Preparation of chloroformates using bis(trichloromethyl)carbonate

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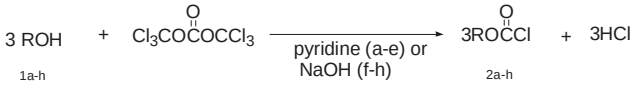
The synthesis of eight chloroformates using bis(trichloromethyl)carbonate(BTC) is reported. It has been found that the yields by this BTC method are improved over the earlier phosgene method, and sodium hydroxide is better than pyridine as catalyst for the preparation of phenyl chloroformate.

Keywords: synthesis, chloroformate, BTC

Chloroformates are versatile intermediates in the synthesis of important organic compounds. The most widely used method for the synthesis of chloroformates is the reaction of phosgene with alcohols or phenols. However, phosgene is a highly toxic gas and inconvenient to transport and store. Therefore, phosgene is disadvantagous for the preparation of chloroformates in the laboratory. Bis(trichloromethyl) carbonate (BTC), also known as triphosgene, has been reported as a safer replacement for phosgene and trichloromethyl chloroformate[1]. BTC is a crystalline, stable solid (m.p.80°C b.p.260°C; at the boiling point, only slight decomposition to phosgene occurs[2]). Also, BTC has the advantages of being much easier and safer to handle than the highly toxic gaseous phosgene. However, see safety note in Experimental section. Under the influence of nucleophiles, 1 mol of BTC reacts similarly to 3 mol of phosgene[1]. So BTC is generally used to substitute for phosgene in the synthesis of chloroformates.

Our research team has studied the synthesis of 1, 4-dihydro-s-tetrazine derivatives and their structure-activity relationships,[3~6] in which chloroformates were important intermediates. Some chloroformates were prepared by the reaction of phosgene with alcohols or phenols as reported in literature. We have studied the literature carefully and have not found any literature indicating that BTC was used to synthesise the chloroformates which we needed, and so we attempted to make use of BTC to synthesise them. The stoichiometric equation is:



R: a, *n*-C_5H_{11}; b, cyclohexyl; c, *i*-C_5H_{11}; d, *n*-C_7H_{15}; e, *n*-C_8H_{17}; f, *m*-CH_3Ph; g, *o*-ClPh; h, Ph

Experimental

Boiling points were uncorrected. Infra-red spectra were recorded on a PK-6000 spectrometer as a neat liquid.

CAUTION: Although BTC is stable, it still liberates small quantities of highly toxic phosgene and has to be handled with extreme care in a fumehood.

General procedure

Procedure A: To a stirred solution of BTC (19.8g, 0.067mol) dissolved in dichloromethane (50ml) and cooled to 0°C was added drop-wise the alcohol (17.6g, 0.2mol) **(1a–e)**, and then a solution of pyridine (16.2ml, 0.2mol) in dichloromethane (10ml) was added over 30 minutes. During the addition, the temperature was kept at 0–5°C. After the addition was completed, the temperature of the mixture was allowed to rise slowly to room temperature and stirring was continued for 2h. The resulting mixture was washed with 3×50ml cooled water, dried over calcium chloride and filtered and then the residue was distilled under vacuum to give the chloroformate(**2a–e**): **2a**, b.p. 65-66°C /10mmHg, ν_{max}[cm^{-1}] (neat) 2963, 1781, 1458, 1164, 820 (lit.[14] ν_{max} [cm^{-1}] 3638, 2963, 2937, 2876, 2865, 2309, 1780, 1468, 1435, 1381, 1294, 1286, 1251, 1160, 1073, 1043, 1016, 966, 837, 822, 812, 776, 730, 690, 482) **2b**, b.p. 73–74°C/14mmHg, ν_{max} [cm^{-1}] (neat) 2934, 2857, 1736, 1451, 1364, 1255, 1060, 966, 844, **2c**, b.p. 98–100°C/20mmHg, ν_{max} [cm^{-1}] (neat) 2963, 1780, 1466, 1386, 1161, 934, 818, 690, **2d**, b.p. 79–82°C/18mmHg, ν_{max} [cm^{-1}] (neat) 2931, 2860, 1780, 1467, 1162, 837, 690 (lit.[14] ν_{max} [cm^{-1}] 2969, 2931, 2874, 2860, 1780, 1468, 1379, 1291, 1262, 1162, 1066, 1002, 930, 837, 819, 725, 690, 623, 482) **2e**, b.p. 90–91°C/11mmHg, ν_{max} [cm^{-1}] (neat) 2929, 2858, 1780, 1467, 1162, 832, 689 (lit.[14] ν_{max} [cm^{-1}] 3639, 2958, 2929, 2873, 2858, 2307, 1780, 1468, 1379, 1281, 1246, 1161, 1071, 1020, 940, 877, 833, 724, 690, 463)

The above method is suitable for preparing alkyl chloroformates.

Procedure B: To a stirred solution of BTC (19.8g, 0.067mol) dissolved in dichloromethane (50ml) and cooled to 0°C, was added drop-wise a solution of the phenol (18.8g, 0.2mol)(**1f–h**) in dichloromethane (10ml) and then a solution of sodium hydroxide (8g, 0.2mol) in 72ml of water was added. During addition, the temperature was kept at 0–5°C. After the addition was completed, the temperature of the mixture was allowed to slowly rise to room temperature and stirring was continued for 2h. The water layer was removed. The organic phase was washed with 3×50ml cooled water, dried over calcium chloride and filtered. Then the residue was distilled under vacuum to give the aryl chloroformate (**2f–h**): **2f**, b.p. 87–88°C/22mmHg, ν_{max} [cm^{-1}] (neat) 3039, 2922, 1788, 1616, 1590, 1489, 1462, 1328, 1281, 1234, 1151, 1040, 910, **2g**, b.p. 66–68°C/10mmHg, ν_{max} [cm^{-1}] (neat) 3077, 1785, 1480, 1452, 1339, 1292, 1250, 1204, 1110, 1058, 1029, 939, 879, **2h**, b.p. 87–88°C/10mmHg, ν_{max} [cm^{-1}] (neat) 3031, 1762, 1608, 1592, 1490,

Table 1 Preparation of chloroformates in contrast to literature **2a–h**

Compd. No.	Literature(phosgene)				Present method(BTC)		
	R	Yield /%	B.p. °C(mmHg)	Ref.	Method	Yield /%	B.p. /°C(mmHg)
2a	*n*-C_5H_{11}	80	68–70(28)	7	A	85.6	65–66(10)
2b	Cyclohexyl	73	38–34(2)	7	A	76.8	73–74(14)
2c	*i*-C_5H_{11}	/	15–151(754)	8	A	83.7	98–100(20)
2d	*n*-C_7H_{15}	68	60–62(4)	9	A	84.6	79–82(18)
2e	*n*-C_8H_{17}	54	119–123(30)	7	A	87.1	90–91(11)
2f	*m*-CH_3Ph	/	96(8)	10	B	87.3	87–88(22)
2g	*o*-ClPh	92	111–113(27)	11/12	B	79.5	66–68(10)
2h	Ph	58	74–75(13)	13	B	88.4	87–88(10)

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1465, 1040, 930, 912 (lit.[14] ν_{max} [cm^{-1}] 3662, 3083, 3066, 3047, 2900, 2232, 1964, 1922, 1788, 1601, 1591, 1493, 1484, 1460, 1389, 1355, 1342, 1330, 1295, 1183, 1163, 1120,1071, 1026, 1006, 916, 883, 866, 803, 744, 6867, 678, 613, 561, 499)

The above method is suitable for preparing aryl chloroformates.

Results and discussion

(1) It was found that the yields by the BTC method were a little bit better as compared with phosgene method (Table 1). The compound's boiling points and IR data were almost as same as that in literature, indicating the purity of the chloroformates synthesised.

(2) It is important to control the rate of addition; if the alcohols, phenols or base were added too rapidly, the reaction temperature will rise significantly and highly toxic phosgene may be given off (see earlier Safety Note) so that the yield will decrease.

(3) When using BTC, the usual base was pyridine. In the experiment using pyridine phenyl chloroformate however, was prepared only in 62.5% yield. When sodium hydroxide was used as a replacement for pyridine (Procedure B), the product was obtained in 88.4% yield. Sodium hydroxide, therefore acted in the reaction as a catalyst.

(4) In comparison with phosgene, BTC, being a solid is convenient to handle. A further advantage is that, only one mole equivalent amount or a little excess of BTC is needed to complete the reaction.

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