Chemistry of Heterocyclic Compounds, Vol.35, No. 4, 1999

ALKYLATION OF HETARYL METHYL KETONES BY PROPARGYL BROMIDE UNDER PHASE-TRANSFER CATALYSIS CONDITIONS*

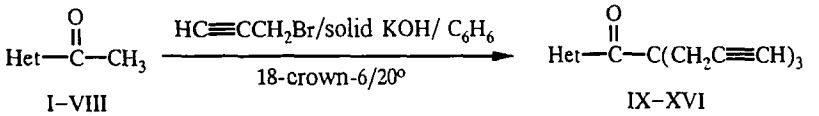
E. Abele, R. Abele, Yu. Popelis, I. Mazheika, and E. Lukevics

The alkylation of aryl and hetaryl methyl ketones by propargyl bromide using the phase-transfer catalysis system KOH (s)/18-crown-6/benzene is studied. The corresponding C-trialkylated products are selectively obtained in 34-78% yields.

Terminal acetylenes, diynes, and polyynes are widely used both as reagents in organic synthesis and in the synthesis of macromolecular compounds [1, 2]. The synthesis of sterically hindered aryl and hetaryl ketones containing three propargyl groups has not previously been studied and is the focus of the present article.

The use of phase-transfer catalysis (PTC) procedure enables the alkylation of ketonic carbanions that are generated by reaction of alkali hydroxides with the acidic C–H bonds [3]. The preparation of sterically hindered ketones by PTC alkylation of acetophenone [4], α-acetylnaphthalene [5], 2-acetylfuran and 2-acetylthiophene [6], 3-acetylthiophene [7], 2-acetylpyrrole [8], and acetylpyridines [9] has recently been described. However, PTC alkylation of aryl and hetaryl ketones by propargyl bromide has not previously been studied.

We developed a new method for synthesis of 1-hetaryl-2,2,2-tripropargylethanones (IX-XVI) by PTC alkylation of the corresponding methyl ketones I-VIII in the propargyl bromide/KOH (s)/18-crown-6/benzene system at room temperature. Under these conditions, the C-tripropargylated products (IX-XVI) are selectively obtained in 34-78% yields.



I–VIII IX–XVI

I and IX, Het = Ph; X, Het = 2-furyl; III and XI, Het = 2-furyl-5-methyl; IV and XII, Het = 2-thienyl; V and XIII, Het = 5-methyl-2-thienyl; VI and XIV, Het = 2-pyridyl; VII and XV, Het = 3-pyridyl; VIII and XVI, Het = 4-pyridyl

According to GLC and mass spectra, formation of the C-tripropargylated products proceeds through the C-monopropargylated and C-dipropargylated ketone intermediates, which completely disappear from the reaction mixtures upon completion of the reaction. Alkylation of the enol form of the ketone to give O-propargyl derivatives was not observed under these conditions.

* Dedicated to Professor Henk van der Plas on his 70th birthday.

Latvian Institute of Organic Synthesis, Riga LV-1006, e-mail: kira@osi.lanet.lv. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 495-497, April, 1999. Original article submitted October 7, 1998.

 0009-3122/99/3504-0436$22.00

EXPERIMENTAL

PMR spectra were recorded on a Bruker WH-90/DS spectrometer in $CDCl_3$ with TMS as internal standard. Mass spectra were obtained with a Hewlett-Packard HP-6890 instrument. GLC analysis was performed on a Chrom-5 chromatograph with a flame-ionization detector and a glass column filled with 5% OV-101 on chromosorb W-HP (80-100 mesh) at 150-210°C. 18-Crown-6, acetophenone (I), 2-acetylfuran (II), 2-acetylthiophene (IV), and acetylpyridine (Fluka) were used without further purification. 2-Acetyl-5-methylfuran (III) and 2-acetyl-5-methylthiophene (V) were prepared from 2-methylfuran and 2-methylthiophene, respectively, by Friedel–Krafts reaction [10]. Elemental analysis of the pyridine-containing ketones' XIV-XVI was not performed owing to the instability of these compounds. They were characterized by mass spectrometry and PMR spectroscopy.

General Method for Alkylation of Aryl and Hetaryl Methyl Ketones (I-VIII) by Propargyl Bromide. 4-Benzoyl-4-propargyl-1,6-heptadiyne (IX). Propargyl bromide (11.26 ml, 150 mmol) was added dropwise to mixture of acetophenone I (3.51 ml, 30 mmol), 18-crown-6 (0.40 g, 1.5 mmol), powdered KOH (8.40 g, 0.15 mol) and benzene (15 ml) over 0.5 h. The mixture was stirred for 6 h at room temperature and filtered through Al_2O_3. The filtrate was concentrated (rotary evaporator) and the residue was purified by column chromatography (eluent benzene). Yield 3.57 g (51%). PMR spectrum: 1.93 (3H, t, J = 2.6 Hz, CH), 2.64 (6H, d, J = 2.6 Hz, CH_2), 7.1-7.6 ppm (5H, m, Ph). Mass spectrum, *m/z* (I_{rel}, %): 234 (1, M^+), 195 (6), 105 (100), 77 (49), 51 (18), 39 (11). Found, %: C 85.75; H 6.13. $C_{17}H_{14}O$. Calculated, %: C 87.15, H 6.02.

1-(2-Furyl)-2,2,2-tripropargylethanone (X) was prepared by reaction of 2-acetylfuran with propargyl bromide for 6 h as described for IX. PMR spectrum: 1.95 (3H, t, J = 2.6 Hz, CH), 2.89 (6H, d, J = 2.6 Hz, CH_2), 6.47 (1H, m, 4-H), 7.22 (1H, m, 3-H), 7.44 ppm (1H, m, 5-H). Mass spectrum, *m/z* (I_{rel}, %): 224 (<1, M^+), 217 (12), 185 (22), 157 (28), 95 (100), 77 (13), 63 (19), 51 (15), 39 (58). Found, %: C 80.29; H 5.56. $C_{15}H_{12}O_2$. Calculated, %: C 80.33; H 5.39. Yield 63%.

1-(5-Methyl-2-furyl)-2,2,2-tripropargylethanone (XI) was prepared by reaction of 2-acetyl-5-methylfuran with propargyl bromide for 8 h as described for IX. PMR spectrum: 1.96 (3H, t, J = 2.6 Hz, CH), 2.39 (3H, s, CH_3), 2.92 (6H, d, J = 2.6 Hz, CH_2), 6.12 (1H, m, 4-H), 7.16 ppm (1H, m, 3-H). Mass spectrum, *m/z* (I_{rel}, %): 237 (1, M^+ - 1), 199 (32), 171 (30), 152 (13), 128 (27), 109 (100), 89 (10), 77 (12), 63 (14), 53 (52), 43 (30). Found, %: C 79.63; H 6.05. $C_{16}H_{14}O_2$. Calculated, %: C 80.65; H 5.92. Yield 65%.

2,2,2-Tripropargyl-1-(2-thienyl)ethanone (XII) was prepared by reaction of 2-acetylthiophene with propargyl bromide for 10 h as described for IX. PMR spectrum: 2.18 (3H, t, J = 2.6 Hz, CH), 2.89 (6H, d, J = 2.6 Hz, CH_2), 7.04 (1H, dd, J_{45} = 4.8 Hz, J_{34} = 3.8 Hz, 4-H), 7.56 (1H, dd, J_{45} = 4.8 Hz, J_{35} = 1.4 Hz, 5-H), 7.71 ppm (1H, dd, J_{34} = 3.8 Hz, J_{35} = 1.4 Hz, 3-H). Mass spectrum, *m/z* (I_{rel}, %): 240 (<1, M^+), 201 (12), 173 (12), 111 (100), 83 (11), 63 (10), 39 (39). Found, %: C 73.87; H 5.03. $C_{15}H_{12}OS$. Calculated, %: C 74.96; H 5.03. Yield 70%.

1-(5-Methyl-2-thienyl)-2,2,2-tripropargylethanone (XIII) was prepared by reaction 2-acetyl-5-methylthiophene with propargyl bromide for 10 h as described for IX. PMR spectrum: 1.93 (3H, t, J = 2.6 Hz, CH), 2.42 (3H, s, CH_3), 2.84 (6H, d, J = 2.6 Hz, CH_2), 6.73 (1H, m, 4-H), 7.56 ppm (1H, m, 3-H). Mass spectrum, *m/z* (I_{rel}, %): 254 (<1, M^+), 215 (16), 187 (14), 125 (100), 97 (11), 63 (10), 53 (36), 39 (19). Found, %: C 74.54; H 5.48. $C_{16}H_{14}OS$. Calculated, %: C 75.55; H 5.54. Yield 78%.

2,2,2-Tripropargyl-1-(2-pyridyl)ethanone (XIV) was prepared by reaction of 2-acetylpyridine with propargyl bromide for 4 h as described for IX. PMR spectrum: 1.87 (3H, t, J = 2.6 Hz, CH), 3.15 (6H, d, J = 2.6 Hz, CH_2), 7.29 (1H, m, 5-H), 7.49 (1H, m, 3-H), 7.84 (1H, m, 4-H), 8.51 ppm (1H, m, 6-H). Mass spectrum, *m/z* (I_{rel}, %): 235 (<1, M^+), 206 (10), 196 (94), 168 (42), 157 (14), 128 (10), 107 (21), 89 (12), 78 (100), 63 (27), 51 (44), 39 (32). Yield 34%.

2,2,2-Tripropargyl-1-(3-pyridyl)ethanone (XV) was prepared by reaction of 3-acetylpyridine with propargyl bromide for 12 h as described for IX. PMR spectrum: 2.00 (3H, t, J = 2.6 Hz, CH), 2.73 (6H, d, J = 2.6 Hz, CH_2), 7.27 (1H, m, 5-H), 7.84 (1H, m, 4-H), 8.62 (1H, m, 6-H), 8.80 ppm (1H, m, 2-H). Mass spectrum, *m/z* (I_{rel}, %): 235 (<1, M^+), 196 (24), 167 (10), 128 (10), 106 (100), 78 (73), 63 (16), 51 (46), 39 (21). Yield 43%.

2,2,2-Tripropargyl-1-(4-pyridyl)ethanone (XVI) was prepared by reaction of 4-acetylpyridine with propargyl bromide for 5 h as described for IX. PMR spectrum: 2.04 (6H, t, J = 2.6 Hz, CH), 2.67 (6H, d, J = 2.6 Hz, CH_2), 7.33 (2H, m, 3-H and 4-H), 8.62 ppm (2H, m, 2H and 6H). Mass spectrum m/z (I_{rel}, %): 235 (2, M^+), 196 (41), 167 (19), 128 (26), 106 (100), 78 (92), 63 (23), 51 (78), 59 (10). Yield 46%.

REFERENCES

1. W. D. Huntsman, *The Chemistry of the Carbon–Carbon Triple Bond*, S. Patai (ed.), Wiley Interscience, London (1978).
2. S. I. Miller and J. I. Dickstein, *Acc. Chem. Res.*, **9**, 358 (1976).
3. E. V. Dehmlow and S. S. Dehmlow, *Phase Transfer Catalysis*, Third, Revised and Enlarged Edition, VCH Publ., Inc., New York (1993), p. 166.
4. M. Lissel, B. Neumann, and S. Schmidt, *Liebigs Ann. Chem.*, No. 3, 263 (1987).
5. E. M. Abele, R. N. Abele, Yu. Yu. Popelis, A. P. Gaukhman, and E. Lukevics, *Zh. Org. Khim.*, **34**, 1391 (1998).
6. E. M. Abele, Yu. Sh. Goldberg, Yu. Yu. Popelis, and M. V. Shymanska, *Zh. Org. Khim.*, **26**, 1784 (1990).
7. Yu. Goldberg, E. Abele, and M. Shymanska, *Synth. Commun.*, **20**, 2741 (1990).
8. Yu. Goldberg, E. Abele, and M. Shymanska, *Synth. Commun.*, **21**, 557 (1991).
9. K. Rubina, Yu. Goldberg, and M. Shymanska, *Synth. Commun.* **19**, 2489 (1989).
10. *Organic Synthesis*, John Wiley & Sons, New York (1932), Vol. 12, p. 62.