REACTIONS OF DIBROMOCARBENE GENERATED FROM BROMOFORM WITH VINYLPYRIDINES UNDER PHASE TRANSFER CATALYSIS CONDITIONS

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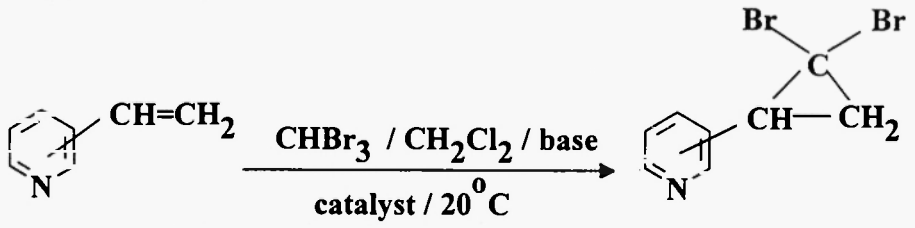
Abstract : Phase transfer catalytic reactions of 2-vinylpyridine (**1**) with dibromocarbene generated from bromoform in the system liquid / liquid and liquid / solid were studied. The PTC system 50% aq. KOH / TEBA / CH_2Cl_2 was found to be most active and was used for preparative synthesis of vinylpyridine dibromocarbene adducts (**4 - 6**).

Introduction

The reactions of dihalocarbenes generated from haloform under phase transfer catalysis (PTC) conditions are widely applied in organic synthesis [1]. Among these carbenes dichlorocarbene was studied most intensively. Dibromocarbene adducts [2] are less studied but they are more advantageous than their chlorine analogues because it is much more easier to modify them in subsequent reactions. In general the PTC chemistry of dibromocarbene is very similar to that of dichlorocarbene, but PTC reactions of dibromocarbene with vinylpyridines are not investigated.

Results and discussion

We studied the phase transfer catalyzed reactions of 2-vinylpyridine (**1**) with dibromocarbene generated from bromoform in the phase transfer catalytic systems liquid / liquid and liquid / solid.



1 - 3 **4 - 6**

It was found that PTC system 50% aq. KOH / triethylbenzylammonium bromide (TEBA) / CH_2Cl_2 was the most active (see Table I). In this PTC system the corresponding 2-(2,2-dibromocyclopropyl)pyridine was obtained in 48% yield. PTC systems 50% KOH / Me_4NBr / CH_2Cl_2 and 50% KOH / Oct_4NBr / CH_2Cl_2 were considerably less active in the dibromocyclopropanation reaction of 2-vinylpyridine. The systems solid K_2CO_3 / 18-crown-6 / CH_2Cl_2 and 50% aq. KOH / $BuNH_2$ / CH_2Cl_2 were inactive in the synthesis of **4** from 2-vinylpyridine (**1**).

The PTC system 50% aq. KOH / TEBA / CH_2Cl_2 as the most active was used in the preparative synthesis of vinylpyridine dibromocarbene adducts **4** - 6 (see **Experimental**). All obtained products **4** - **6** were very unstable in the contact with air and were isolated as hydrochlorides.

Table I Dibromocyclopropanation of 2-vinylpyridine (**1**) under phase transfer catalysis conditions at room temperature

N°	Base	Catalyst	Reaction time, h	Yield of IV, %[a]
1	solid KOH	18-crown-6	4	18
2	solid K_2CO_3	18-crown-6	11	3
3	50% aq. KOH	$BuNH_2$	11	4
4	50% aq. KOH	Me_4NBr	13	25
5	50% aq. KOH	Et_3BnNBr	15	48
6	50% aq. KOH	Oct_4NBr	15	33

[a] GLC control

Conclusion

Thus, simple PTC method for the preparation of 2,2-dibromocyclopropylpyridine was developed and products were isolated in 29 - 37% yield.

Experimental

^{1}H NMR spectra were recorded on a Bruker WH - 90/DS (90 MHz) instrument using DMSO-d_6 as solvent and Me_4Si as internal standard. Mass spectra were registered on a MS-25 spectrometer (Kratos, 70 eV). GC analysis was performed on a Chrom - 5 instrument equipped with a flame-ionization detector using glass column packed with 5% OV-101 / Chromosorb W-HP (80 - 100 mesh) (1.2 m x 3 mm). 2-, 3- and 4-Vinylpyridines and 18-crown-6 were Fluka products. Vinylpyridines were purified by distillation *in vacuo* prior the use.

General procedure for dibromocyclopropanation of 2-vinylpyridine (1) under PTC conditions on semi-micro scale. 2-Vinylpyridine (0.216ml, 2 mmol), base (solid KOH or K_2CO_3 (16 mmol) or 50% aq. KOH (1 ml); see Table I), catalyst (0.1 mmol) and bromoform (0.53 ml, 6 mmol) in dichloromethane (0.5 ml) were placed in a Pierce reacti-vial (5 ml). The reaction mixture was stirred at room temperature with GLC control. The results are shown in Table I.

General procedure for the synthesis of 2,2-dibromocyclopropylpyridines 4 - 6. 2-(2,2-Dibromocyclopropyl)pyridine hydrochloride (4·HCl). To a solution of 2-vinylpyridine (4.32 ml, 40 mmol), bromoform (10.6 ml, 0.16 mol), TEBA (0.45 g, 2 mmol) in dichloromethane (10 ml) was added 50% aq. KOH (10 ml). The mixture was stirred 15 h at room temperature (GLC control), organic layer separated and filtered over Al_2O_3. Product **4** was isolated as hydrochloride by extraction with 5% aq. HCl solution (30 ml) and evaporation of water phase. Yield of **4**·HCl (yellow-brown oil) was 3.66 g (29%). ^{1}H NMR , δ ppm: 1.18 (m, 3H, $CHCH_2$), 7,69 (m,1H, H-5), 8.20 (m, 1H, H-3), 8.40 (m, 1H, H-4), 8.71 (m, 1H, H-6). Mass-spectra of 4, m/z (rel. abundance): 277 (M^+, 37), 196 (100), 117 (84), 90 (40), 63 (42), 50 (14), 39 (12).

Compounds **5, 6** were prepared similarly.

3-(2,2-Dibromocyclopropyl)pyridine hydrochloride (5·HCl). Obtained from 3-vinylpyridine. Reaction time 15 h. ^{1}H NMR , δ ppm: 1.29 (m, 3H, $CHCH_2$), 7.82 (m, 1H, H-5), 8.18 (m, 1H, H-4), 8.40 (m, 1H, H-6), 8.67 (m, 1H, H-2). Mass-spectra of **5**, m/z (rel. abundance): 277(M^+, 32), 196 (100), 117 (81), 90 (41), 63 (45), 51 (16), 38 (14). Yield 37%.

4-(2,2-Dibromocyclopropyl)pyridine hydrochloride (6·HCl). Obtained from 4-vinylpyridine. Reaction time 12 h. ^{1}H NMR: δ ppm : 1.22 (m, 3H, $CHCH_2$), 8.13 (m, 2H, H-3 and H-5), 8.82 (m, 2H,H-2 and H-6). Mass-spectra of **6**, m/z (rel. abundance): 277(M^+, 6), 196 (7), 117 (100), 89 (22), 63 (18), 51 (14), 39 (10). Yield 30%.

References

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