Mild and Selective Phase Transfer Catalysed Bromination of Terminal Acetylenes Using Carbon Tetrabromide as Reagent†

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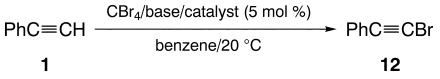
Terminal acetylenes were successfully brominated under phase transfer conditions using a CBr_4/solid KOH/18-crown-6/benzene system.

Brominated terminal acetylenes are of interest as potential biologically active substances or intermediates. Usually this type of organic compound is obtained from terminal acetylenes by bromination in Bu^nLi/*N*-bromosuccinimide,[1] Bu^nLi/Br_2,[2] $NaOH/Br_2$[3] and DBU/Cl_3CBr[4] systems as well as by treating with hypobromite solution.[5–7] It is also known that phenylacetylene is successfully chlorinated in the carbon tetrachloride/50% aq. NaOH/TEBA PTC system.[8]



Scheme 1

We have developed a new, simple and selective PTC bromination method for a variety of terminal acetylenes. The influence of catalyst, base and amounts of brominating agent (CBr_4) was studied in the bromination reaction of phenylacetylene (**1**). Surprisingly, the PTC system CBr_4 (0.75 equiv. to phenylacetylene)/solid KOH/18-crown-6 in benzene was found to be the most active (Table 1). In the presence of this system phenylbromoacetylene was obtained in 79% yield. Increase in the amount of carbon tetrabromide to $\geqslant$1 equiv. diminishes the desired product (**12**) yield owing to brominated product side reactions. The PTC systems solid CBr_4/KF/18-crown-6 and CBr_4/50% KOH/triethylbenzylammonium chloride (TEBAC) were less active in bromination of **1**. Interestingly, bromination of phenylacetylene also proceeds in the presence of the PTC system bromoform (1 equiv.)/solid KOH/18-crown-6 and product **12** was obtained in 6% yield. This suggests that as well as carbon tetrabromide, bromoform can also serve as a source of Br^+ ion. The PTC system CBr_4/solid K_2CO_3/18-crown-6 was inactive in phenylacetylene bromination.

Table 1 PTC bromination of phenylacetylene[a]

Base (equiv.)	Catalyst	CBr_4 (equiv.)	Reaction time/h	Yield (%) (GLC data)
KOH (3)	18-crown-6	0.5	13	58
KOH (3)	18-crown-6	0.75	11	79
KOH (3)	18-crown-6	1.0	11	67
KOH (2)	18-crown-6	1.5	8	42
KOH (3)	18-crown-6	1.5	8	36
K_2CO_3 (3)	18-crown-6	1.0	9	0
KF (3)	18-crown-6	1.0	9	22
50% KOH (4 ml)	TEBAC	1.5	8	41
KOH (3)	18-crown-6	1.0[b]	11	6

[a]Reaction conditions: phenylacetylene (0.11 ml, 1 mmol), catalyst (0.05 mmol), base and brominating agent (see table) in benzene (1 ml), 20 °C. [b]$CHBr_3$ as a bromination agent.

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Table 2 PTC bromination of terminal acetylenes **2–11** with carbon tetrabromide in the system solid KOH/18-crown-6/benzene at room temperature

R	Reaction time/h	Product	Isolated yield (%)	Mp/°C
2	2	13	37	—[a]
3	2.5	14	53	—[a]
4	1	15	16	—[a]
5	4	16	66	—[a]
6	7	17	60	—[a]
7	12	18	42	123–126
8	4	19	59	107–110
9	4	20	64	61–63
10	4	21	42	129–131
11	2	22	84	—[a]

[a]Oil, boiling point was not determined.

The PTC system carbon tetrabromide (0.75 equiv.)/solid KOH/18-crown-6/benzene being the most active was then used in bromination of terminal acetylenes of different types.

All reactions proceed selectively and afford the corresponding bromoacetylenes **13–22** in 16–84% yield (Table 2, Scheme 2). Double bond bromination in compounds **8–11** as well as formation of addition products of dibromocarbene generated from $CHBr_3$ or CBr_4 to C=N double and C≡C triple bonds was not observed. Bromination of *E*-ketoxime and aldoxime *O*-propargyl ethers **8–11** proceeds stereoselectively giving only *E*-isomers of brominated products **19–22** (Table 2). PTC bromination of terminal acetylenes **2–11** with carbon tetrabromide in the system solid KOH/18-crown-6/benzene takes place at room temperature.

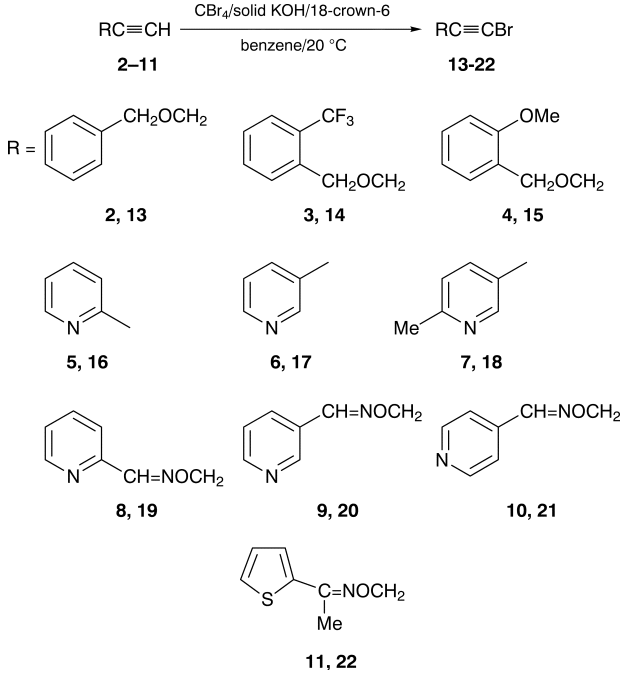
Experimental

^{1}H NMR spectra were recorded with a Bruker WH-90/DS (90 MHz) spectrometer using $CDCl_3$ as solvent and Me_4Si as internal standard. Mass spectra were recorded on a MS-25 spectrometer (Kratos, 70 eV). GC analysis was performed on a Chrom-5 instrument equipped with a flame-ionization detector using a glass column packed with 5% OV-101/Chromosorb W-HP (80–100 mesh), 1.2 m × 3 mm.

Typical Procedure. Synthesis of **13**.—Finely powdered KOH (0.336 g, 6 mmol) was added to a solution of **2** (0.29 g, 2 mmol), CBr_4 (0.498 g, 1.5 mmol) and 18-crown-6 (26 mg, 0.1 mmol) in 2 ml of benzene. The reaction mixture was stirred for 2 h at room temperature until the substrates disappeared (GC and GC–MS). The solid substance was filtered off and the filtrate evaporated under reduced pressure. The residue was purified by column chromatography using light petroleum (bp 45–60 °C)–benzene (2:1) as eluent. Isolated yield was 0.164 g (37%).

^{1}H NMR ($CDCl_3$, 90 MHz) and MS Data for Isolated Compounds.—**13**. ^{1}H NMR: δ 4.11 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 7.27 (m, 5H, Ph). MS: *m/z* 225 (M^+, 1), 119 (12), 117 (36), 116 (22), 115 (100), 105 (14), 92 (14), 91 (60), 89 (10), 79 (26), 77 (38), 65 (19), 51 (21), 50 (10), 39 (23), 38 (11).

14. ^{1}H NMR: δ 4.22 (s, 2H, OCH_2), 4.74 (s, 2H, CH_2), 7.11–7.69 (m, 4H, Ph). MS: *m/z* 293 (M^+, $<$1), 193 (12), 185 (31), 184 (20),



Scheme 2

183 (75), 173 (19), 165 (17), 164 (12), 160 (14), 159 (100), 158 (17), 155 (16), (32), 137 (11), 133 (12), 127 (77), 125 (10), 120 (16), 119 (52) 118 (18), 117 (39), 109 (54), 107 (12), 95 (10), 91 (22), 89 (13), 77 (12), 75 (16), 63 (12), 55 (12), 51 (15), 50 (12), 49 (49), 37 (11).

15. ^{1}H NMR: δ 3.76 (s, 3H, OCH_3), 4.04 (s, 2H, OCH_2), 4.56 (s, 2H, CH_2), 6.71–7.36 (m, 4H, Ph). MS: m/z 255 (M^+, 2), 211 (68), 209 (67), 146 (10), 145 (54), 135 (13), 131 (11), 121 (30), 119 (20), 117 (27), 115 (35), 109 (13), 107 (17), 94 (15), 93 (10), 92 (20), 91 (100), 79 (10), 78 (42), 65 (28), 63 (15), 52 (11), 51 (22), 50 (11), 39 (26), 38 (15).

16. ^{1}H NMR: δ 7.16 (m, 1H, H-5), 7.34 (m, 1H, H-3), 7.61 (m, 1H, H-4), 8.49 (m, 1H, H-6). MS: m/z 181 (M^+, 100), 154 (11), 130 (25), 128 (23), 102 (95), 75 (48), 74 (37), 61 (10), 51 (31), 50 (30), 37 (14).

17. ^{1}H NMR: δ 7.16 (m, 1H, H-5), 7.27 (m, 1H, H-4), 7.48 (m, 1H, H-6), 8.49 (m, 1H, H-2). MS: m/z 181 (M^+, 100), 154 (10), 130 (20), 128 (27), 102 (90), 76 (40), 74 (33), 51 (23), 50 (19), 37 (12).

18. ^{1}H NMR: δ 2.54 (s, 3H, CH_3), 7.09 (m, 1H, H-3), 7.59 (m, 1H, H-4), 8.51 (m, 1H, H-6). MS: m/z 195 (M^+, 89), 130 (17), 128 (20), 116 (23), 89 (100), 74 (22), 63 (25), 62 (19), 50 (14), 40 (21), 39 (16).

19. ^{1}H NMR: δ 4.83 (s, 2H, OCH_2), 7.15–7.35 (m, 1H, H-5), 7.55–7.89 (m, 2H, H-3,4), 8.19 (s, 1H, CH), 8.54–8.67 (m, 1H, H-6). MS: m/z 239 (M^+, 10), 210 (30), 209 (10), 208 (30), 131 (12), 129 (44), 119 (32), 117 (34), 104 (10), 79 (19), 78 (100), 66 (16), 64 (12), 63 (16), 52 (20), 51 (44), 50 (15), 39 (14), 38 (25).

20. ^{1}H NMR: δ 4.76 (s, 2H, OCH_2), 7.13–7.36 (m, 1H, H-5), 7.91 (dt, 1H, $J_1 = 7.6$, $J_2 = 1.6$ Hz, H-4), 8.07 (s, 1H, CH), 8.54 (dd, 1H, $J_1 = 6.0$, $J_2 = 1.6$ Hz, H-6), 8.67 (d, 1H, $J = 2.0$ Hz, H-2). MS: m/z 239 (M^+, 46), 238 (12), 237 (48), 159 (13), 131 (27), 130 (11), 129 (72), 119 (92), 117 (100), 106 (11), 105 (20), 104 (27), 103 (12), 91 (15), 79 (12), 78 (69), 77 (17), 76 (12), 66 (23), 64 (36), 63 (49), 52 (27), 51 (74), 50 (35), 39 (23), 38 (48), 37 (16).

21. ^{1}H NMR: δ 4.76 (s, 2H, OCH_2), 7.38 (dd, 2H, $J_1 = 6.2$, $J_2 = 2.0$ Hz, H-3,5), 7.97 (s, 1H, CH), 8.56 (dd, 2H, $J_1 = 6.2$, $J_2 = 2.0$ Hz, H-2,6). MS: m/z 239 (M^+, 13), 237 (13), 131 (30), 130 (15), 129 (100), 119 (84), 117 (90), 105 (16), 104 (21), 78 (44), 77 (12), 66 (15), 64 (18), 63 (29), 52 (14), 51 (66), 50 (33), 39 (26), 38 (29), 37 (12).

22. ^{1}H NMR: δ 2.20 (s, 3H, CH_3), 4.67 (s, 2H, CH_2), 6.87 (m, 1H, H-4), 7.11 (m, 1H, H-3), 7.20 (m, 1H, H-5). MS: m/z 259 (M^+, 15), 148 (49), 110 (82), 109 (66), 99 (100), 84 (21), 66 (27), 57 (13), 39 (36).

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