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TRIMETHYLSILYLCYANATION OF HETEROAROMATIC KETONES IN THE CsF/18-CROWN-6/BENZENE PHASE-TRANSFER CATALYTIC SYSTEM

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

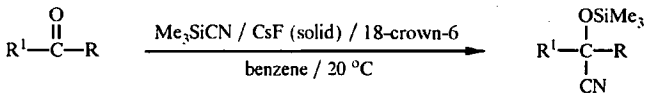
The trimethylsilylcyanation of heteroaromatic ketones in the Me_3SiCN/CsF/18-crown-6/benzene phase-transfer catalytic system has been studied. The reaction products have been isolated selectively in yields of up to 95%.

Cyanohydrins are widely used as intermediates in organic synthesis [1]. One of the most widely used methods for the synthesis of these compounds is the addition of trimethylcyanosilane to aldehydes and ketones. The catalysts commonly used in this reaction are $ZnCl_2$, KCN/18-crown-6 [2], AgCN [3], montmorillonites [4, 5], HgI_2 [6], $AlCl_3$ [7], trimethylsilylbis(fluorosulfonyl)imide [8], dialkyldichlorostannanes [9], and Bu_3SnCN [10].

It has recently been shown that it is possible to enantioselectively trimethylsilylcyanate carbonyl compounds in the presence of the chiral complexes salen-Ti(IV) [11-15], dialkyl tartrate-Ti(IV) [16], binaphthol-Ti(IV) [17], Pybox-$AlCl_3$ [18], diethyl tartrate-Bi(III) [19], bisoxazoline-Mg(II) [20], and phosphineoxide-$SmCl_3$ [21], and also 1,3-bis(2-methylferrocenyl)propan-1,3-dione [22] and lanthanide alkoxides [23]. The addition of trimethylcyanosilane to aldehydes in acetonitrile in the absence of a catalyst is also known [24]. However prolonged boiling of the reaction mixture is normally required in this case. The reaction of ketones with trimethylcyanosilane in effect does not occur in the absence of a catalyst [24].

We have developed a new, mild, and selective phase-transfer catalytic method for the trimethylsilylcyanation of heteroaromatic ketones, including sterically hindered examples.

Compounds I–XIII readily react with trimethylcyanosilane at room temperature in a medium of low polarity (benzene) in the presence of catalytic amounts of CsF (20 mol.%) and 18-crown-6 (10 mol.%). The high effectiveness of slightly polar media (benzene or dichloromethane) in phase-transfer catalysis systems with CsF/18-crown-6 has been observed in the hydrosilylation of ketones [25].



I–XIII XIV–XXVI

I, XIV R^1 = Ph, R = Me; II, XV R^1 = Ph, R = $CHMe_2$; III, XVI R^1 = Ph, R = $CHEt_2$; IV, XVII R^1 = 2-furyl, R = Me; V, XVIII R^1 = 2-furyl, R = $C(CH_2CH{=}CH_2)_3$; VI, XIX R^1 = 2-thienyl, R = Me; VII, XX R^1 = 2-thienyl, R = $CHMe_2$; VIII, XXI R^1 = 2-pyridyl, R = Me; IX, XXII R^1 = 2-pyridyl, R = Ph; X, XXIII R^1 = 3-pyridyl, R = Me; XI, XXIV R^1 = 3-pyridyl, R = Ph; XII, XXV R^1 = 4-pyridyl, R = Me; XIII, XXVI R^1 = 4-pyridyl, R = Ph

Latvian Institute of Organic Synthesis, Riga LV-1006, Latvia; e-mail: abele@osi.lanet.lv. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1073-1076, August 1999. Original article submitted February 8, 1999.

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TABLE 1. Trimethylsilylcyanation of Heteroaromatic Ketones I-XIII Catalyzed by CsF/18-Crown-6 in Benzene at Room Temperature

R^1	R	Reaction time, h	Reaction product	Yield, %	Ref.
Ph	Me	5	XIV	67	[26]
Ph	$CHMe_2$	4	XV	79	
Ph	$CHEt_2$	5	XVI	83	
2-Furyl	Me	5	XVII	74	
2-Furyl	$C(CH_2CH=CH_2)_3$	5	XVIII	88	
2-Thienyl	Me	6	XIX	71	[27]
2-Thienyl	$CHMe_2$	4	XX	89	
2-Pyridyl	Me	3	XXI	95	[28]
2-Pyridyl	Ph	3	XXII	92	
3-Pyridyl	Me	3	XXIII	91	
3-Pyridyl	Ph	4	XXIV	89	
4-Pyridyl	Me	3	XXV	82	
4-Pyridyl	Ph	4	XXVI	85	

The trimethylsilylcyanation products XIV–XXVI were isolated in 67-95% yields (Table 1). All the synthesized products were identified by ^{1}H NMR and mass spectroscopy (Tables 2 and 3).

Thus the phase-transfer catalysis method we have developed for the trimethylsilylcyanation of hetarylketones is mild, selective, and successful; reaction products were isolated in yields of up to 95%.

TABLE 2. ^{1}H NMR Spectral Data for Products XIV–XXVI

Compound	Chemical shift, ppm, and coupling constants (J), Hz
XIV	0.16 (9H, s, $SiMe_3$); 2.52 (3H, s, CH_3); 7.33 and 7.82 (5H, m and m, Ph)
XV	0.16 (9H, s, $SiMe_3$); 1.16 (6H, d, J = 7.0 Hz, CH_3); 3.49 (1H, m, CH) 7.42 and 7.91 (5H, m and m, Ph)
XVI	0.16 (9H, s, $SiMe_3$); 0.96 (6H, m, $CH(CH_2C\underline{H}_3)_2$); 1.38 (4H, m, $CH(C\underline{H}_2CH_3)_2$) 3.69 (1H, m, CH); 7.40 (5H, m, Ph)
XVII	0.13 (9H, s, $SiMe_3$); 2.52 (3H, s, CH_3); 6.58 (1H, m, 4-H); 7.25 (1H, m, 3-H) 7.65 (1H, m, 5-H)
XVIII	0.18 (9H, s, $SiMe_3$); 2.40 (6H, m, $C\underline{H}_2CH=CH_2$); 4.88 (6H, m, $CH_2CH=C\underline{H}_2$) 5.89 (3H, m, $CH_2C\underline{H}=CH_2$); 6.47 (1H, m, 4-H); 6.64 (1H, m, 3-H); 7.53 (1H, m, 5-H)
XIX	0.16 (9H, s, $SiMe_3$); 2.49 (3H, s, CH_3); 7.06 (1H, m, 4-H); 7.62 (2H, m, 3-H and 5-H)
XX	0.13 (9H, s, $SiMe_3$); 1.56 (6H, d, J = 6.8 Hz, CH_3); 2.10 (hept, 1H, J = 6.8 Hz, CH) 6.91 (1H, m, 4-H); 7.16 (1H, m, 3-H); 7.25 (1H, m, 5-H)
XXI	0.22 (9H, s, $SiMe_3$); 1.84 (3H, s, CH_3); 7.15 (1H, m, 5-H) 7.47-7.66 (2H, m, 3-H and 4-H); 8.58 (1H, m, 6-H)
XXII	0.16 (9H, s, $SiMe_3$); 7.20 (1H, m, 5-H); 7.42-7.55 (2H, m, 3-H and 4-H) 8.49 (1H, m, 6-H)
XXIII	0.18 (9H, s, $SiMe_3$); 1.80 (3H, s, CH_3); 7.27 (1H, m, 5-H); 7.76 (1H, m, 4-H) 8.49 (1H, m, 6-H); 8.71 (1H, m, 2-H)
XXIV	0.17 (9H, s, $SiMe_3$); 7.28 (6H, m, Ph and 5-H); 7.67 (1H, m, 4-H); 8.53 (1H, m, 6-H) 8.68 (1H, m, 2-H)
XXV	0.22 (9H, s, $SiMe_3$); 1.78 (3H, s, CH_3); 7.42 (2H, m, 3-H and 5-H) 8.62 (2H, m, 2-H and 6-H)
XXVI	0.18 (9H, s, $SiMe_3$); 7.36 (7H, m, Ph, 3-H and 5-H); 8.86 (2H, m, 4-H and 6-H)

TABLE 3. Mass Spectral Data for Products XIV–XXVI

Compound	m/z (I_{rel}, %)
XIV	219 (<1, M^+), 204 (70), 177 (95), 135 (32), 105 (79), 75 (100), 51 (14), 45 (25)
XV	247 (1, M^+), 205 (15), 204 (24), 105 (100), 77 (14), 73 (12), 45 (8)
XVI	275 (1, M^+), 233 (4), 205 (56), 178 (18), 163 (10), 116 (9), 105 (100), 91 (9), 73 (26) 43 (17)
XVII	209 (3, M^+), 194 (58), 167 (30), 120 (24), 95 (54), 76 (100), 65 (20), 59 (9), 45 (23) 39 (17)
XVIII	329 (1, M^+), 195 (55), 194 (35), 168 (15), 135 (15), 107 (12), 95 (100), 79 (24), 73 (45) 41 (30)
XIX	225 (5, M^+), 210 (47), 183 (16), 136 (17), 111 (80), 84 (10), 75 (100), 45 (29)
XX	253 (1, M^+), 211 (75), 184 (75), 153 (6), 141 (7), 111 (100), 73 (24), 57 (19), 45 (16)
XXI	220 (2, M^+), 205 (100), 190 (20), 178 (64), 104 (12), 78 (23), 52 (7), 45 (17)
XXII	282 (75, M^+), 267 (52), 240 (23), 192 (55), 182 (9), 167 (10), 155 (37), 105 (100) 77 (30), 75 (35), 45 (23)
XXIII	220 (2, M^+), 205 (66), 178 (100), 136 (22), 106 (41), 84 (15), 75 (75), 51 (17), 45 (25)
XXIV	282 (10, M^+), 267 (100), 204 (9), 193 (45), 192 (36), 166 (16), 139 (9), 105 (36), 84 (12) 73 (19), 45 (17)
XXV	220 (1, M^+), 205 (37), 178 (100), 136 (7), 106 (13), 84 (15), 75 (25), 51 (13), 45 (16)
XXVI	282 (2, M^+), 267 (100), 204 (15), 192 (25), 166 (9), 139 (13), 105 (44), 84 (18), 73 (13) 45 (13)

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker WH-90/DS spectrometer in $CDCl_3$ solution with TMS as internal standard. Mass spectra were recorded with a chromato-mass spectrometer GC-MS HP 6890 (70 eV). GLC analysis was carried out with a Chrom-5 chromatograph with flame ionization detector and a glass column filled with 5% OV-101 on W-HP chromosorb (80-100 mesh) and an analysis temperature of 170-230°C. Ketones I, II, IV, VI, VIII–XIII (Aldrich) were used without additional purification. 1-Phenyl-2-ethylbutanone (III), 1-(2-furyl-2,2,2-triallylethanone (V), and 2-methyl-(2-thienyl)-1-propanone (VII) were prepared from acetophenone, 2-acetylfuran, and 2-acetylthiophene by phase-transfer catalytic alkylation as previously described [29]. CsF was dried at 250°C for 1 h before use. Elemental analysis was impossible because of the instability of compounds XIV–XXVI.

General Method for the Trimethylsilylcyanation of Hetarylketones I-XIII. 1-(2-Furyl)-1-trimethylsiloxy-cyanoethane (XVII). To a solution of 2-acetylfuran IV (0.22 g, 2 mmol) and 18-crown-6 (0.052 g, 0.2 mmol) in dry benzene (2.5 ml), CsF (0.0602 g, 0.4 mmol) was added followed by trimethylcyanosilane (0.266 ml, 2 mmol) under argon. The mixture was stirred for 5 h, filtered through Al_2O_3, and the solvent was evaporated from the filtrate to give compound XVII as a yellowish oil. Yield 0.31 g (74%).

Compounds XIV–XVI and XVIII–XXVI were prepared analogously. The characteristics of products XIV–XXVI are given in Tables 1-3.

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