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Application of trichloroethylene in organic synthesis. VIII. Competitive reactions of dichloroacetylene with secondary amines and carbazole. New evidence for the reaction mechanism

Dariusz Bogdał*, Jan Pielichowski

Institute of Organic Chemistry and Technology, Politechnika Krakowska, ul Warszawska 24, 31-155 Krakow, Poland

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Summary – Dichloroacetylene (DCA), which is generated *in situ* from trichloroethylene, reacts with carbazole and secondary aliphatic amines under phase-transfer catalytic conditions to yield 9-((*E*)-1,2-dichlorovinyl)carbazole **4**, 1-(9-carbazolyl)-1-dialkylamino-2-chloroethylenes **5** and *N*,*N*-dialkyl-2-(9-carbazolyl)acetamides **6** in a one-pot synthesis. The compounds **5** and **6** are formed as the result of direct addition of secondary amines to the triple bond of DCA followed by the reactions of intermediate products with either carbazole or hydroxyl anions.

dichloroacetylene / secondary amine / carbazole / reaction mechanism / phase-transfer catalytic conditions

Many polychloroethanes and polychloroethylenes undergo β-elimination reactions in phase-transfer (PTC) systems [1,2]. For example, trichloroethylene easily forms the trichlorovinyl anion **2** and then dichloroacetylene (DCA)** under PTC conditions as reported by Makosza [3]. The formation of the vinyl anion **2** was proved by reaction with CCl_4, which resulted in the formation of tetrachloroethylene [4], whereas the formation of DCA was confirmed by the isolation of the compound from the reaction mixture (fig 1) [5, 6].

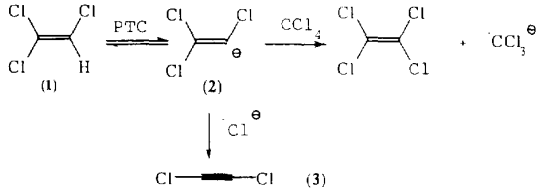

Fig 1. The formation of dichloroacetylene from trichloroethylene under PTC conditions

Direct nucleophilic substitution of chlorine atoms connected to an alkenyl carbon atom is difficult because of their low reactivity. For that reason, few reactions of trichloroethylene with nucleophilic reagents are known, although it does react with thiols and their salts in alkaline medium to give corresponding dichlorovinyl thioethers and thiolo-substituted ethylenes [7-9] and with phenolates or alcoholates of alkali metal to yield aryl- or alkyldichlorovinyl ethers [10, 11]. Benechie *et al* [12] and Kende *et al* [13] have applied the reaction of trichloroethylene with certain enolates to introduce the 1,2-dichlorovinylic group into the α-position of ketones. Under the action of strong bases (*eg*, BuLi), trichloroethylene forms a metalloorganic compound which gives trichloroacrylic acid with CO_2 [14, 15]. Aromatic Grignard compounds react with trichloroethylene in the presence of $CoCl_2$ to form diaryl derivatives of acetylene [16].

Among the reactions of trichloroethylene with amines, Shklyar [17] has described the reaction of trichloroethylene with aniline at 120°C which provides a mixture of anilinium chloride, azobenzene, 1,3-diphenylurea, and traces of dichloroacetylene. Rene *et al* [18] obtained bis (dimethylamino)acetylene from trichloroethylene and dimethylamine in the presence of sodium amide. It was reported that trichloroethylene reacted with liquid ammonia under pressure at increased temperature to yield glycine or aminoacetonitrile depending on the conditions [19].

Recently. Heiden and Brandsma [20] obtained 1,2-dichloro-1-(*N*,*N*-dialkylamino)ethylenes **7** by the reaction of lithium dialkylamide and diethylamine with DCA prepared *in situ* from trichloroethylene. The same products, the 1,2-dichloroenamines **7**, have been obtained previously by Ott *et al* in direct reaction of DCA and secondary amines [21]. The 1,2-dichloroenamines **7** were

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** DCA is a toxic and unstable compound which explodes in contact with air.

so unstable that they reacted vigorously with moisture and water or formed brown resins upon exposure to air. Furthermore, under the reaction conditions, they easily underwent the subsequent reaction with excess secondary amine to give 1,1-bis(dialkylamino)-2-chloroethylenes **8** [20, 21].

Owing to the transformation of trichloroethylene to DCA (*ie*, the preparation of DCA *in situ*) under PTC conditions, we can react it with both carbazole and secondary amines under mild conditions to give a number of compounds. In order to exploit the chemistry of DCA under such conditions, we have undertaken further studies of the reactions of DCA in the PTC systems, and, in the present paper, we describe the competitive reactions of DCA with both carbazole and secondary amines.

Result and discussion

Our previous investigations have showed that DCA generated *in situ* from trichloroethylene under PTC conditions reacted with secondary aliphatic amines or with carbazole and its derivatives to form *N*,*N*,*N*′,*N*′-tetraalkylglycinamides [22] and 9-((*E*)-1,2-dichlorovinyl)carbazole [23], respectively. In the course of these investigations, we recently reported that DCA underwent competitive reactions with the mixed reagents (*ie* carbazole and primary amines) to afford 1-(alkylimino)-1,2-di(9-carbazolyl)ethanes and 9-(1,2-dichlorovinyl)carbazole [24]. These compounds were formed in a multistage process of addition/elimination to the triple bond of DCA, and our investigations provided data useful to understand the mechanism of DCA reactions with primary amines [25].

The investigation of competitive reaction of DCA with both carbazole and secondary amines has been performed in a PTC system containing diethyl ether, 50% aqueous solution of NaOH, and DMSO as a phase-transfer catalysts. DCA was generated *in situ* from trichloroethylene, which was added to the reaction mixtures. Finally, mixtures of 9-((*E*)-1,2-dichlorovinyl)carbazole **4**, 1-(9-carbazolyl)-1-(dialkylamino)-2-chloroethylenes **5** and *N*,*N*-dialkyl-2-(9-carbazolyl)acetamides **6** (fig 2) were obtained as the reaction products.

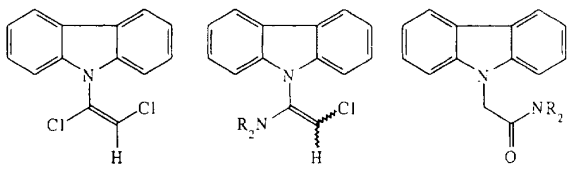

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Fig 2. The products of the reaction of trichloroethylene with both carbazole and secondary amine under PTC conditions.

Since the vinylcarbazole **4** is formed as the result of direct addition of carbazole to the triple bond of DCA and is stable under the reaction conditions [23], the (dialkylamino)ethylene **5** and the amide **6** must be formed by the direct addition of a secondary amine to the triple bond of DCA followed by the reactions of an intermediate product with either the carbazole or the hydroxyl anion. As mentioned above, the reactions of DCA and secondary amines are known and resulted in the formation of 1,2-dichloroenamines **7** followed by the formation of 1,1-bis(dialkylamino)-2-chloroethylenes **8** [20, 21].

In the PTC system, carbazole is present as the carbazolyl anion [26], which is a stronger nucleophile than secondary aliphatic amines. The 1,2-dichloroenamine **7** therefore reacted mostly with carbazole instead of secondary amines to yield the dialkylaminoethylene **5**, which could be isolated from the reaction mixtures.

The substitution of the α-chlorine atom in the 1,2-dichloroenamine **7** can also be accomplished with the hydroxyl anions present in the PTC system to give *N*,*N*-dialkyl-2-chloroacetamides **9** [21, 27]. We confirmed the above reaction and obtained 4-(chloroacetyl)morpholine in the rapid reaction of DCA morpholine under PTC conditions [22]. *N*,*N*-Dialkyl-2-chloroacetamides **9** underwent easily further reactions with secondary amines to form *N*,*N*,*N*′,*N*′-tetraalkylglycinamides **10**, as was described in our previous papers [6, 21]. However, both carbazole and amines were present in the reaction mixtures. The substitution of the chlorine atom in the chloroacetamide **9** was therefore accomplished predominantly by the carbazole anion to yield the amide **6**, whereas the glycinamides **10** were the final products of the reaction of the chloroacetamide **9** and a secondary amine in the absence of carbazole [22].

Moreover, it was reported that 1,1-bis(diethylamino)-2-chloroethylenes **8** could be transformed into *N*,*N*,*N*′,*N*′-tetraethylglycinamides **10** in the presence of diethylamine in concentrated sodium hydroxide solutions [21, 27]. Similarly, *N*,*N*-diethylamides of phenoxyacetic acid were obtained from 1,1-bis(diethylamino)-2-chloroethylenes **8** and phenoxides in sodium hydroxide solutions [21]. The mechanism consists of multistep addition/elimination processes, which are typical for halogenoacetylenes and substituted ethylenes under basic conditions [28]. Therefore, we assume that similar transformations of the (dialkylamino)ethylene **5** into the amide **6** took place in the described syntheses. This hypothesis was confirmed by the reaction of carbazole and a secondary amine with the isolated (dialkylamino)ethylene **5** under PTC conditions, which led to the formation of the amide **6**. In addition, we found that when the reaction mixture was stirred after all of carbazole was consumed, the concentration of the amide **6** gradually increased, while the concentration of the (dialkylamino)ethylene **5** decreased, and the amount of the vinylcarbazole **4** remained constant. The best yields of the (dialkylamino)ethylene **5** were obtained after relatively short reaction times (table I). When the reaction mixture was left sealed for a few weeks, the concentration of the (dialkylamino)ethylene **5** dropped to a few percent, and the concentration of the amide **6** was correspondingly higher.

It is well known that substituted ethylenes with hydrogen and halogen in the geminal position undergo a Fritsch–Buttenberg–Wiechell (FWB) rearrangement to 1,2-substituted acetylenes in the presence

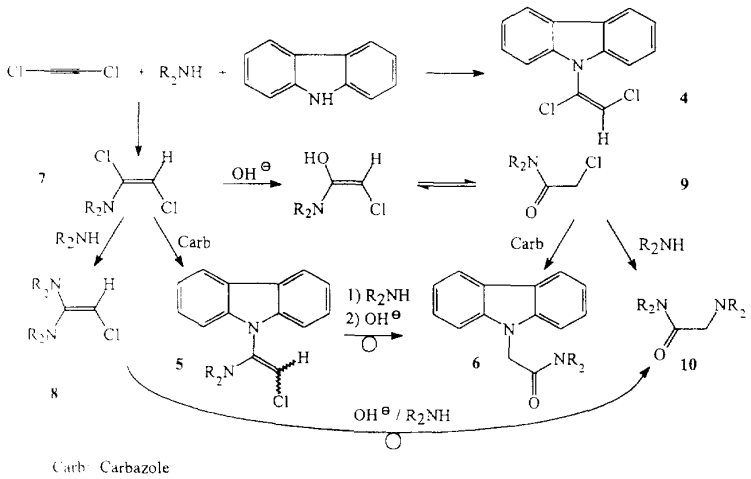

Fig 3. The mechanism of the reaction of trichloroethylene with both carbazole and a secondary amine under PTC conditions.

of base [29-32]. According to the FWB rearrangement, 1-carbazolyl-2-(dialkylamino)acetylenes can be formed from (dialkylamino)ethylenes **5**, and the subsequent addition of water to the triple bond of 1-carbazolyl-2-(dialkylamino)acetylene results in the formation of the amide **6**.

In summary, we would like to emphasize that, due to unusual reactivity of DCA compared with 1,2-dichloroenamine **7**, secondary amines reacted exclusively with DCA to yield 1,2-dichloroenamine **7**. DCA is a strong electrophile with the reactivity of acid chlorides [33], and so the reactivities of carbazole and amines towards DCA played minor roles, thus allowing an amine to react with DCA in the first stage of the reactions. 1,2-Dichloroenamine **7** is a vinyl derivative which is much less reactive than DCA towards nucleophilic addition. Therefore the vinyl compound **7** could only react with a strong nucleophile such as carbazole. We noticed that even in the presence of excess amine, the consumption of carbazole was always total when the carbazole/DCA ratio was 1:1. If an amine had reacted with the 1,2-dichloroenamine **7**, all the carbazole would not have been used.

The reaction of trichloroethylene with both carbazole and a secondary amine allowed us to obtain compounds **4–6** in one-pot syntheses, because the appropriate yield of the desired compound can be obtained by the adjustment of reaction conditions such as temperature, catalyst type, reagent ratio and time. The products are easy to separate by means of flash chromatography; the results are gathered in table I.

Table I. The product yield[a] in the competitive reactions of trichloroethylene with carbazole and secondary aliphatic amines under PTC conditions.

		DMSO			TEBA		
Compound	Molar ratio[b]	**4**	**5**	**6**	**4**	**5**	**6**
	C:D:A	(%)	(%)	(%)	(%)	(%)	(%)
Diethylamine	1:1:2				71	13	10
	1:2:2	52	24	19	63	16	14
	1:2:5	21	43	32			
Di-*n*-propylamine	1:1:2				80	7	6
	1:2:2	73	11	13	74	9	10
	1:2:5	38	22	36			
Piperidine	1:1:2				82	6	6
	1:2:2	52	26	20	73	13	10
	1:2:5	30	34	31			
Morpholine	1:1:2				80	11	
	1:2:2	75	17		69	23	
	1:2:5	43	48				

[a] Relative to DCA; [b] C: carbazole, D: dichloroacetylene, A: amine.

Experimental section

Elemental analyses were performed on a Perkin-Elmer 240 microanalyzer. Melting points were measured on a Boetius-PHMK 05 microscope plates and are uncorrected. The reactions were monitored by means of TLC. ^1H and ^{13}C NMR spectra were recorded with a TESLA 487 C spectrometer, TMS being used as an internal standard; the chemical shifts are expressed in δ values downfield from TMS. MS spectra were recorded on a Hewlet-Packard 5985 spectrometer. IR spectra were performed on a UR-20 spectrophotometer, and the wave numbers are given with a precision of 5 cm^{-1}.

1-(Diethylamino)-1-(9-carbazolyl)-2-chloroethylene 5a

A 150 mL three-necked flask equipped with a thermometer, an upright condenser and an efficient stirrer was charged with NaOH (8.0 g, 200 mmol), water (8 mL), carbazole (1.0 g, 6.0 mmol, 1 equiv), diethyl ether (10 mL), DMSO (2 mL) and diethylamine (2.2 g, 30 mmol, 5 equiv). The mixture was heated to 30°C and a solution of trichloroethylene (0.6 mL, 6.0 mmol, 1 equiv) in diethyl ether (10 mL) was then added dropwise within 1 h, with vigorous stirring. After 2 h the reaction was stopped by addition of water (50 mL). The organic solvent was distilled off and the remaining aqueous phase was extracted with CH_2Cl_2 (2 × 40 mL). The extract was washed with saturated aqueous NaCl and dried over $MgSO_4$. The reaction products were separated by flash chromatography (silica gel 60, 70–270 mesh) using hexane

as an eluent. The (dialkylamino)ethylene **5a** was obtained as a second fraction very quickly after the vinylcarbazole **4**. The attempts at crystallization from heptane or ethanol gave only an oil, **5a** (0.7 g, 42%).

IR (film): 3 060, 2 980, 2 830, 1 680, 1 615, 1 480, 1 455, 1 335, 1 235, 1 165, 820, 765, 730 cm^{-1}.

^1H NMR ($CDCl_3$): δ 1.04 (t, J = 7.1 Hz, 6H, 2 × (-CH_3)), 2.89 (q, J = 7.1 Hz, 4H, 2 × (-CH_2-)), 5.35 (s, 1H, vinyl), 7.20–8.13 (m, 8H, aromatic protons).

^{13}C NMR ($CDCl_3$): δ 12.9, 14.0, 40.3, 41.8, 108.4, 119.7, 120.1, 120.6, 123.3, 126.1, 126.3, 140.5.

Anal calc for $C_{18}H_{19}ClN_2$: C, 72.35; H, 6.41; N, 9.38. Found C, 72.7; H, 6.2; N, 9.2.

The syntheses of **5b–d** were carried out in a similar way as that described for **5a**.

5b: oil, yield 37%.

IR (film): 3 060, 2 975, 2 830, 1 675, 1 610, 1 480, 1 450, 1 340, 1 235, 1 165, 825, 760, 730 cm^{-1}.

^1H NMR ($CDCl_3$): δ 0.88 (t, J = 7.0 Hz, 6H, 2 × (-CH_3)), 1.26–1.82 (m, 4H, 2 × (-CH_2-)), 3.08–3.43 (m, 4H, 2 × (N-CH_2-)), 5.36 (s, 1H, vinyl), 7.23–8.15 (m, 8H, aromatic protons).

^{13}C NMR ($CDCl_3$): δ 10.8, 11.2, 20.9, 22.0, 48.4, 49.2, 108.5, 119.6, 120.3, 120.6, 123.2, 126.4, 126.7, 140.6.

Anal calc for $C_{20}H_{23}ClN_2$: C, 73.50; H, 7.09; N, 8.57. Found: C, 73.1; H, 6.8; N, 8.3.

5c: yield 45%, mp 118–120°C.

IR (KBr): 3 060, 2 965, 2 860, 2 810, 1 690, 1 600, 1 480, 1 455, 1 340, 1 240, 1 210, 1 165, 760, 730 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.10–2.05 (m, 6H, -CH_2-CH_2-CH_2-), 2.67–3.19 (m, 4H, 2 × (N-CH_2-)), 5.43 (s, 1H, vinyl), 7.23–8.15 (m, 8H, aromatic protons).

^{13}C NMR ($CDCl_3$: δ 24.5, 25.3, 25.9, 45.5, 46.3, 108.2, 119.5, 120.1, 120.4, 123.2, 126.1, 126.3, 140.6.

Anal calc for $C_{19}H_{19}ClN_2$: C, 73.42; H, 6.16; N, 9.01. Found: C, 73.0; H, 5.9; N, 8.7.

5d: yield 52%, mp 140–141°C.

IR (KBr): 3 050, 3 010, 2 980, 2 910, 2 860, 1 650, 1 590, 1 480, 1 450, 1 320, 1 260, 1 215, 1 200, 1 100, 1 020, 840, 800, 740, 705 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.75 (t, J = 4.7 Hz, 4H, CH_2-N-CH_2), 3.64 (t, J = 4.7 Hz, CH_2O-CH_2), 5.48 (s, 1H, vinyl), 7.25–8.15 (m, 8H, aromatic protons).

Anal calc for $C_{18}H_{17}ClN_2O$: C, 69.11; H, 5.48; N, 8.95. Found: C, 69.43; H, 5.2; N, 8.7.

N,N-*Diethyl-2-(9-carbazolyl)acetamide* **6a**

A 150 mL three-necked flask equipped with a thermometer, an upright condenser and an efficient stirrer was charged with NaOH (8.0 g, 200 mmol), water (8 mL), carbazole (1.0 g, 6.0 mmol, 1 equiv), diethyl ether (10 mL), DMSO (2 mL) and diethyl amine (2.2 g, 30 mmol, 5 equiv). The mixture was heated to 35–40°C and a solution of trichloroethylene (0.6 mL, 6 mmol, 1 equiv) in diethyl ether (10 mL) was then added dropwise 1 h, with vigorous stirring. After 8 h the reaction was stopped by addition of water (50 mL). The organic solvent was distilled off and the remaining aqueous phase was extracted with CH_2Cl_2 (2 × 40 mL). The extract was washed with saturated aqueous NaCl and dried over $MgSO_4$. The reaction products were separated by flash chromatography (silica gel 60, 70–270 mesh) using hexane/CH_2Cl_2 (4:1) as eluent. The amide **6a** was obtained as a last fraction after the vinylcarbazole **4** and the (dialkylamino)ethylene **5a**. Recrystallization from heptane gave **6a** (0.9 g, 55%), mp 140–142°C.

IR (KBr): 3 055, 2 990, 2 970, 2 930, 1 665, 1 600, 1 490, 1 465, 1 330, 1 270, 1 220, 1 145, 755, 725 cm^{-1}.

^1H NMR ($CDCl_3$): δ 1.01 (t, J = 7.8 Hz, 3H, -CH_3), 1.11 (t, J = 7.8 Hz, 3H, -CH_3), 3.36–3.51 (m, 4H, 2 × (N-CH_2-)), 4.98 (s, 2H, N-CH_2-CO-N), 7.15–8.10 (m, 8H, aromatic protons).

^{13}C NMR ($CDCl_3$): δ 12.9, 14.0, 40.0, 41.7, 45.7, 108.5, 118.4, 120.4, 123.2, 125.9, 140.7, 166.4.

MS (EI, 70 eV): m/z = 280 (38%, M^+, 180 (100%, carbazolyl-CH_2^+).

Anal calc for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 10.00. Found: C, 77.2; H, 7.14; N, 9.9.

The syntheses of **6b** and **6c** were carried out in a similar way as that described for **6a**.

6b: yield 60%, mp 132–134°C.

IR (KBr): 3 060, 2 965, 2 960, 2 880, 1 670, 1 600, 1 490, 1 475, 1 330, 1 220, 1 150, 760, 725 cm^{-1}.

^1H NMR ($CDCl_3$): δ 0.74 (t, J = 7.1 Hz, 3H, -CH_3), 0.83 (t, J = 7.1 Hz, 3H, -CH_3), 1.12–1.94 (m, 4H, 2 × (-CH_2-)), 3.17–3.43 (m, 4H, 2 × (N-CH_2-)), 4.99 (s, 2H, N-CH_2-CO), 7.23–8.14 (m, 8H, aromatic protons).

^{13}C NMR ($CDCl_3$): δ 10.9, 11.3, 20.8, 22.0, 45.7, 48.2, 49.2, 108.5, 119.4, 120.4, 123.2, 125.8, 140.7, 166.8.

MS (EI, 70 eV): m/z = 308 (41%, M^+), 180 (100%, carbazolyl-CH_2^+).

Anal calc for $C_{20}H_{24}N_2O$: C, 77.88; H, 7.84; N, 9.08. Found: C, 77.8; H, 7.9; N, 8.9.

6c: yield 63%, mp 170–172°C.

IR (KBr): 3 050, 2 945, 2 860, 1 670, 1 600, 1 490, 1 475, 1 330, 1 255, 1 225, 755, 725 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.17–1.82 (m, 6H, -CH_2-CH_2-CH_2-), 3.23–3.74 (m, 4H, 2 × (N-CH_2-)), 4.98 (s, 2H, N-CH_2-CO), 7.23–8.15 (m, 8H, aromatic protons).

^{13}C NMR ($CDCl_3$): δ 24.3, 25.5, 26.1, 43.5, 45.6, 46.3, 108.5, 119.4, 120.4, 123.2, 125.8, 140.6, 165.5.

Anal calc for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.90; N, 9.58. Found: C, 77.8; H, 6.9; N, 9.5.

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