Pak. j. sci. ind. res., vol. 32, no. 6, June 1989

RING EXPANSION REACTIONS OF TRICHLOROMETHYL RADICALS WITH PYRAZOLES AND THE EFFECT OF SUBSTITUENTS ON THE YIELD

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(Received November 6, 1988; revised May 16, 1989)

Vapour phase reactions of carbon tetrachloride with substituted pyrazoles in a flow system at 550° provide a convenient method for ring expansion. Effect of increasing the number of electron donating methyl group on the nature of products and the over all yields was investigated. An increase in the overall yield of the reaction products (75%) was observed while the presence of a benzene ring decreased the yield. Results were compared with those obtained from the reactions of chloroform and substituted pyrazoles under identical conditions.

Key words : Ring expansion, Trichloromethyl radicals pyrazoles, Effect of substituents.

INTRODUCTION

Earlier papers [1-2] described ring expansion reactions of trichloromethyl radicals, generated in the vapour phase from carbon tetrachloride in a flow system at 550° with N-substituted and *C*-substituted pyrroles and pyrazoles. L Zor [3] has established that trichloromethyl radicals generated from chloroform in the vapour phase at 550° in a flow system react with a substrate molecule to give ring expanded products. With the information available in the literature [4] that trichloromethyl radicals can be generated from CCl_4 as well as from chloroform [5], ring expansion reactions with CCl_4 were considedred worthwhile.

This communication presents reactions of 3-methylpyrazole 3,5-dimethylpyrazole and indazole with CCl_4 separately. As expected, ring expanded products were obtained. The reaction products of these heterocycles with CCl_4 differed markedly from those obtained from chloroform [6-7]. It was further observed that an increase in the number of electron donating methyl groups in the substrate molecule increases the overall yield of the reaction products while the presence of a benzene ring decreases it.

EXPERIMENTAL

A Pye series 105 Automatic Preparative Chromatograph, Model 15 was used for both analytical and preparative work. All infra-red spectra were recorded on Unicam SP200 Spectrometer. The spectrum of a solid sample was examined as a film between sodium chloride plates. Mass spectra were recorded with Perkin-Elmer model 990 Chromatograph while NMR spectra were obtained with Varian T 60 Spectrometer. The pyrolytic apparatus consisted of nitrogen cylinder, a gas flow-meter containing dibutyl-phthalate as the manometric fluid to measure the flow rate of nitrogen, a preheater made of pyrex glass tube maintained a temperature above the boiling point of the substrate and a horizontal carbolite furnace maintaining a constant temperature of 550°. A reaction tube was inserted into this furnace. The volatile reaction products were then cooled by ice and cardice in the cooling traps.

The pyrolysate from the reaction tube and the cooling traps was treated with 10% hydrochloric acid followed by neutralization with 30% sodium hydroxide. The alkaline solution was extracted with chloroform, and then the solvent removed.

1-Methylindazole was prepared as described in the literature [8].

1-Reaction of carbon tetrachloride with 3-methylpyrazole. A solution of 3-methylpyrazole (8.0 g) in carbon tetrachloride (53.0 cm^3) was pyrolysed [1-2] and the reaction mixture of product was carefully collected. The basic components of pyrolysate were analysed by GLC with Carbowax 20M as the stationary phase at 185°. The components were isolated by preparative GLC; NMR and mass spectra were obtained for each component. The spectral data and the comparison of the retention distances with those of the respective authentic samples of each component showed the following reaction products:-

(1) 4-Methylpyrimidine; (2) 2-Chloro-4-methylpyrimidine; (3) 3-Methylpyrazole.

Spectral data of 4-methylpyrimidine. I.R. [7] (Liquid film) υmax 675m (possibly C-H vib), 1600m (C=C and C=N str. vib), 3050W (C-H stgr. vib) cm^{-1}., N.M.R. ($CDCL_3$) 9.10 (2-H), 2.55m (3H, mCH3), 7.17d (5-H), 8.39d (6-H), MS M/z 94 (100), 93 (6), 79 (8), 67 (18), 66 (6), 53 (25), 52 (9), 40 (15), 39 (9), 26 (9).

Spectral data of 2-chloro-4-methylpyrimidine. Colourless solid, m.p., 47-48° I.R. [7] υmax (KBR) 720. s.sh (possibly C-H or C-C1 vib), 1575s (possibly C=C and C=N str)/ cm^{-1} NMR δ ($CDC1_3$) 2.52s (intensity = 3 protons) CH_3 groups), 7.10 d (5-H), 8.41 (6-H), MS m/z 130 (33), 33, 129 (7) 128 (100), 93 (27), 92 (35), 87 (11), 66 (18), 65

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(12), 40 (22).

2-Reaction of carbon tetrachloride with 3, 5-dimethylpyrazole. A solution of 3, 5-dimethylpyrazole (6.0 g) in carbon tetrachloride (40.0 cm^3) was pyrolysed and the reaction mixture of products was carefully collected. The components were isolated by preparative GLC; IR, NMR, and mass spectra were obtained for each component. The spectral data and the comparison of retention distances with those of the respective authentic samples of each component showed the following reaction products:-

(1). 4, 6-Dimethylpyrimidine; (2) 2-Chloro-4, 6-dimethylpyrimidine; (3). 2, 5-Dichloro-4, 6-dimethylpyrimidine.

Spectral data of 4, 6-dimethylpyrimidine. Colourless liquid, b.p. 154°; I.R. liquid film [10] υmax 1050m (possibly ring vib) 1600vs (C-C and C-N str/.vib), 3000m (possibly C-H str. vib), CM^{-1}, NMR δ ($CDC1_3$), 2.5 s (intensity = 6 protons) 4-CH_3 and 6-CH_3 groups, 9.0s (2-H), 7.1s (5-H); MS m/z, 108 (100), 107 (19), 81 (16), 80 (14), 66 (11), 42 (45), 41 (11), 40 (33), 39 (38), 28 (42).

Spectral data of 2-chloro-4, 6-dimethylpyrimidine. M.P. 38.5-40°, IR (KBr) [7] υmax (possibly C-H and C-Cl vib), 1590vs (C-C and C-N str. vib) 2950 m (possibly C-H str. vib of CH_3 group) cm^{-1}., N.M.R. δ ($CDC1_3$) 2.52 s (intensity = 6 protons) 4-Ch_3 and 6-CH_3 groups, 7.00s (5-H)., MS m/z 144 M+2 (33), 143 (5), 142 (100), 107 (29), 106 (16), 105 (9), 80 (8), 66 (46), 41 (13), 39 (11), 38 (39).

This component contains one chlorine atom as indicated by M+2.

Spectral data of 2, 5-dichloro-4, 6-dimethylpyrimidine. Colourless solid, m.p. 62-63°, I.R. (KBr) [7] υmax 840m (C-Cl or C-H vib), 1600m (aromatic ring), 3400-3500s, cm^{-1}, MS m/z 180 (12), 178 (75), 176 (100), 141 (80), 106 (40), 79 (45), 52 (58), 39 (80).

3-Reaction of carbon tetrachloride with 1-methylindazole. A solution of 1-methylindazole (8.0 g) in carbon tetrachloride (33.cm^3) was pyrolysed and the reaction mixture of the products was carefully collected. The basic components of pyrolysate were analysed by GLC with OV-17 as the stationary phase at 170°. The components were isolated by preparative GLC; IR, NMR, and mass spectra were obtained for each component. The spectral data and the comparison of retention distances with those of the respective authentic samples of each component showed the following reactions products:-

(1) 1-Methylindazole. (2) Quinazoline, (3) 2-Chloroquinazoline.

Spectral data of quinazoline. M.P., 46-48°, IR liquid film [11] υmax 752vs, 1071s, 148 vs (quinoline band), 1620 vs, 3064 (C-H str. vib) cm^{-1} NMR δ (CCl_4) 9.41s (2-H) 9.71s (4-H), 8.66m (5-H) 7.9 t (6-H), 9.14m complex intensity = 2 protons (3-H and 8-H) MS m/z 131 (8), 130 (100), 129 (12), 104 (6), 103 (58), 102 (8), 76 (38), 75 (12).

Spectral data of 2-chloroquinazoline. IR [12] (KBr) υmax 795s, 1620s, 3500s, cm^{-1}., N.M.R. δ ($CDCl_3$) 9.72s (4-H), 8.0m complex intensity = 4 protons (5-H, 6-H, 7-H and 8-H): MS m/z 165 (11), 164 (100), 139 (6), 137 (19), 129 (52), 102 (22), 77 (24), 76 (10, 50 (19) M+2.

This contains one chlorine atom as indicated by M+2 (M=parent peak).

DISCUSSION

Reaction of 3-methylpyrazole. A solution of 3-methylpyrazole in carbon tetrachloride on pyrolysis at 550° yielded:- (i) 4-methylpyrimidine (37.5%) and (ii) 2-chloro-4- methylpyrimidine (62.5%) unlike the reaction of 3-methylpyrazone in chloroform which gave only 2-chloro-4-methylpyrimidine under identical conditions. Increase in the percentage of unchlororinated products from N-substituted pyrazole, compared with C-substituted pyrazoles was observed. (63% pyrimidine from 1-methylpyrozole and 37.5% 4-methylpyrimidine from 3-methylpyrazole). This was attributed to the consequence of higher acidity of *N*-methyl group compared with C-methyl group.

Reaction of 3, 5-dimethylpyrazole. The pyrolysis of 3, 5-dimethylpyrazole in carbon tetrachloride yielded a mixture of ring expansion products:-

(i) 4, 6-dimethylpyrimidine (20%); (ii) 2-chloro-4, 6-dimethylpyrimidine (65%) and (iii) 2, 5-dichloro-4, 6-dimethylpyrimidine (15%).

The aim of the study of the reaction of 3, 5- dimethylpyrazole was to investigate the effect of increasing the number of electron-donating methyl groups on the nature of products and the overall yield. As expected, an increase in yield of the reaction products (75%) was observed indicating that the molecule became more active towards electrophilic attack due to the presence of two methyl groups.

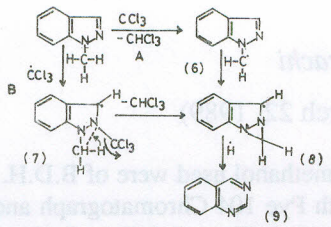
The reaction products of 3, 5-dimethylpyrazole with carbon tetrachloride differed markedly from those obtained in the reaction of 3, 5-dimethylpyrazole [7] and chloroform in that the former yielded, 4, 6-dimethylpyrimidine, 2-chlolro-4, 6-dimethylpyrimidine and 2, 5-dichloro-4, 6-dimethylpyrimidine while the later gave only 2-chloro-4, 6-dimethylpyrimidine. Results are different because in the case of CCl_4, chlorine radical is generated while in case of $CHCl_3$ hydrogen radical is produced and the effects naturally should be different.

Reaction of 1-methylindazole. After studying the nature of reaction of alkyl substituted pyrazoles, it was thought worthwhile to determine the effect of benzene ring on the type of the reaction products. A decrease was observed in the overall yield possibly due to the presence of benzene ring.

1-Methylindazole in carbon tetrachloride, on pyrolysis at 550°, gave a mixture of (i) quinazoline (57.6%) and (ii), 2-chloroquinazoline (42.3%). The pyrolysis of indazole [7] in chloroform at 550° gave only 2-chloroquinazoline. The

mechanism for the formation of these ring expansion products may be explained by a mechanism as suggested for the formation of pyrimidines and 2-chloropyrimidines from pyrazoles [2].

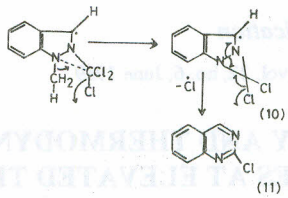
Quinazoline



It is possible that the trichloromethyl radical attacks the methyl group by abstracting a hydrogen atom from it and so forms the radical (6), which rearranges to the tricyclic system (8) and this is, in turn, converted into quinazoline (9) by the loss of a hydrogen atom. The relatively easy loss of hydrogen radical [9] is common under the high temperature conditions of the reaction.

It is also possible that the trichloromethyl radical attacks at the 2-position of the indazole ring to produce the radical (7), which rearranges to the tricyclic system (8). The tricyclic system is transformed into quinazoline (9) by the loss of a hydrogen radical.

2-Chloroquinazoline. The mechanism for the formation of 2-chloroquinazoline is explained as under:-



The formation of the reaction products obtained by the pyrolysis of 3-methylpyrazole, 3, 5-dimethylpyrazole can be explained by the mechanism similar to that given for the formation of corresponding products from 1-methylindazole.

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