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# REACTION OF TRIPHENYLPHOSPHINE-CARBON TETRAHALIDE REAGENT WITH α-KETO-γ-LACTONE

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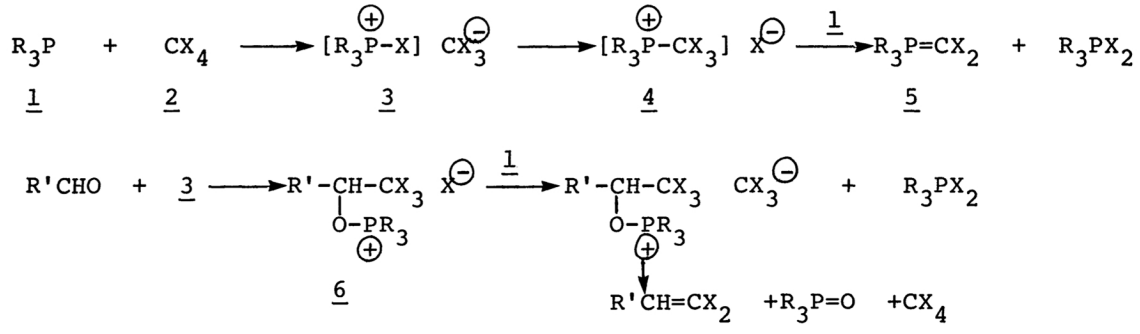
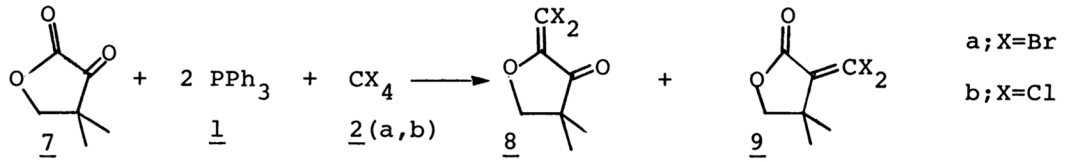
Triphenylphosphine-carbon tetrahalide reagent reacts with 4,4-dimethyloxolan-2,3-dione to afford two dihalomethyleneoxolanes, 8 and 9. The major reaction course can be changed by the addition order of the reagents. Reaction mechanisms are discussed.

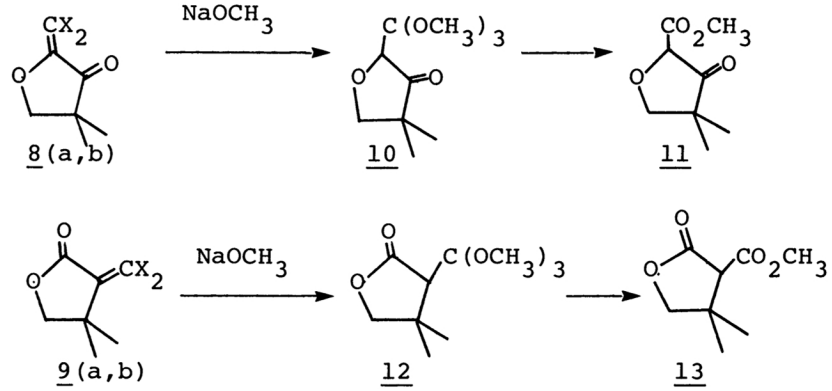
Triphenylphosphine 1 (R=Ph) with carbon tetrahalide 2 ($CBr_4$ and $CCl_4$) has been known to react with carbonyl compounds to produce 1,1-dihalogeno-olefins.[1] This reagent is also useful for the exchange of hydroxy group with a halogen atom.[2] In the former transformation, phosphonium salt 4, which is produced from 1 and 2 via 3, reacts further with 1 to form a ylid 5 (R=Ph). This ylid has been believed to react with carbonyl compounds (Wittig type reaction) to afford 1,1-dihalogeno-olefins. On the other hand, when tris(dimethylamino)-phosphine 1 ($R=NMe_2$) is used in place of triphenylphosphine, no ylid of the type 5 has been claimed to be formed.[3] Instead, carbonyl compounds react with phosphonium salt 3 ($R=NMe_2$) producing an adduct 6. Subsequent transformation shown in the following scheme generates 1,1-dihalogeno-olefins. In this report, we present our findings that more than one reaction pathways are involved in this dihalomethylenation reaction using triphenylphosphine-carbon tetrahalide system, suggesting the presence of an interaction between 3 and carbonyl group prior to the ylid formation.



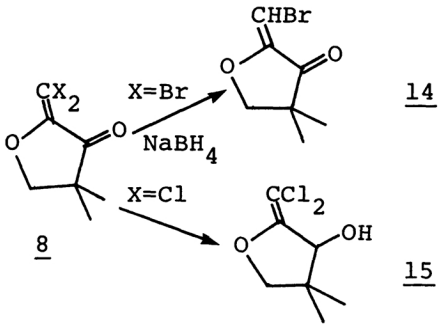
In connection with our project to prepare new derivatives of α-methylene-γ-lactones, which are expected to exhibit biological activities, we examined a reaction of 1(R=Ph)+2 reagent with 4,4-dimethyloxolan-2,3-dione 7 and found that two dihalogeno-olefins were produced. Experimentally, when 1 (R=Ph) was added in small portions into a solution of 2 (X=Br) and 7 in dichloromethane (Method A), two dibromoolefins 8a[4] and 9a[5] were isolated in 21 and 58% yields, respectively. On the other hand, when ylid 5 (R=Ph, X=Br), which was produced by mixing 1 (R=Ph) and 2 (X=Br) in dichloromethane, was treated with 7 (Method B), the same products were obtained, but in this case the yields were 57% for 8a and 13% for 9a. This diverse reactivity was also observed with triphenylphosphine-carbon tetrachloride reagent; 8b and 9b were isolated in 5 and 59% yields, respectively, in Method A, while isolated yields in Method B were 44% for 8b and 38% for 9b.

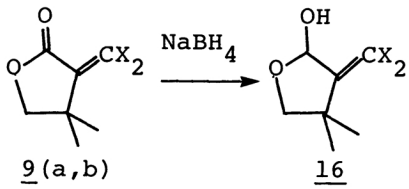



The structures of these products were determined from spectroscopic data and by chemical transformations. When 8(a,b) was treated with excess sodium methoxide an orthoester 10[6] was obtained. This was hydrolyzed upon standing at room temperature to a ketoester 11.[7] Reaction of 9(a,b) with sodium methoxide formed similarly an orthoester 12,[8] and its hydrolysis afforded a diester 13.[9] Chemical shifts of methyne protons in these products [δ 4.12(10), 4.58(11),2.59 (12), and 3.22(13)] in NMR spectra clearly distinguish the structures. Also, mass spectra of 8 show a strong fragmentation peak at $M^+$-84, corresponding to $CX_2$=C=O.



Sodium borohydride reduction was rather deceptive. Reduction of 8a and 8b produced 14[10] and 15,[11] while 9(a,b) was reduced to lactol 16(a,b).[12]




In order to know the mechanism of this dihalomethylenation reaction, several control experiments were performed using $CBr_4$ in Method A, and we obtained following observations. 1) Even when 1/10 of the required amount of 1 (R=Ph) was added, 9a was formed. 2) When the added amount of 1 (R=Ph) was less than a half of the total, only 9a was produced. 8a appeared near the end of addition of 1. This suggests that 8 and 9 are not produced from a common intermediate. 3) Addition of triphenylphosphine dibromide had no effect on the reaction course. 4) When reagent 5 (R=Ph, X=Br) was prepared either from 1 (R=Ph), 2 (X=Br), and zinc,[13] or from 1 (R=Ph), $CHBr_3$, and potassium t-butoxide,[14] and treated with 7, both 8a and 9a were obtained in very low yields. Furthermore, similar diverse reactivity of (1 + 2) reagent has been reported in the reaction with alcohols. Namely, halides are obtainable only when the alcohol is present in the reaction mixture before the addition of 1[15] (this corresponds to Method A in this report).

Above results suggest that no ylid intermediate of the type 5 was formed in Method A, at least at the early stage of addition of 1 (R=Ph). In Method A, initially formed phosphonium salt 3 (R=Ph, X=Br) reacts with ketone carbonyl in 7 preferentially before the formation of ylid 5. And once a ylid 5 (R=Ph) is formed, it reacts with both carbonyl groups in 7 affording 8 as the major product. This indicates that besides the accepted ylid reaction via 5 (R=Ph), dihalomethylenation of carbonyl compounds using triphenylphosphine proceeds by direct interaction between phosphonium salt 3 and carbonyl compound prior to ylid formation (a mechanism similar to the one using tris(dimethylamino)phosphine). And the chemoselectivity of these two nucleophilic reagents (3 and 5) toward 7 was quite marked.

In the above, we showed that two different pathways seems to be involved in the dihalomethylenation of α-keto-γ-lactone by triphenylphosphine-carbon tetrahalide reagent, and major reaction course can be controlled by changing the addition order of reagent.

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L. Gruber, I. Tomoskozi, and L. Radics, Synth., 1975, 708.
3) J. C. Combret, J. Villieras, and G. Lavielle, Tetrahedron Lett., 1971, 1035.
G. Lavielle, J. C. Combret, and J. Villieras, Bull. Soc. chim. Fr., 1971, 2047.
4) Bp 76-78°C/0.5 Torr.; NMR δ 1.22(6H,s), 4.15(2H,s); IR 1740, 1590, 1465, 1270, 1180, 1160, 1000, 860, 740 $cm^{-1}$; MS m/e 286(24%), 284(49), 282(26), 271 (6), 269(13), 267(7), 202(41), 200(84), 198(44), 174(7), 172(15), 170(8), 56 (73), 41(100).
5) Mp 84-85°C; NMR δ 1.44(6H,s), 3.88(2H,s); IR 1760, 1600, 1470, 1255, 1150, 1050, 1030, 770 $cm^{-1}$; MS m/e 286(16%), 284(30), 282(15), 271(22), 269(43), 267(22), 243(20), 241(41), 239(21), 228(6), 226(19) 224(10), 205(49), 203(45), 161(48), 159(46), 147(93), 145(89), 65(76), 39(100).
6) NMR δ 1.15(6H,s), 3.40(9H,s), 3.85(1H,d,J=8Hz), 4.07(1H,d,J=8Hz), 4.12(1H,s).
7) NMR δ 1.17(3H,s), 1.20(3H,s), 3.80(3H,s), 3.98(1H,d,J=9Hz), 4.15(1H,d,J=9Hz), 4.58(1H,s); IR 1750, 1230, 1100, 1070 $cm^{-1}$.
8) NMR δ 1.17(3H,s), 1.21(3H,s), 2.59(1H,s), 3.37(9H,s), 3.75(1H,d,J=8Hz), 4.03 (1H,d,J=8Hz); IR 1780, 1080 $cm^{-1}$; MS m/e 187(49%, $M^+-OCH_3$).
9) NMR δ 1.15(3H,s), 1.30(3H,s), 3.22(1H,s), 3.78(3H,s), 3.97(1H,d,J=9Hz), 4.15(1H,d,J=9Hz); IR 1790, 1720, 1160, 1025 $cm^{-1}$; MS m/e 173(5%, $M^+$+1).
10) NMR δ 1.22(6H,s), 4.22(2H,s), 6.27(1H,s); IR 3090, 1740, 1625,1300, 1140, 995, 720 $cm^{-1}$; MS m/e 206(26%), 204(25).
11) NMR δ 1.05(3H,s), 1.13(3H,s), 2.40(1H,d,J=3Hz,OH), 3.86(1H,d,J=8Hz), 4.08 (1H,d,J=8Hz), 4.28(1H,d,J=3Hz); IR 3200, 1020 $cm^{-1}$; MS m/e 200(5%), 198(30), 196(45).
12) 16a; NMR δ 1.33(3H,s), 1.37(3H,s), 3.30(1H,OH), 3.73(1H,d,J=8Hz), 4.08(1H, d,J=8Hz), 5.75(1H,d); IR 3390, 1650, 1620, 1115 1070, 1035, 770 $cm^{-1}$; MS m/e 287(2%), 285(3), 283(2).
16b; NMR δ 1.29(3H,s), 1.35(3H,s), 3.67(1H,d,J=8Hz), 4.02(1H,d,J=8Hz),4.27 (1H,d,J=4Hz), 5.81(1H,d,J=4Hz); IR 3370, 1640, 1120, 1070, 1030, 1015, 890 $cm^{-1}$; MS m/e 183(1%), 181(8), 179(12)($M^+$-OH).
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