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TRICHLOROETHYLENE IN ORGANIC SYNTHESIS: II.
REACTION OF TRICHLOROETHYLENE WITH SECONDARY AMINES

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Abstract - In a novel reaction, trichloroethylene reacts with secondary aliphatic amines in the presence of aqueous solution of NaOH and catalytic quantity of benzyltriethylammonium chloride to give the corresponding **N,N,N,N′-tetraalkylsubstituted** glycinamides. The following glycinamides were obtained with high yield: **/N-morpholine/acetic** acid morpholide, **N-/piperidineacetyl/piperidine, N,N,N,N′-tetra-n-butylglycinamide** and **N,N,N,N′-tetraethylglycinamide.** Mechanism of the reaction is discussed.

INTRODUCTION

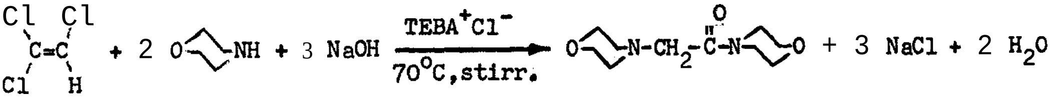
Direct, nucleophilic substitution of chlorine atoms connected to alkenyl carbon atom is difficult, because of its low reactivity. For that reason, there are known relatively few reactions of trichloroethylene with nucleophilic reagents, although it does react with thiols and their salts in alkaline medium to give corresponding dichlorovinyl thioethers or thiolosubstituted ethylenes[1-6] - and with phenolates or alcoholates of alkali metal to form aryl- or alkyldichlorovinyl ethers[7-10], Benechie et.al.[11] and Kende and Fludzinski[12] have applied the reaction of trichloroethylene with certain enolates to introduce the **α,β-dichlorovinylic** group into thea-position of ketones. Under the action of strong bases, such as BuLi, triohloroethylene forms a metalloorganic compound, which with CO_2 gives trichloroacrylic acid[13,14] whilst aromatic Grlgnard aompounds react with trichloroethylene in the presence of $CoCl_2$ to yield diary1 derivatives of acetylene[15] .

From among the reactions of trichloroethylene with amines, Shklyar[16] has described the reaction of trichloroethylene with aniline at 120 °C, which provides a mixture of: anilinium chloride, hydrazobenzene, azobenzene, sym-diphenylurea and traces of dichloroacetylene. Also Rene et.al.[17] have obtained bis-/dimethylamino/acetylene from trichloroethylene and dimethylamine in the presence of sodium amide. Recently, it was reported that trichloroethylene reacts with liquid ammonia under pressure at increased temperature to yield glycine or aminoacetonitrile depending on the conditions[18,19].

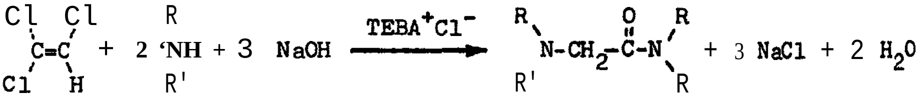
Under phase-transfer catalytic conditions[20,21] we have achieved[22] so an increase in the reactivity of trichloroethylene, such that one can react it with nucleophilic reagents under much milder conditions than previously to give interesting, new compounds. In order to exploit this new chemistry of trichloroethylene, we have undertaken further studies of the reactions of trichloroethylene under phase-transfer catalytic conditions. In the present paper we report the reactions of trichloroethylene with secondary amines.

RESULTS AND DISCUSSION

During our investigations on a behaviour of polyhalogen organic compounds under phase-transfer catalytic conditions, we have observed that trichloroethylene unexpeotedly reaoted exothermally with morphollne to give a crystalline compound (m.p. 69 °C), which on the basis of elemental analysis, mass spectrum, ^{1}H.NMR and IR spectroscopy showed the substance to be (N-morpholine)acetic acid morpholide, formed according to summary eqation:



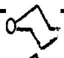
Further investigations have showed that other secondary amines react similarly with trichloroethylene to give the corresponding N,N,N',N'-tetraalkylglycinamides in high yield (Table 1), according to general equation:



$$Cl_2C{=}CHCl + 2\ RR'NH + 3\ NaOH \xrightarrow{TEBA^+Cl^-} RR'N{-}CH_2{-}C(O){-}NRR' + 3\ NaCl + 2\ H_2O$$

The reaction of trichloroethylene with secondary aliphatic or alicyclic amines seems to be a new general method for the preparation of symmetrically substituted N,N,N',N'-tetraalkylglycinamides and in many cases is superior and more convenient to those hitherto known[23-27].

Table 1. Substituted glycinamides: $R_2NCH_2CONR_2$, obtained from trichloroethylene and secondary amines under phase-transfer catalytic conditions.

Procedure	R_2N-	Yield (%)	m.p. (°C)	b.p. (°C/Tr)	$\delta^{**}_{CH_2CO}$ (ppm)	$\nu^{\dagger}_{CO}$ (cm^{-1})
8a	 N-	71	69-70		2.81	1652
8b	 N-	a3	38		2.98	1638
8c	n-Bu$_2$N-	81	-	150-5/3.5	3.26	1648
8d	Et$_2$N-	79	-	118/15	3.14	1647
	Me$_2$N-*	51		66-70/6	2.97	1655

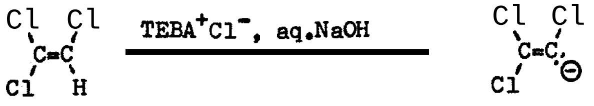
* - synthesis of N,N,N',N'-tetramethylglycinamide was reported as example in lit:22,
** - chemical shift for ^{1}H,
† - absorption maximum situation (for carbonyl group.)

Less nucleophilic, aromatic amine6 behave differently and an attempt to react diphenylamine or N-methylaniline with trichloroethylene failed. When the aromatic amines were heated with trichloroethylene under phase-transfer catalytic conditions however, a gaseous product was evolved, which exploded in contact with air, and only the unchanged anilines were isolated.

As the formation of N,N,N',N'- tetraalkylglyoinamides from the reactions of the secondary amines with trichloroethylene under the conditions favourable for the anionic reactions was surprising, we have attempted to explain the mechanism.

TEBA$^+$Cl$^-$ - benzyltriethylammonium chloride.

As reported earlier[28], in the presence of $TEBA^+Cl^-$ and aqueous sodium hydroxide, trichloroethylene easily forms the trichlorovinylic anion 2.

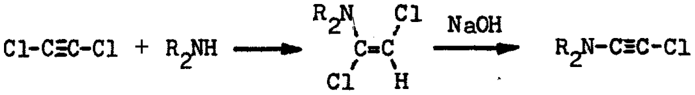


1 a

Direct reaction of anion 2 with amine is impossible, because of both are nucleophilic, but dichlorcacetylene 3 formed as a result of decay of anion 2 at increased (above 40°C) temperatures, is capable to reaction with the amine.

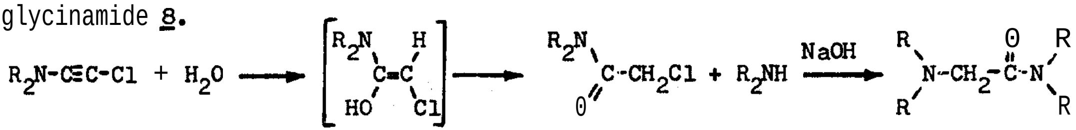
2 3

We have already reported[22] the isolation of dichloroacetylene in high yield as a complex with diethyl ether from the reaction of trichloroethylene under phase-transfer catalytic conditions in the absence of aliphatic amines. Dichloroacetylene forms an explosive mixture with air[29] and hence, in the case of less reactive aromatic amines it is the volatile dichloroacetylene, which explodes in the condenser, whereas aliphatic amines react instantenously with the highly electrophilic[30] dichloroacetylene with the same energy as acid chlorides to give α,β-dichloroenamine 5.



3 4 5 6

The compounds 5 (R = alkyl) are highly unstable in the presence of water[30] and are hydrolyzed in the alkaline medium to yield di-N-substituted chloroacetamides 7, which react with a second molecule of the amine to give the N,N,N,N'-tetraalkylglycinamide 8.



6 enolic form of 7 7 4 8

In order to confirm the proposed mechanism, attempts were undertaken to isolate the intermediate compounds 5 - 7. Neither of compounds 5 and 6 could be isolated from the reaction mixture in pure form, because of their unstability under reaction conditions. Although, in case of morpholine reaction with trichloroethylene at room temperature, extraction of products with benzene gave a solution, which, when dropped on a filter paper, spontaneously became yellow, then brown-red and HCl was secreted. An attempt to-distill off the solvent resulted in an explosion and the formation of dark-brown, viscous substance. Similar behaviour has been observed previously for 1,2-dichloro-1-(diethylamino)ethylene[30]. Moreover, when the extract was shaken with water, the aqueous phase became acidic from released HCl. It is therefore possible that 1,2-dichloro-1-(N-morpholine)-ethylene was present in the solution. The observed behaviour can be explained by decomposition with loss of HCl from dichloroenamine 5 and the formation of the chloroinamine 6, which cationically polymerized to give the dark, viscous product. In the case of the morpholine reaction with trichloroethylene we have isolated and identified pure intermediate product 7 (R_2N = morpholino) in a low yield. It, as well as above mentioned observations, confirm the postulated mechanism.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Tesla 487C spectrometer. TMS was used as internal reference standard and the chemical shifts are expressed in t-values (ppm) downfield from TMS=0. The IR spectra were recorded on a Carl-Zeiss UR-20 spectrophotometer. Mass spectra were recorded on LKB 9000-S mass spectrometer. The microanalyses were performed on Perkin-Elmer 240 microanalyzer. M.ps and b.ps are uncorrected.

Materials: Trichloroethylene and diethylamine (POCH), di-n-butylamine and morpholine (Fluka) and piperidine (BDH Ltd.) were obtained commercially. Benzyltriethylammonium chloride was synthesized according to literatur procedure. The reactants and solvents were distilled before use.

(N-morpholine)acetic acid morpholide 8a. In a 250 ml round bottom flask equipped with an efficient stirrer, thermometer and upright condenser were placed a solution of 50 g (1.25 mole) NaOH in 50 ml water, 43.5 ml (0.5 mole) morpholine and 1.1 g (0.005 mole) benzyltriethylammonium chloride (TEBA $^+$Cl$^-$) in 2 ml water. The mixture was stirred and heated up to 70°C and 22.5 ml (0.25 mole) trichloroethylene was added dropwise through the upright condenser. The temperature was maintained between 70 and 100 °C and the reaction flask was cooled if necessary. After all of trichloroethylene was added (2 h), the reaction mixture was refluxed for 1 hour. The water was then evaporated from the mixture under slightly reduced pressure end the residue was extracted with 500 ml CH_2Cl_2. The extract was dried with anhyd. Na_2SO_4 and evaporated from a water bath to give crude morpholide 8a, which was recrystallized from ligroine. Yield: 38 g, m.p. 69-70 °C (lit.[23]: 70-71 °C) MS: m/e = 214(M^+). Found: C:55.7; H:8.33; N:13.05, calcd for $C_{10}H_{18}N_2O_3$(214.27): C:56.06; H:8.47; N:13.07,%.

N-(piperidineacetyl)piperidine 8b. This was obtained as for 8a from 22.5 ml (0.25 mole) trichloroethylene and 49.5 ml (0.5 mole) piperidine. Main part of crude 8b was isolated by separation of organic layer, after the reaction had finished. Additional part was obtained from the water phase as for 8a. Crude 8b was recrystallized from ligroine. It is recommended to cool the mother liquora to avoid considerable losses. Yield: 43.5 g mol.weight: 212(acidimetric), calcd: 210.3, m.p. 38 °C (lit.23: 38-9, lit.26: 48-9). Found: C:68.7; H:10.2; N:13.6, calcd for $C_{12}H_{22}N_2O$: C:68.53; H:10.54; N:13.33,% .

N,N,N',N'-tetra-n-butylglycinamide 8c. The compound was obtained as for 8a from 39 ml (0.23 mole di-n-butylamine, 10.5 ml (0.117 mole) trichloroethylene and 20 g (0.5 mole) NaOH 50 % aq.sol.) in the presence of 0.5 g (0.0025 mole) TEBA $^+$Cl$^-$. The temperature was maintained between 100 and 120 °C. After the reaction finished, the product was extracted with benzene (3 x 50 ml). The extracts were dried with Na_2SO_4 and the solvent was evaporated. The residue was distilled under vacuum. Yield: 28.5 g, Found: C:72.2; H:12.4; N:9.37, calcd for $C_{18}H_{38}N_2O$(298.52): C:72.42; H:12.83; N:9.38,%.

N,N,N',N'-tetraethylglycinamide 8d. This was obtained as for 8c from 52 ml (0.5 mole) diethylamine, 22.5 ml (0.25 mole) trichloroethylene and 50 g (1.25 mole) NaOH. The reaction was conducted at the boiling point of diethylamine. The extraction was made with chloroform (3 x 150 ml). Yield: 37 g. Found: C:64.1; H:11.5; N:15.0, calcd for $C_{10}H_{22}N_2O$(186.3): C:64.47; H:11.90; N:15.04,% .

N-(chloroacetyl)morpholine 7a. The reaction was carried out in the same apparatus as for 8a. In the flask were placed 22.5 ml (0.25 mole) trichloroethylene, 22 ml (0.25 mole) morpholine and a solution of 1.1 g (0.005 mole) TEBA $^+$Cl$^-$ in 2 ml water. To the mixture was added dropwise a solution of 40 g (1 mole) NaOH in 50 ml wager within 1 hour. The flask was cooled such that the temperature didn't exceed 30 °C. After all of the solution had been added, stirring was continued for a further 2 hours. Then 60 ml benzene was added and after stirring 5 min, the organic layer was separated. It consisted of in addition to the unreacted substrates, 1,2-dichloro-I-(N-morpholino)ethylene, which behaved as described in the preceding section. The extract was shaken with 100 ml water for 0.5 hour and was then separated and dried with $MgSO_4$. The solvent was evaporated and the residue was distilled under vacuum. Yield: 7 g (17 %). Found: C:43.87; H:6.10; N:8.32, calcd for $C_6H_{10}NO_2Cl$(163.6): C:44.05; H:6.16; N:8.56,% . IR: V = 1660(CO) cm^{-1}, PMR: δ (CCl_4): 4.04(s,2H), 3.4-3.7(m,8H),ppm.

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