DMSO. However, the extensive formation of triphenylphosphine oxide led to the conclusion that the solvent was reactive under the reaction conditions. See Ref. 19.
18. Appel, R.; Knoll, F.; Michel, W.; Morbach, W.; Wihler, H.-D.; Veltman, H. *Chem. Ber*. **1976**, *109*, 58–70.
19. Rapid disappearance of **22** in DMSO was observed by ^{31}P NMR corresponding to the reduction of DMSO. Analogous reduction of DMSO by triphenylphosphine and carbon tetrachloride by a yet unknown mechanism has been already described: Szmant, H. H.; Cox, O. *J. Org. Chem*. **1966**, *31*, 1596–1598. The present work provides evidence that the phosphorane is likely to be the active species.