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Phase Transfer Catalyzed Reactions of Chloroform with Methacrylic Esters*

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Chloroform reacts with an excess of methyl methacrylate in the presence of 50% aq NaOH and benzyltriethylammonium chloride (TEBA) as a catalyst (phase transfer catalysis, PTC) to give a mixture of dichlorocarbene and trichloromethyl anion adducts, **1** and **2**, respectively. These additions proceed as parallel processes, there is a slow conversion of **2** → **1**, which proceeds as an intramolecular process.

Key words: phase transfer catalysis, dichlorocarbene, trichloromethyl anion, Michael reaction, gem-dichlorocyclopropanes

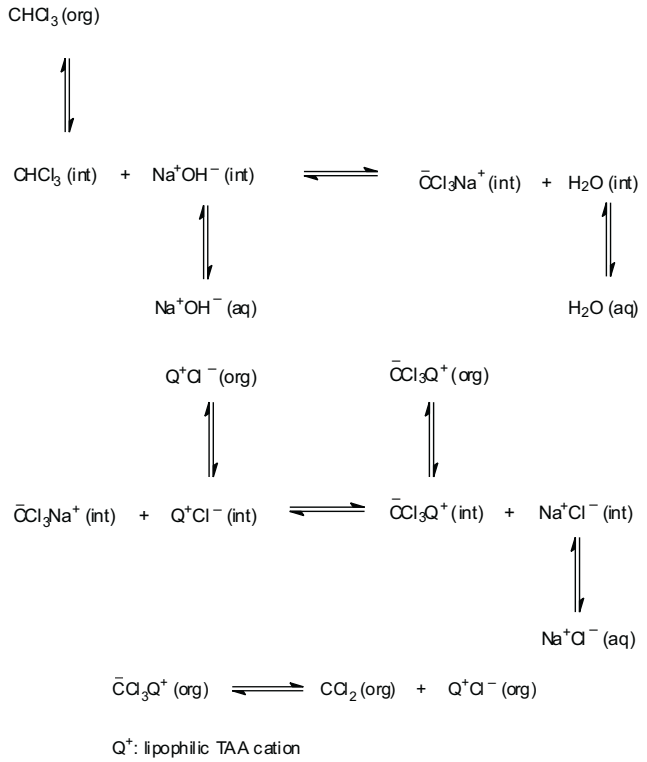
Dichlorocarbene is the most efficiently generated *via* α-elimination of hydrogen chloride from chloroform by action of concentrated aqueous sodium hydroxide and tetraalkylammonium (TAA) salt in two phase system, phase transfer catalysis, PTC [1]. These the most convenient and simple conditions also assure highest yields of the products of reactions of dichlorocarbene.

In this system deprotonation of chloroform takes place at the phase boundary and the trichloromethyl anions generated there are transferred into the organic phase as lipophilic ion pairs with TAA cations. Further dissociation of trichloromethyl anions to dichlorocarbene is a truly reversible process because all components of the equilibrium are soluble in the organic phase, whereas no base and its conjugated acid: hydroxide anions and water, are present there [2]. Thanks to this situation dichlorocarbene is kept in "ready for use state" in the organic phase, hence it gives products in high yields (Scheme 1).

As a consequence of the equilibrium one can expect that depending on the character of the reagent introduced to the system both partners of the equilibrium – nucleophilic trichloromethyl anions and electrophilic dichlorocarbene would enter the reaction. Indeed, electrophilic reagents, *e.g.* aldehydes, acrylonitrile or alkyl acrylates, react with trichloromethyl anion, whereas nucleophilic partners: alkenes, ammonia derivatives *etc.* react with dichlorocarbene [1]. Alkyl methacrylates occupy

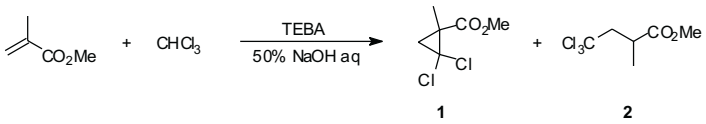
*Dedicated to the memory of Professor Stanisław Malinowski in appreciation of his outstanding contributions to acid-base catalysis.

Scheme 1



intermediary position, in such system produce both: dichlorocyclopropanes **1** and the Michael adducts **2** [3]. Some experimental observations, for instance change of ratio of **1** to **2** with change of the conditions, indicate however that this simple picture could be inadequate. Thus, it was reported that when the PTC reaction of chloroform was carried out in the presence of an excess of the methyl methacrylate, **2** was the dominant product [3], whereas use of an excess of chloroform gave exclusively dichlorocyclopropane derivative **1** [4] (Scheme 2).

Scheme 2

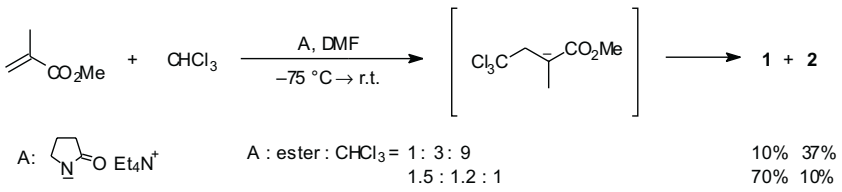


Taking into account that independent on the amount of chloroform and its ratio to the methacrylate, concentration of trichloromethyl anions together with dichlorocarbene cannot exceed concentration of the catalyst – typically 1–2% molar, and that ratio of chloroform to the ester does not affect the ratio of acceptor of the trichloromethyl anion

and dichlorocarbene, this observation can be provisionally rationalized as follows. Excess of the ester, by a simple concentration effect, favors addition of trichloromethyl anion, thus, the formation of **2** become faster than equilibration of trichloromethyl anion with dichlorocarbene and chloride anion, thus, the process become kinetically controlled. This supposition suggests that factors favoring the equilibration shifts the process to addition of dichlorocarbene.

This rationalization is based on the assumption that formation of **1** proceeds *via* direct addition of dichlorocarbene to the double bond. However, there is an alternate possibility that **1** can be formed *via* initial addition of the trichloromethyl carbanion to the methacrylate and subsequent reaction of **2** in the presence of base. Thus, it was reported that in the reaction of chloroform with methyl methacrylate promoted by tetraethylammonium salt of pyrrolidone (A) a mixture of esters **1** and **2** is formed [5]. The authors suggest that **1** is formed *via* cyclization of the initially produced carbanionic Michael adduct **2** (Scheme 3).

Scheme 3



Cyclization of **2** to produce **1** can proceed on two ways: direct intramolecular replacement of the halogen or the halophilic reaction that produces dichlorocarbanion and α-chloroester followed by intramolecular replacement of the latter. Conversion of **2** → **1** can proceed also *via* the retro Michael reaction followed by dissociation of the produced trichloromethyl carbanion to dichlorocarbene and its addition to the double bond. The aim of this paper is to clarify these questions.

RESULTS AND DISCUSSION

First we have studied how degree of conversion affect ratio of **2** to **1** when the methacrylate was used in excess in relation to chloroform. For this reason the reaction of methyl methacrylate with chloroform was carried out when these reagents in ratio 8:1 were vigorously stirred with 50% NaOH aq and benzyltriethylammonium chloride (TEBA) – 2% molar in relation to chloroform – at 27°C [3] and samples of the mixture analyzed every 30 min. We have observed that ratio of the products **2:1** increase with time (degree of conversion) (Table 1).

Table 1. Reaction of chloroform with an excess of methyl methacrylate in PTC system.

Time (min)	30	60	90	120	150	180	210	240
2:1 ratio	1.57	1.65	1.72	1.81	1.87	2.01	2.06	2.20

This ratio was not affected by possible partial hydrolysis of **1** or **2**, since we have not found the corresponding acids in the aqueous phase. Thus, the reaction proceeds *via* parallel addition of trichloromethyl anions and dichlorocarbene to the double bond, because in the case that formation of **1** takes place *via* conversion **2** → **1**, contrary to this observation the ratio should decrease in time.

Next we have clarified whether under the reaction conditions conversion of **2** → **1** takes place at all. For this **2** dissolved in methylene chloride was vigorously stirred with 50% NaOH aq and TEBA, 2% mol., at 22°C, and the mixture analyzed by GLC. Slow conversion of **2** → **1** proceeded as shown in Table 2.

Table 2. Conversion of **2** → **1** in PTC system.

Time (h)	Content in reaction mixture (%)	
	2	**1**
2	97.8	2.2
3.5	96.6	3.4
5	95.0	5.0
10	90.0	10.0
12[a]	84.1	15.9

[a]last two hours at reflux.

However, the conversion was much slower than formation of **1** in the direct reaction, thus it appears that the conversion **2** → **1** has negligible contribution to formation of **1** in the PTC reaction of methyl methacrylate with chloroform.

It should be also clarified how the conversion **2** → **1** proceeds: *via* direct intramolecular reaction or *via* dissociation of **2** to produce trichloromethyl anion (retro Michael reaction) followed by conversion of this anion to dichlorocarbene and its addition to the double bond. This question was clarified in a simple experiment in which **2** mixed with a good dichlorocarbene acceptor – 2-methyl-2-butene was treated with 50% NaOH aq and TEBA. Even after prolonged reaction time – 5 h, so the conversion **2** → **1** attained 12%, no traces of the dichlorocarbene adduct to 2-methyl-2-butene were detected in the reaction mixture (Table 3).

Table 3. Reaction of **2** carried out in the presence of 2-methyl-2-butene.

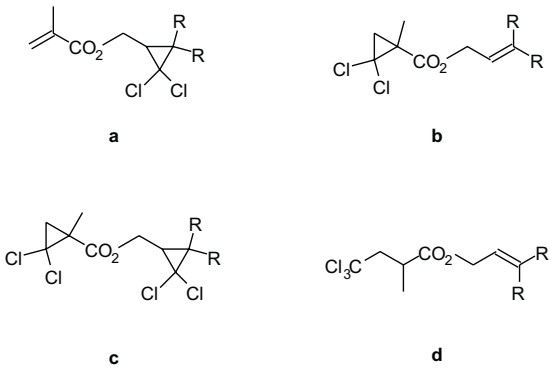
Time (h)	Content in reaction mixture (%)	
	2	**1**
2	93.1	6.9
3	92.0	8.0
4	91.1	8.9
5	88.1	11.9

An interesting piece of evidence that ethyl 2,2-dichloro-1-methylcyclopropane carboxylate is formed *via* direct addition of dichlorocarbene, not *via* cyclization of the Michael adduct of trichloromethyl anion, came from analysis of the relative rates of addition of dichlorocarbene to various alkenes estimated by Dehmlow in competitive experiments [4b]. Thus competition between cyclohexene and ethyl methacrylate indicated that dichlorocarbene adds to cyclohexene 3.4 times faster than to the ester, whereas the latter adds dichlorocarbene 3.8 times faster than 1-pentene. From these data it can be simply calculated that addition of dichlorocarbene to cyclohexene is 3.4×3.8 = 12.9 faster than to 1-pentene. Direct comparison of rates of these reactions made by Doering [6] gave value 13.8. Thus, the value calculated on the basis of competitive experiments with ethyl methacrylate and from direct comparison are in good agreement, which can be the case only when all these reactions proceed *via* addition of dichlorocarbene.

We have approached this question also in a different way, namely studying intramolecular competition of the addition of dichlorocarbene to prenyl methacrylate **3** and allyl methacrylate **4**.

All samples of the expected products: **3a–d** and **4a–d** (Scheme 4, Table 4) were prepared independently, see Experimental part.

Scheme 4



3a-d, R = Me
4a-d, R = H

Assuming that products type **a**, **b**, **c** under typical PTC conditions are formed *via* electrophilic addition of dichlorocarbene to the double bonds one can expect preference for the addition to more nucleophilic double bonds namely relations of rates of the adduct formation should be **3a** > **3b**, **4b** > **4a**. On the other hand, in the case when the dichlorocyclopropanes are produced *via* cyclization of the initially formed adducts of trichloromethyl anions for both esters **3** and **4** there should be preference for **b** type products namely **3b** > **3a** and **4b** > **4a**. Since in the reaction of **3** ratio of the pro-

Table 4. Yields, physical properties and ^{1}H NMR data of **3a–d** and **4a–d**.

Comp.	Yield %	Purity (GC) %	b.p., °C/Torr	^{1}H NMR, δ	MW	Analysis					
						Calcd			Found		
						C	H	Cl	C	H	Cl
3a	66	96.0	60–62/0.1	1.27 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.63 (t, J = 7.4, 1H, CH_{cycl}), 1.96 (dd, J = 1.3, 1.3, 3H, CH_3), 4.27 (dd, J = 7.4, 2.0, 2H, OCH_2), 5.58–5.62 (m, 1H, = CH), 6.13–6.16 (m, 1H, =CH)	$C_{10}H_{14}Cl_2O_2$ (237.13)	50.65	5.95	29.90	50.41	6.01	30.18
3b	51	99.7	127–128/15	1.40 (d, J = 7.5, 1H, CH_{cycl}), 1.57 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.76 (d, J = 1.0, 3H, CH_3), 2.27 (d, J = 7.5, 1H, CH_{cycl}), 4.65 (d, J = 7.3, 2H, OCH_2), 5.32–5.40 (m, 1H, =CH)	$C_{10}H_{14}Cl_2O_2$ (237.13)	50.65	5.95	29.90	50.50	6.03	30.21
3c	43	98.0	116–117/0.4	1.26 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.42–1.47 (m, 1H, CH_{cycl}), 1.60 (d, J = 1.6, 3H, CH_3), 1.62–1.66 (m, 1H, CH_{cycl}), 2.26–2.31 (m, 1H, CH_{cycl}), 4.26–4.32 (m, 2H, OCH_2)	$C_{11}H_{14}Cl_4O_2$ (320.04)	41.28	4.41	44.31	41.23	4.33	44.35
3d	74	98.0	86–87/0.6	1.29 (d, J = 7.2, 3H, CH_3), 1.67 (d, J = 0.8, 3H, CH_3), 1.72 (d, J = 0.8, 3H, CH_3), 2.60 (dd, J = 14.8, 2.8, 1H, $CHCCl_3$), 2.92 (ddq, J = 7.2, 2.8, 8.4, 1H, C**H**CH_3), 3.43 (dd, J = 14.8, 8.4, 1H, $CHCCl_3$), 4.56 (d, J = 7.2, 2H, OCH_2), 5.30 (t sep, J = 7.2, 0.8, 1H, =CH)	$C_{10}H_{15}Cl_3O_2$ (273.59)	43.90	5.53	38.88	43.81	5.40	39.01
4a	70	98.8	51–54/0.15	1.35 (dd, J = 10.6, 7.3, 1H, CH_{cycl}), 1.71 (dd, J = 7.5, 7.3, 1H, CH_{cycl}), 1.97 (dd, J = 1.55, 1.0, 3H, CH_3), 2.01–2.13 (m, 1H, CH_{cycl}), 4.15 (dd, J = 12.0, 8.2, 1H, OCH), 4.42 (dd, J = 12.0, 9.1, 1H, OCH), 5.60–5.63 (m, 1H, =CH), 6.16–6.18 (m, 1H, =CH)	$C_8H_{10}Cl_2O_2$ (209.07)	45.96	4.82	33.91	45.81	4.72	33.71
4b	55	98.4	86–90/12	1.43 (d, J = 7.55, 1H, CH_{cycl}), 1.60 (s, 3H, CH_3), 2.29 (d, J = 7.55, 1H, CH_{cycl}), 4.65–4.69 (m, 2H, OCH_2), 5.23–5.41 (m, 2H, CH_2=), 5.84–6.04 (m, 1H, =CH)	$C_8H_{10}Cl_2O_2$ (209.07)	45.96	4.82	33.91	46.35	4.79	33.63

Table 4 (continuation)

4c	51	96.0	79/0.04	1.31–1.39 (m, 1H, CH_{cycl}), 1.43–1.48 (m, 1H, CH_{cycl}), 1.61 (d, J = 1.5, 3H, CH_3), 1.66–1.76 (m, 1H, CH_{cycl}), 2.00–2.35 (m, 1H, CH_{cycl}), 2.27–2.33 (m, 1H, CH_{cycl}), 4.10–4.22 (m, 1H, OCH), 4.39–4.48 (m, 1H, OCH)	$C_9H_{10}Cl_4O_2$ (291.99)	37.02	3.45	48.57	36.98	3.47	48.28
4d	48	100.0	60–62/0.25	1.35 (d, J = 7.3, 3H, CH_3), 2.65 (dd, J = 15.0, 2.9, 1H, $CHCCl_3$), 3.00 (ddq, J = 7.3, 8.0, 2.9, 1H, C**H**CH_3), 3.48 (dd, J = 15.0, 8.0, 1H, $CHCCl_3$), 4.60–4.64 (m, 2H, OCH_2), 5.22–5.39 (m, 2H, CH_2=), 5.82–6.02 (m, 1H, =CH)	$C_8H_{11}Cl_3O_2$ (245.53)	39.13	4.52	43.32	38.97	4.44	42.70

ducts **3a:3b** was close to twelve after 3 h and in the reaction of **4** ratio of the products **4b:4a** was fifteen the pathway *via* initial addition of trichloromethyl anion and intermediacy of **3d** or **4d** shall be excluded. In reactions of **3** and **4** the appropriate diadducts **3c** and **4c** were formed in minute amounts, no traces of **3d** or **4d** were detected.

Thus, we can conclude that in the PTC reaction of alkyl methacrylate with chloroform addition of trichloromethyl anions and dichlorocarbene giving **2** and **1** proceeds as parallel processes. Under such conditions there is a slow conversion of **2** → **1**, which proceeds as an intramolecular process.

EXPERIMENTAL

Melting point was determined with a capillary melting-point apparatus. Melting point and boiling points are uncorrected. ^{1}H NMR spectra were measured on a Varian Gemini spectrometer at 200 MHz or Varian Mercury 400BB at 400 MHz, as solutions in $CDCl_3$. Coupling constants are given in Hz. Gas chromatography (GC) analyses were performed on a Hewlett-Packard 5890 series II chromatograph, equipped with HP50+ capillary column (30 m).

Commercial allyl methacrylate, 3-methyl-2-buten-1-ol, allyl alcohol (all from Aldrich) were used. Other typical reagents and solvents were commercial grade and were used without further purification.

Compounds **1** [4a], **2** [3], 1,1-dichloro-2-hydroxymethylcyclopropane [7] and 1,1-dichloro-2,2-dimethyl-3-hydroxymethylcyclopropane [8] were prepared by literature procedures.

4,4,4-Trichloro-2-methylbutanoic acid was obtained by alkaline hydrolysis of **2** [3] (15% NaOH aq, 50°C, 1.5 h, then acidification) in 74% yield, m.p. 46–47°C, ^{1}H NMR, δ: 1.41 (d, J = 7.2, 3H, CH_3), 2.66 (dd, J = 15.2, 2.8, 1H, $CHCCl_3$), 3.00 (ddq, J = 7.2, 2.8, 8.0, 1H, C**H**CH_3), 3.48 (dd, J = 15.2, 8.0, 1H, $CHCCl_3$), 11.79 (br, 1H, COOH). Anal. Calcd. for $C_5H_7Cl_3O_2$ (205.47): C, 29.23; H, 3.43; Cl, 51.76. Found: C, 29.02; H, 3.47; Cl, 51.84.

Preparation of prenyl methacrylate, esters 3a–d and 4a–d. General procedure: Acid chlorides were prepared by refluxing appropriate carboxylic acid (0.05 mol) and thionyl chloride (7.14 g, 0.06 mol) for 2.5–3 h. After cooling, methylene chloride (25 ml) was added and the excess of thionyl chloride evaporated with the solvent. Methacroyl chloride was distilled, b.p. 68–72°C/12 Torr, other acid chlorides were used without purification.

Acid chlorides obtained as above were refluxed with an appropriate alcohol (0.05 mol) and N,N-dimethylaniline (6.7 g, 0.055 mol) in diethyl ether (15 ml) for 2.5 h. The reaction mixture was washed with diluted HCl and brine, the organic phase dried ($MgSO_4$) and the products were distilled *in vacuo*.

Prenyl methacrylate: b.p. 132–138°C/15 Torr, yield 62%, purity (GC) 99%, ^{1}H NMR, δ: 1.73 (s, 3H, CH_3), 1.76 (d, J = 1.0, 3H, CH_3), 1.94 (dd, J = 1.6, 1.0, 3H, $=CCH_3$), 4.64 (d, J = 6.9, 2H, OCH_2), 5.33–5.41 (m, 1H, =CH), 5.52–5.55 (m, 1H, $CH=CCH_3$), 6.08–6.10 (m, 1H, $CH=CCH_3$). Anal. Calcd. for $C_9H_{14}O_2$ (154.21): C, 70.09; H, 9.15. Found: C, 70.19; H, 9.12. Yields, b.p's, ^{1}H NMR data and analyses for compounds **3a–d** and **4a–d** are given in Table 4.

Reactions of chloroform with methyl methacrylate and esters 3 and 4 in PTC system. General procedure: A mixture of an ester, 50% NaOH aq, TEBA (2% molar) and chloroform were vigorously stirred and the samples for GC analyses were taken.

Reaction with methyl methacrylate [3], Table 1: Methyl methacrylate (33.6 g, 0.34 mol), chloroform (5.04 g, 0.042 mol), TEBA (0.18 g, 0.8 mmol), 50% NaOH aq (6.72 g, 0.084 mol); t. 20–22°C, 4 h.

Reaction with 3: Ester **3** (3.85 g, 0.025 mol), chloroform (29.9 g, 0.25 mol), TEBA (0.12 g), 50% NaOH aq (2.0 g, 0.025 mol); t. 27°C, 3 h. The reaction mixture contained (GC) **3** (66.7%), **3a** (28.9%), **3b** (2.4%) and **3c** (1.1%). Ratio of **3a:3b** = 12.0.

Reaction with 4: Ester **4** (6.3 g, 0.05 mol), chloroform (59.7 g, 0.5 mol), TEBA (0.23 g), 50% NaOH aq (4.0 g, 0.05 mol), t. 26–30°C, 3 h. The reaction mixture contained (GC) **4** (86.2%), **4a** (0.85%), **4b** (12.7%) and **4c** (0.2%). Ratio of **4b: 4a** = 14.9.

Cyclization of 2 to 1 in PTC system (Table 2): Compound **2** (2.0 g, 0.0091 mol), CH_2Cl_2 (8 ml), 50% NaOH aq (0.73 g, 0.0091 mol) and TEBA (0.04 g) were vigorously stirred at 22–23°C for 10 h, and, after addition of 10 ml of CH_2Cl_2, at reflux for 2 h.

Reaction of 2 carried out in the presence of 2-methyl-2-butene in PTC system (Table 3): Compound **2** (4.0 g, 0.018 mol), 2-methyl-2-butene (5.1 g, 0.073 mol), 50% NaOH aq (4.4 g, 0.055 mol), TEBA (0.08 g) and CH_2Cl_2 (25 ml) were stirred at 23°C for 5 h.

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