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FORMATION OF A REASONABLY STABILIZED TRICHLOROMETHYL ANION BY THE REACTION OF CHLOROFORM WITH ELECTROGENERATED BASE, AND ITS 1,4-ADDITION TO α,β-UNSATURATED CARBONYL COMPOUNDS[1]

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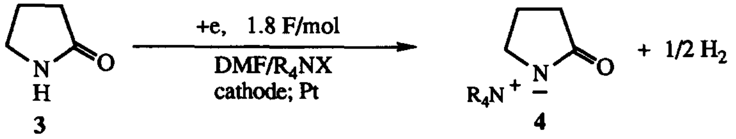
A reasonably stabilized trichloromethyl anion (TCMA) was formed by the reaction of chloroform with an electrogenerated base prepared by the electroreduction of 2-pyrrolidone, and the addition of this TCMA to α,β-unsaturated esters gave the corresponding β-trichloromethyl esters in good yields.

1,4-Addition of trichloromethyl anion (TCMA) to α,β-unsaturated carbonyl compounds is usually hardly applicable to the synthesis of β-trichloromethylcarbonyl compounds since TCMA is unstable and shows a strong tendency toward formation of dichlorocarbene through the elimination of chloride ion. Although a number of methods have already been exploited for the formation of TCMA,[2,3] this TCMA is not stable enough to use for the 1,4-addition. For example, it has been reported that the addition of TCMA to methyl acrylate (**1a**) gave methyl β-trichloromethylpropionate (**2a**) in only 10-18% yield.[4-7] Although it was recently reported that rather stable TCMA was formed in liq.NH_3, the yield of **2a** formed through its addition to **1a** was still only 22%.[8]

On the other hand, we have previously reported[9,10] that the electroreduction of 2-pyrrolidone (**3**) in DMF (Scheme 1) using tetraalkylammonium salts (R_4NX) as supporting electrolytes yielded the corresponding anionic species **4** (**4a**; R=Et, **4b**; R= n-Bu) possessing interesting reactivities as bases.

Scheme 1

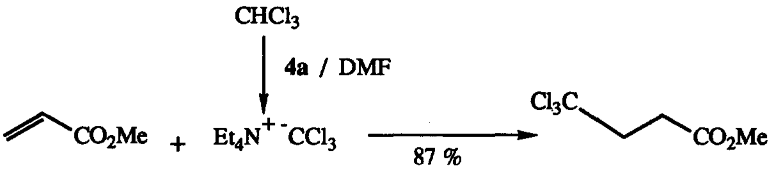


4a; R=Et, X=OTs; **4b**; R=n-Bu , X=BF_4

In this paper, we wish to report that a reasonably stabilized TCMA[10] was formed by the reaction of chloroform with **4a** (Scheme 2), and the 1,4-addition of this TCMA to α,β-unsaturated esters and nitriles proceeded in excellent yields with affording β-trichloromethyl substituted compounds.

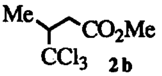
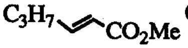
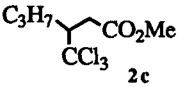
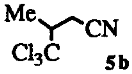
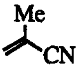
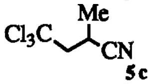
For example, it was found that the addition of a solution of a catalytic amount of **4a** into DMF solution of methyl acrylate (**1a**) and chloroform gave methyl β-trichloromethylpropionate (**2a**) in 87% yield.

Scheme 2



As the other examples summarized in Table 1 show, using **4a** as the base is effective to the 1,4- addition of TCMA to α,β-unsaturated ester (**1b**, run 1) and nitriles (runs 4-6), whereas it is not effective to the reaction of methyl hexenoate (**1c**, run 2). Since it has already been reported in our previous study[9] that the activity of **4** as a base was largely influenced by the type of counter cation (R_4N^+), the base **4b** instead of **4a** was utilized for the reaction of **1c** with chloroform, and a reasonable increase in the yield of **2c** was observed (run 3).

Table 1. 1,4-Addition of TCMA.

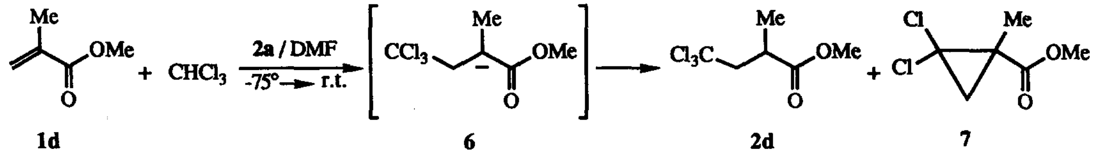
run	Ester	Product	Yield (%)[a]	run	Nitrile	Product	Yield (%)[a]
1	 **1b**	 **2b**	78	4		 **5a**	67
2	 **1c**	 **2c**	18	5		 **5b**	70
3	**1c**	**2c**	35[b]	6		 **5c**	82

a) Isolated yields based on α,β–unsaturated esters and nitriles. b) **4b** was used as the base.

A typical procedure for the preparation of **2a** is as follows: A solution of **4a** or **4b** in DMF was prepared by the electroreduction of 2-pyrrolidone in DMF.[9,10] Into a solution of methyl acrylate (**1a**) (15 mmol) and chloroform (45 mmol) in 5 mL of DMF was added a solution of **4a** (5 mmol) at -70°C, and the mixture was stirred for 1 hr at the same temperature and for the additional 4 hr at room temperature. The reaction mixture was then poured into an aqueous solution of NH_4Cl (100 ml) and extracted with ether. The product **2a** was obtained in 87% yield after distillation. The structures of the products shown in Table 1 were determined by the comparison of spectroscopic data with authentic samples (**2a** and **5a**)[11] and/or elemental analysis (**2b**,**2c**,**5b**, and **5c**).

Interestingly, the reaction of chloroform with methyl methacrylate (**1d**) carried out under the same typical reaction conditions (**4a** : chloroform = 1 : 9) gave considerably different results from the other α,β-unsaturated esters (**1a** and **1b**). Namely, the reaction gave a mixture of β-trichloromethyl ester (**2d**) and dichlorocyclopropane type compound (**7**) (Scheme 3). Furthermore, when much amount of **4a** was used (**4a** : chloroform = 1.5 : 1), **7** was obtained as the main product. Under the typical reaction conditions, the anion intermediate **6** is easily protonated by the excess amount of chloroform before **7** is formed through the intramolecular substitution , while using **4a** in excess will retard the protonation of **6** since pyrrolidone formed from **4a** by proton abstraction is a much poor proton donor than chloroform. The presence of a methyl group at the carbon atom bearing the negative charge seems to be an additional essential factor to favor the formation of **7** since the methyl group will increase the reactivity of the anion.

Scheme 3

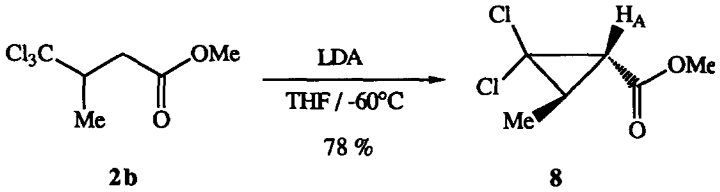


	2d	7
Reaction conditions ; **4a** (5 mmol), **1d** (15 mmol), $CHCl_3$ (45 mmol)	37 %	10 %
4a (15 mmol), **1d** (12 mmol), $CHCl_3$ (10 mmol)	10 %	70 % [12]

Although the reaction of methyl crotonate (**1b**) and chloroform with excess **4a** did not give the corresponding dichlorocyclopropane type product but yielded β-trichloromethyl ester **2b**,[13] we have found that treatment of **2b** with LDA (Scheme 4) led to the formation of a single stereoisomer of dichlorocyclopropanecarboxylic acid derivative **8**.[14]

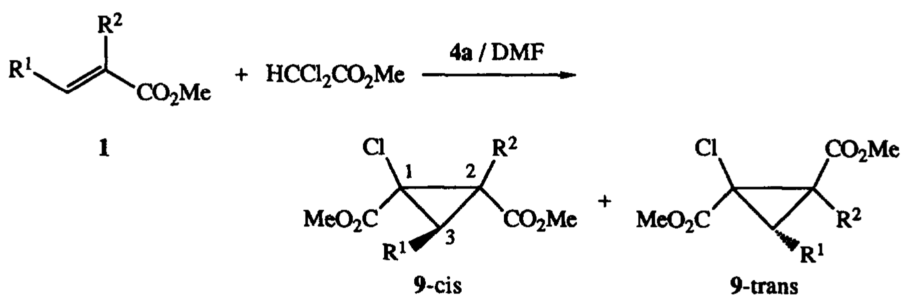
β-Trichloromethyl esters **2** are important materials to flame retardants of cotton,[11] and also **7** and **8** are key intermediates for the synthesis of insecticides.[15,16] The new method shown in this report certainly provides a convenient tool to the synthesis of these important compounds.

Scheme 4



Methyl dichloroacetate also showed a similar reactivity to chloroform in the reaction with unsaturated esters (**1a**, **1b**, and **1d**) in the presence of **4a** (Scheme 5). The reaction carried out in DMF gave the addition products **9** (**9a**,[17] **9b**,[18] and **9d**[19]) with yields remarkably higher than those obtained in the similar type of reactions using usual bases.[20]

Scheme 5



	Total yield (%)[21]	
9a; R^1=H, R^2=H	61	only **9a**-trans
9b; R^1=Me, R^2=H	59	**9b**-cis : **9b**-trans = 5 : 3
9d; R^1=H, R^2=Me	97	**9d**-cis : **9d**-trans = 1 : 1

Reaction conditions ; **4a** (20 mmol), **1** (50 mmol), $HCCl_2CO_2Me$ (10 mmol)

References and Notes

1) Electroorganic Chemistry. 126.

2) J.Mathieu and J.Weill-Raynal "Formation of C-C Bonds", Georg Thieme Publishers Stuttgart (1973), Vol I, pp 260.

3) J.M.Wyvratt, G.G.Hazen, and L.M.Weinstock, *J. Org. Chem.*, **1987**, 52, 944 and other references cited therein.

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5) H.G.Viehe and P.Valange, *Chem. Ber.*, **1963**, 96, 420.

6) Although it has has been reported that the cathodic reduction of CCl_4 gave TCMA and it added to **1a**,[7] the isolated yield of **2a** was low.

7) M.M.Baizer and J.L.Chruma, *J. Org. Chem.*, **1972**, 37, 1951.

8) G.S.Matosyan, M.A.Dzhragatspanyan, and A.A.Gevorkyan, *Arm. Khim. Zh.*, **1984**, 37, 593, *Chem. Abstr.* **1985**, 102, 220392u.

9) T.Shono, S.Kashimura, M.Sawamura, and T.Soejima, *J. Org. Chem.*, **1988**, 53, 907.

10) T.Shono, S.Kashimura, K.Ishizaki, and O.Ishige, *Chem. Lett.*, **1983**, 1311.

11) L.H.Chance and J.D.Timpa, *Chem. Eng. Data*, **1977**, 22, 116.

12) Yield based on chloroform.

13) The use of excess **4a** (1.5 eq. based on **1a**) in the reaction of **1a** with chloroform gave **2a** as the single product in 87 % yield.

14) Confirmed by ^{13}C-NMR ($CDCl_3$) ; δ 13.72, 31.18, 38.83, 52.74, 63.47, 168.22.
The stereochemistry of **8** was determined by ^{1}H-NMR using NOE between H_A and methyl protons. That is, the irradiation of H_A (δ 2.09) showed strong NOE at methyl protons (δ 1.36), and this result indicated that the configuration between H_A and the methyl group is cis.

15) R.Y.Wong, US 4,579,850 ; *Chem. Abstr.*, **1986**, 105, P42664m.

16) Nihon Nohyaku Co. Ltd. JP 6,041,667 ; *Chem. Abstr.*, **1985**, 103, P37474d.

17) **9a** was formed as a single product. **9a** ; ^{13}C-NMR ($CDCl_3$) δ 23.10, 30.82, 42.43, 52.79, 54.03, 167.63, 169.46. Trans configuration with respect to two methoxycarbonyl groups was determined by the known method.[20]

18) **9b** was a mixture of two stereoisomers with respect to the two methoxycarbonyl groups, cis : trans = 5 : 3). **9b**; trans isomer ^{1}H-NMR ($CDCl_3$) δ 1.24 (d, J=6.4Hz, 3H), 2.31 (m, 1H), 2.71 (d, J=8.3Hz, 1H), 3.77, 3.84 (s, 6H) ; cis isomer δ 1.36 (d, J=6.3Hz, 3H), 2.04 (d, J=7.9 Hz, 1H), 2.31 (m, 1H), 3.70, 3.78 (s, 6H). In each isomer, the stereochemical relation between a methyl group at 3-position and a methoxycarbonyl group at 2-position was determined to be trans since the irradiation of methyl group (δ 1.24 or 1.36) showed NOE at proton at 2-position.

19) **9d** was formed as a mixture (1 : 1) of cis and trans isomers with respect to two methoxycarbonyl groups. cis-isomer ; ^{1}H-NMR ($CDCl_3$) δ 1.28 (d, J=6.5Hz, 1H), 1.59 (s, 3H), 2.32 (d, J=6.5Hz, 1H), 3.69, 3.76 (s, 6H) ; trans isomer ; δ 1.43 (s, 3H), 1.88 (d, J=6.7Hz, 1H), 2.08 (d, J=6.6Hz, 1H), 3.79, 3.84 (s, 6H).

20) L.L.McCoy and G.W.Nachtigall, *J. Org. Chem.*, **1962**, 27, 4312.

21) Yields based on methyl dichloroacetate.

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