Application of phase-transfer catalysis (PTC) to reactions of C-H acids with chloroethylenes

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Dedicated to Professor Mieczysław Mąkosza on his 70th birthday

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Abstract

2-Phenylalkanenitriles **1** react under PTC conditions with 1,1- or *cis*-dichloroethylene giving ethynylated products **2**. Nitriles **1**, α-substituted desoxybenzoines **6**, 2-substituted phenylacetaldehydes **8**, 1,3-dialkylindene **10** and substituted diethylmalonates **12** afford with trichloroethylene 1,2-dichlorovinylated derivatives, respectively **3**, **7**, enol ethers **9**, **11** and **13**. PTC reaction of *trans*-dichloroethylene with **1** or **10** lead to formation of 2-chlorovinylated **14** or ethynylated **16** products, respectively. In majority of cases the products were formed in good yield. The course of these reactions is rationalized.

Keywords: Phase-transfer catalysis, chloroethylenes, carbanions

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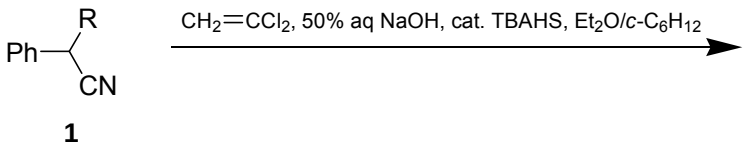
1. Introduction

1,1-Dichloroethylene (vinylidene chloride, VC), *cis*-1,2-dichloroethylene (*cis*-DE) or trichloroethylene (TRI) easily eliminate hydrogen chloride with formation of chloroacetylene (CA) [1] or dichloroacetylene (DCA), [2,3] respectively when treated with alkali metal hydroxide in the presence of a catalyst, a quaternary ammonium salt [1,2] or in aprotic dipolar solvent [3] (phase-transfer catalysis, PTC [4-7]). Both CA and DCA exhibit electrophilic properties hence easily add nucleophiles. From practical point of view the nucleophiles are usually present in reaction mixtures, adding to *in situ* generated CA or DCA. Thus, PTC technique was successfully applied to reactions of TRI with oxygen,[8] selenium [9-11] and nitrogen [2,12-15] nucleophiles leading to formation of the corresponding 1,2-dichlorovinyl substituted derivatives and/or other products. However, PTC has not been used to reactions of C-H acids with dichloroethylenes or TRI. The results of experiments carried out by us in this subject are briefly reviewed below.

2. Reactions of 2-substituted phenylacetonitriles with vinylidene chloride (VC) or *cis*-dichloroethylene (*cis*-DE)

Nucleophiles, including carbanions, add to mono substituted triple bond usually in *trans*-fashion with formation of *cis*-products.[16-18] *cis*-Adducts formed from carbanions and CA should easily eliminate hydrogen chloride giving ethynylated C-H acids. Indeed, stirring of 2-alkyl substituted phenylacetonitriles **1a-g** with VC, 50% aq. sodium hydroxide and tetra-*n*-butylammonium hydrogensulfate (TBAHS) as a catalyst, resulted in 2-ethynyl substituted nitriles **2a-g** in good yield [19,20] (Scheme 1).



1 **2**

1, 2	A	b	C	d	e	F	G
R	Me	Et	*i*-Pr	CH_2=$CHCH_2$	$PhCH_2$	Ph_2CH	*i*-$Pr_2N(CH_2)_2$
2, yield (%)	61	81	70	75	83	89	90
purity (%)	≥ 98	≥ 98	95	92	92	≥ 98	≥ 98

Scheme 1

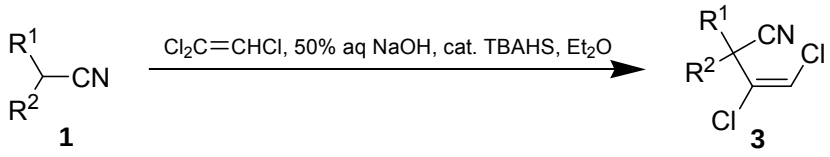
The process was carried out at reflux (ca. 40°C) of cyclohexane-ethyl ether mixture, for 2.5-5 h, but preparation of sterically crowded *i*-propyl derivative **1c** required longer time, under inert gas. The use of the latter is essential to prevent oxidation of nitriles **1** to the corresponding phenones and violent burning of chloroacetylene in air. For the latter reason the use of ethyl ether is very

desirable since it stabilizes chloroacetylenes by formation of the complexes.[21] The process did not take place without the catalyst. Essentially the same results gave *cis*-DE, but its use did not show any advantages, also it is much more expensive than VC. Careful examination of a mixture from the reaction of **1a** with VC carried out at 18°C revealed the presence of a small amount of *trans*-2-chlorovinyl- and 1-chlorovinyl substituted derivative, the latter was converted into **2a** after prolonged reaction. These compounds may result from *cis*-addition of $\mathbf{1a}^-$ to CA and its addition to C-1 of CA, respectively.

3. Reactions of C-H acids with trichloroethylene (TRI)

3.1. Reactions of 2-substituted phenylacetonitriles and 2-phenylthiopropionitrile

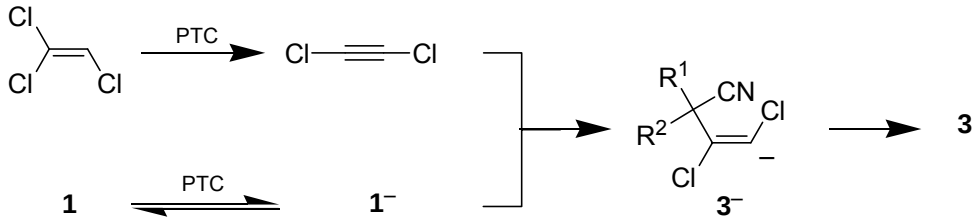
Different products - namely *trans*-1,2-dichlorovinyl substituted nitriles **3** - were formed in high yield when 2-substituted phenylacetonitriles **1** and 2-phenylthiopropionitrile (**1n**) were allowed to react with TRI under PTC conditions [22] (Scheme 2).



1, 2	a	b	C	e	H	i	j	k	l	M	n
R^1	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Me
R^2	Me	Et	*i*-Pr	$PhCH_2$	$Me_2N(CH_2)_2$	Me_2N	$O(CH_2CH_2)_2N$	MeO	*i*-PrO	CH_2=$CHCH_2O$	PhS
Yield **3** (%)	66	67	75	76	70	60	69	65	65	61	67

Scheme 2

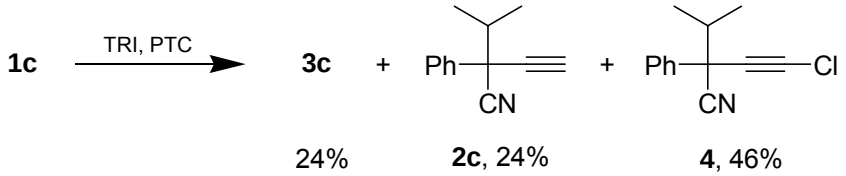
Reasonable route of their formation is given on Scheme 3.



Scheme 3

The carbanions $\mathbf{1}^-$ by *trans*-addition to DCA produced highly basic dichlorovinyl anions $\mathbf{3}^-$ which after protonation afforded *trans*-products **3**. The process was carried out at 5-10°C in ethyl ether, benzyltriethylammonium chloride (TEBAC) as a catalyst was less effective than TBAHS.

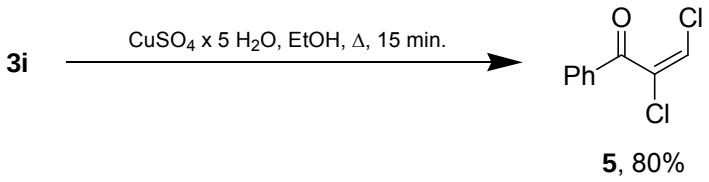
When the reaction of nitrile **1c** with TRI was performed at ca 35°C products **2c** and **4** predominated (Scheme 4, yields determined by GC).



Scheme 4

The product **4** may be formed either via a *cis*-addition of $\mathbf{1c}^-$ to DCA and subsequent elimination of hydrogen chloride, via halogenophilic reaction of $\mathbf{1c}^-$ with DCA or, less probably, via addition of this anion to TRI, followed by elimination of two equivalents of hydrogen chloride. All these mechanisms were identified in reactions of nucleophiles with TRI or DCA.[23,24] Ethynyl substituted derivative **2c** probably results from a halogenophilic attack of any anion present in the system on **4.**

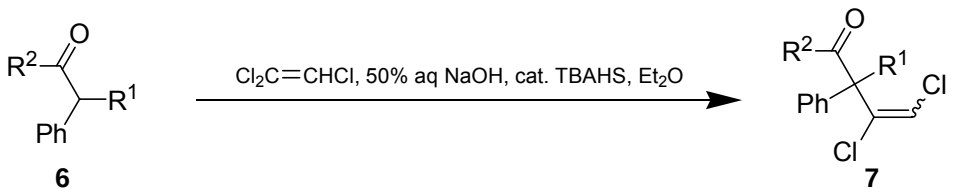
Dichlorovinylation of nitriles substituted at C-2 with a heteroatom afforded products **3i-m** which after unmasking of the carbonyl group should give dichlorovinyl-substituted ketones. This transformation was exemplified by efficient conversion of nitrile **3i** into *trans*-dichlorovinylphenyl ketone (**5**, Scheme 5).



Scheme 5

3.2. Reactions of α-substituted desoxybenzoines and α-substituted phenylacetaldehydes

PTC dichlorovinylation is not restricted to nitriles **1**. Desoxybenzoines α-substituted with alkyl **6a-e** or heteroatom **6f-h** group reacted with TRI in the presence of 50% aq. sodium hydroxide and TBAHS as a catalyst in ethyl ether to give the expected products **7** usually as mixtures of *trans*- and *cis*-isomers [25] (Scheme 6).



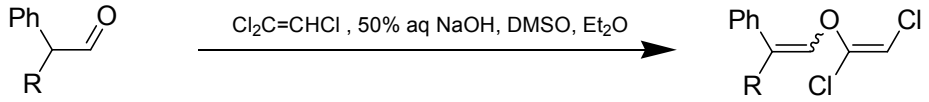
6 **7**

6, 7	**a**	**B**	**c**	**d**	**e**	**f**	**g**	**H**	**i**
R^1	Et	*n*-C_4H_9	*n*-C_6H_{13}	CH_2=$CHCH_2$	$PhCH_2$	Cl	PhO	PhS	CN
R^2	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Me
Yield **7** (%)	63	71	62	54	79	62	76	83	40

Scheme 6

Because of larger steric crowding in enolate anions, in comparision with nitrile ones, the formation of both stereoisomers of products **7** is probably a result of competitive *trans* (major pathway) and *cis* (minor pathway) addition of enolate anions $\mathbf{6}^-$ to DCA. The result of PTC reaction of ketone **6b** with independently synthesized DCA [3] confirmed participation of the latter in the process with TRI. While α-(phenyl)alkylmethyl ketones formed rather complex products mixtures with TRI under PTC conditions (probably isomeric methyl enolate anion was involved), α-(cyano)-α-(phenyl)acetone (**6i**) afforded dichlorovinylated product **7i** in moderate yield (Scheme 6).

Ambident character of enolate anions generated from phenylacetaldehyde derivatives **8** was evidenced in their reactions with TRI: only O-*trans*-dichlorovinyl substituted derivatives **9** were isolated in good yield, the best results gave 50% aq. sodium hydroxide/DMSO base/solvent system [25] (Scheme 7).



8a, R = Me
8b, R = Ph

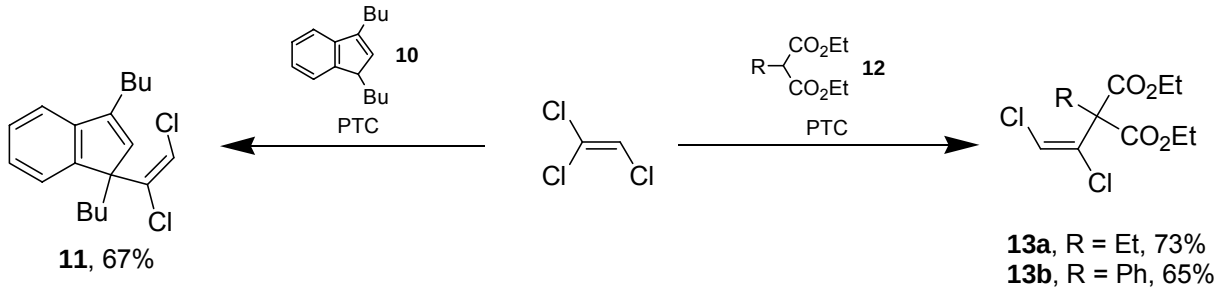
9a, 70%
9b, 75%

Scheme 7

Apart from spectral data, structure of **9** was confirmed by acid catalyzed hydrolysis which led to formation of the starting aldehyde **8** and others products, due to possible cleavage of both carbon-carbon double bonds.

3.3. Reactions of 1,3-dibutylindene and substituted diethylmalonates

We also succeded in dichlorovinylation of 1,3-di-n-butylindene (**10**) or substituted diethylmalonates **12** with TRI under PTC conditions which led to formation of the products **11** or **13**, respectively [26] (Scheme 8).



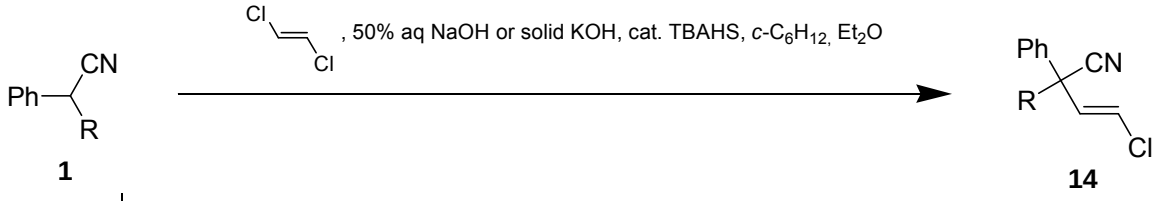
Scheme 8

Reaction with less acidic ethyl diethylmalonate (**12a**) did not occur in the presence of solid potassium carbonate and TBAHS or in DMSO, while the product **13a** was obtained in good yield when 50% aq. sodium hydroxide and TBAHS as a catalyst in diluted with ethyl ether organic phase, were used (with lesser amount of ethyl ether ester functionalities in **12a** hydrolyzed). On the other hand, in the case of more acidic phenyl diethylmalonate (**12b**) solid-liquid carbonate system was sufficiently basic for preparation of **13b**.

4. Reactions of C-H acids with *trans*-dichloroethylene (*trans*-DE)

4.1. Reactions of 2-substituted phenylacetonitriles

trans-DE eliminates hydrogen chloride on treatment with base, but not as easily as the *cis*-isomer does.[17] Therefore we doubted its usefulness in PTC reactions with C-H acids. Much to our surprise, phenylacetonitriles substituted at C-2 with alkyl **1a-c,e,h** or a heteroatom group **1j** entered reaction with *trans*-DE under typical PTC conditions giving *trans*-2-chlorovinyl substituted nitriles **14** [20,27] (Scheme 9).

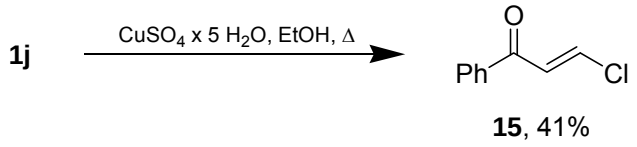


1, 14	A	B	C	e	h	J
R	Me	Et	*i*-Pr	$PhCH_2$	$Me_2N(CH_2)_2$	$O(CH_2CH_2)_2N$
Yield **14** (%)	71	79	12	82	68	68

Scheme 9

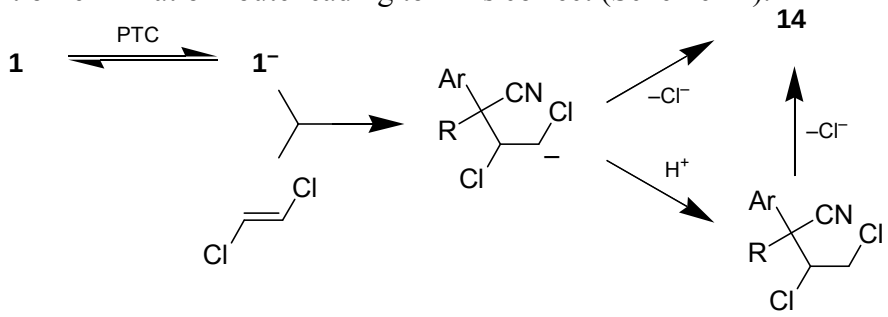
Steric crowding around a carbanion center in **1c** required the use of a solid-liquid system (powdered potassium hydroxide and TBAHS as a catalyst) to prepare nitrile **14c**, albeit in low

yield. Cleavage of **14j** with Cu(II) salt gave *trans*-2-chlorovinylphenylketone (**15**) in moderate yield (Scheme 10).



Scheme 10

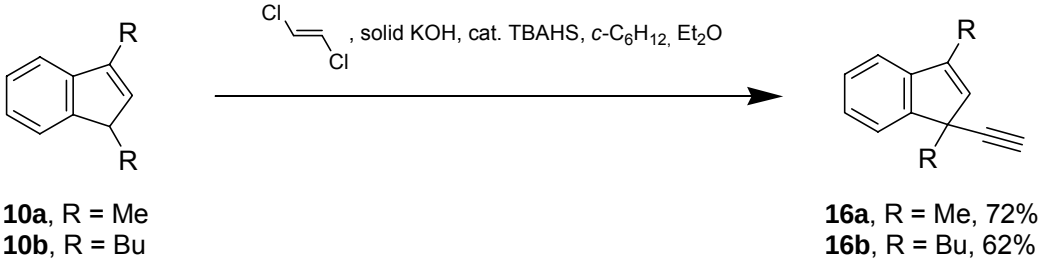
Some C-H acids like diphenylacetonitrile, phenylacetonitrile substituted at C-2 with oxy or thio group and 1,3-diphenylbutan-1-one proved inert toward *trans*-DE. Furthermore, we did not observe formation of CA from *trans*-DE under PTC conditions, and the products **14** were formed under slightly stronger reaction conditions than used for the typical ethynylation process. Therefore addition-elimination route leading to **14** is correct (Scheme 11).



Scheme 11

4.2. Reactions of 1,3-dialkyl indenes

Also, we expected chlorovinylation of 1,3-dialkylsubstituted indenes **10** by means of *trans*-DE under PTC condition but these C-H acids formed ethynylated products **16**, instead [27] (Scheme 12).



Scheme 12

The reactions described above were carried out in a solid-liquid PTC system, in the presence of powdered potassium hydroxide and TBAHS as a catalyst in ethyl ether-cyclohexane mixture (in liquid-liquid PTC system much indenes **10** remained intact). There are two routes according to

which ethynylation of indenes **10** may occur.[26] *trans*-DE is not so prone to eliminate hydrogen chloride like other dichloethylenes but this process may take place by means of basic indene anions [pK_a of heptamethylindene and 2-phenylpropionitrile (**1a**) are 27.4 and 23, respectively [28]]. If so, addition-elimination route with participation of CA is possible. Another approach consists of addition of indene anions to *trans*-DE followed by elimination of two equivalents of hydrogen chloride. Detailed investigation revealed that indene anion is indeed basic enough to promote elimination of hydrogen chloride from both *trans*-DCE as well as from chlorovinylated intermediates. So, these routes probably compete during formation of ethynylated indenes **16**.

5. Conclusions

Results of our investigations indicate that simple PTC methodology allows to synthesize variety of ethynylated, 1,2-dichlorovinylated or 2-chlorovinylated C-H acids using cheap chloroethylenes. Utilization of other C-H acids, elucidation of mechanistic aspects of these processes as well as application of the products formed in organic synthesis is actually searched.

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