Tetramethylammonium Salts: Highly Selective Catalysts for the Preparation of *gem*-Dichlorocyclopropanes from Electrophilic Alkenes and Chloroform under Phase-Transfer Catalysis Conditions

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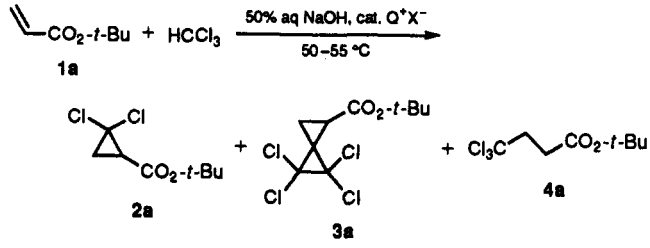
Haloform treated with concentrated aqueous sodium hydroxide and a quaternary ammonium salt (Q^+X^-) as a catalyst (phase-transfer catalysis, PTC[1]) generates trihalomethyl anion which further splits into dihalocarbene. Depending on the kind of the alkene present in the system, each of these particles may be trapped. When simple, nucleophilic alkenes smoothly add dihalocarbene; those substituted by an electron-withdrawing group, EWG (alkoxycarbonyl, cyano, etc.) usually afford trihalomethyl anion adducts and/or other products if a typical phase-transfer catalyst, like benzyltriethylammonium chloride (TEBA), is applied.

Since *gem*-dihalocyclopropanes substituted with EWG are attractive synthetic substrates,[2,3] searching for the catalysts which promote the selective addition of dihalocarbenes to electrophilic alkenes is an important preparative target. The addition of dichlorocarbene, generated from phenyl(trichloromethyl)mercury[4] or sodium trichloroacetate,[5] to a few electrophilic alkenes has already been described.

Our preliminary reports that methyl, ethyl,[6] or *tert*-butyl acrylate[2,6] add selectively dichlorocarbene generated by PTC in the presence of tetramethylammonium salt as a catalyst have been confirmed in the case of *tert*-butyl acrylate.[7] The same particle was added to *tert*-butyl 3-methyl-2-butenoate in a PTC system, in the presence of a mixture of alkylphenylpoly(ethylene glycol) (Triton N-101) and tricaprylmethylammonium chloride (Aliquat 336) as a catalyst.[8] Peculiar properties of tetramethylammonium salts as phase-transfer catalysts were also evidenced in monodichlorocyclopropanation of unconjugated polyenes,[9] dibromocyclopropanation of allyl bromide,[10] and in the selective preparation of *gem*-bromochlorocyclopropanes.[11]

Following our preliminary reports,[2,6] we would like to describe now in detail the selective dichlorocyclopropanation of acrylates and some other electrophilic alkenes **1a–g**. Initial investigations were carried out on the reaction of *tert*-butyl acrylate (**1a**) with chloroform under PTC conditions.



Without the catalyst, with a 12-fold excess of chloroform, only a small amount of **1a** is slowly converted into **2a**, exclusively (1.5% after 39 h), and the rest of **1a** remained intact. On the other hand, Dehmlow and Wilkenloh[7] have shown that in the presence of TEBA—a typical PTC catalyst—the mixture of **2a** (25%), **3a**[12] (7%), and **4a** (9%) resulted. In the light of these results, the use of the catalyst of low lipophilicity might favor the selective formation of **2a** and increase its yield. Indeed, with tetramethylammonium bromide (TMABr) as a catalyst, and a large excess (at least 12-fold) of chloroform, **2a** was formed with a yield of 57%, accompanied with a small amount of **4a** (5%).

With this information in hand, the esters **1b–f** were allowed to react under the conditions mentioned above to afford the corresponding dichlorocarbene adducts **2b–f** with low to good yields (Table I).

In the case of esters **1b,c** which are prone to hydrolysis, an even larger excess of chloroform is needed, and the yields of **2b,c** are meager. Furthermore, the addition of trichloromethyl anion competes with cyclopropanation if $HCCl_3/\mathbf{2b} \leq 20$. The product **2d** is accompanied by small amounts of other products, but it was easily isolated by a simple distillation. The reaction of **1e** with chloroform afforded the mixture of **2e** (main product) and isopropyl 3-methyl-2-(trichloromethyl)-1-cyclopropenecarboxylate (which were separated by distillation on efficient fractionating column), as well as a few other products in minute amounts. Products of the same type were obtained in TMACl-catalyzed reaction of chloform with *tert*-butyl crotonate, yet their yields were low.[7] Methacrylonitrile (**1g**) which with chloroform and TEBA in PTC system yielded the mixture of trichloromethyl anion and dichlorocarbene adducts,[14,15] in the presence of TMABr cleanly produced the latter product, **2g** (Table I).

The formation of only one product **2** in the majority of reactions mentioned above greatly simplifies its isolation by distillation. Generally, the reactions performed with TMAX as a catalyst proceeded at a slower rate than those carried out with typical Q^+X^-.

Both acrylonitrile and phenyl vinyl sulfone gave trichloromethyl anion adducts irrespective of the kind of the catalyst applied (TMABr or TEBA[14,15]). Furthermore,

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(12) The formation of **3a** is visualized below:[2,13]

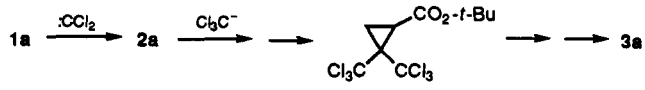

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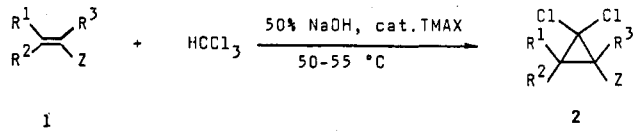
Table I. Preparation of 2 and Their Physical Properties and Yields

	condns						
product	$HCCl_3$/1 (mol/mol)	TMAX (mol %)	50% NaOH/1 (mol/mol)	time (h)	T (°C)	bp (°C/Torr)	yield (%)
2a[a]	12	TMABr (2)	22.5	8	45–50	97–100/20	57
2b	30	TMABr (10)	18.75	9	50–55	77–79/16	11
2c	30	$TMAHSO_4$ (5)	15.0	7	45	74–76/14	25
2d	12	$TMAHSO_4$ (2)	22.5	8	50	107–109/12	17
2e	20	$TMAHSO_4$ (5)	37.7	8	45–50	90–92/8	49
2f	12	TMABr (10)	7.5	24	50–55	101–105/10[b]	42
2g	12	TMABr (10)	10.0	10	45	71/10[c]	78

[a] Data taken from ref 2. [b] Lit.[8] bp 41–43 °C/0.2 Torr. [c] Lit.[13] bp 72 °C/11 Torr.

Table II. ^{1}H-NMR Data of *gem*-Dichlorocyclopropanes 2b–f ($CDCl_3$)

compd	chemical shifts (ppm), *J* (Hz)
2b	3.79 (s, 3 H, OCH_3), 2.66–2.48 and 2.16–1.80 (m, 3 H, CH_2CH)
2c	4.26 (q, J = 7.1, 2 H, OCH_2), 2.64–2.41 and 2.14–1.71 (m, 3 H, CH_2CH), 1.28 (t, J = 7.1, 3 H, CH_3)
2d	4.20 (t, J = 6.5, 2 H, OCH_2), 2.66–2.44 and 2.15–1.70 (m, 3 H, CH_2CH), 1.70–1.17 (m, 4 H, CH_2CH_2), 0.92 (t, J = 6.5, 3 H, CH_3)
2e	5.01 [septet, J = 6.25, 1 H, $CH(CH_3)_2$], 2.13 (dq, J = 6.22, J_{AB} = 7.95, 1 H, CH_3CH), 1.99 (d, J_{AB} = 7.95, 1 H, $CHCO_2$), 1.29 (d, J = 6.22, 3 H, CH_3CH), 1.23 and 1.22 [two d, J = 6.25, 6 H, $(CH_3)_2CH$]
2f	2.01 (s, 1 H, CH), 1.48 [s, 9 H, $(CH_3)_3C$], 1.45 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3)



1 2

1,2	R^1	R^2	R^3	Z
a	H	H	H	CO_2-t-Bu
b	H	H	H	CO_2Me
c	H	H	H	CO_2Et
d	H	H	H	CO_2Bu
e	Me	H	H	CO_2-i-Pr
f	Me	Me	H	CO_2-t-Bu
g	H	H	Me	CN

Figure 1.

bromoform proved to be much less selective, affording the mixture of tribromomethyl anion and dibromocarbene adducts to *tert*-butyl and methyl acrylate with each of the catalysts mentioned above.[7]

The reason why TMAX favor *gem*-dichlorocyclopropanation of some electrophilic alkenes by PTC is not clear at present. It has been shown that in the 50% aqueous sodium hydroxide/benzene/cat. TMABr system, the ammonium salt resides in the aqueous phase.[16] One may assume that $Me_4N^+CCl_3^-$ ion pairs, formed in low concentration from chloroform and TMAX at the interphase, cannot penetrate into the organic phase. Due to the small size (low lipophilicity) of tetramethylammonium cation, these ion pairs are rather tight and hydrated; therefore, the activity of the trichloromethyl anion is insufficient to add to 1. Thus, the reaction of alkene with dichlorocarbene takes place.

These conclusions are supported by the experiment carried out without the catalyst. In this case, $CCl_3^-Na^+$ ion pairs have to be formed at the interphase, with a particularly inactive trichloromethyl anion. Consequently, the adduct of dichlorocarbene **2a** is produced, though with a very low yield.

To conclude, we have presented a significant improvement of the preparation of **2**, which opens up some interesting mechanistic questions as well.

Experimental Section

Boiling points are uncorrected. GC analyses were performed on OV-17 (5%) on Chromosorb W-HP (80–100 mesh) column. ^{1}H NMR spectra were recorded at 200 MHz.

Ester **1e** was prepared from crotonic acid (43.0 g, 0.5 mol) and 2-propanol (130.3 g, 191.4 mL, 2.5 mol) in the presence of sulfuric acid (4 mL) (reflux, 24 h): bp 51–52 °C/20 Torr (48%) (lit.[17] bp 140 °C/640 Torr); ^{1}H NMR δ 6.92 (dq, ^3J = 15.5 Hz, ^3J = 6.88 Hz, 1 H, CH_3CH), 5.79 (dq, ^3J = 15.5 Hz, ^4J = 1.68 Hz, 1 H, $CHCO_2$), 5.02 [septet, J = 6.24 Hz, 1 H, $(CH_3)_2CH$)], 1.84 (dd, ^3J = 6.88 Hz, ^4J = 1.68 Hz, 3 H, CH_3), 1.23 [d, J = 6.24 Hz, 6 H, $(CH_3)_2CH$]. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.86; H, 9.37.

tert-Butyl 3-methyl-2-butenoate (**1f**) was prepared by literature procedure.[18]

General Procedure for the Preparation of *gem*-Dichlorocyclopropanes 2b–g. Electrophilic alkene **1b–g** (0.05–0.10 mol), chloroform (Table I), and a catalyst (Table I) were stirred while 50% aqueous sodium hydroxide (Table I) was added. The mixture was stirred at the temperature and for the time given in Table I and diluted with water, the organic phase was separated, and the water phase was extracted with chloroform. The combined organic extracts were washed with water, diluted hydrochloric acid (ca. 2%), and then water and dried over $MgSO_4$, the solvent was evaporated, and the residue was vacuum distilled to give **2** (Table I). ^{1}H NMR data for **2b–f** are given in Table II.

The mixture from the reaction of **1e** with chloroform was distilled in a Fisher apparatus (SPALTROHR column) to give **2e** (Table I) and isopropyl 3-methyl-2-(trichloromethyl)-1-cyclopropene carboxylate (6%): bp 104–105 °C/7 Torr; ^{1}H NMR δ 5.08 [septet, J = 6.2 Hz, 1 H, $(CH_3)_2CH$], 3.57 (q, J = 6.8 Hz, 1 H, CH_3CH), 1.38 (d, J = 6.8 Hz, CH_3CH), 1.29 [d, J = 6.2 Hz, 6 H, $(CH_3)_2CH$]. Anal. Calcd for $C_9H_{11}Cl_3O_2$: C, 41.97; H, 4.30; Cl, 41.30. Found: C, 42.04; H, 4.29; Cl, 41.15.

2b. Anal. Calcd for $C_5H_6Cl_2O_2$: C, 35.53; H, 3.58; Cl, 41.95. Found: C, 35.74; H, 3.26; Cl, 42.22.

2c. Anal. Calcd for $C_6H_8Cl_2O_2$: C, 39.37; H, 4.41; Cl, 38.74. Found: C, 39.52; H, 4.44; Cl, 38.96.

2d. Anal. Calcd for $C_8H_{12}Cl_2O_2$: C, 45.52; H, 5.73; Cl, 33.59. Found: C, 45.64; H, 5.75; Cl, 33.74.

2e. Anal. Calcd for $C_8H_{12}Cl_2O_2$: C, 45.52; H, 5.73; Cl, 33.59. Found: C, 46.09; H, 5.78; Cl, 33.69.

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