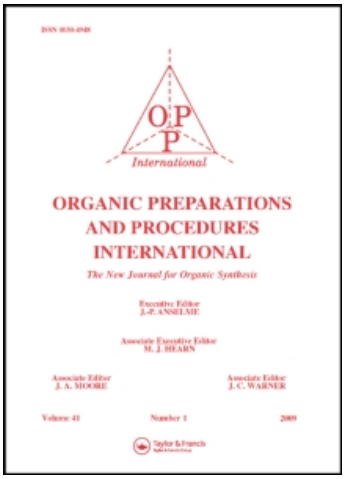

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ALKOXYETHYNYL KETONES

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Stannyl groups at the β-position of ynamines[1] and ynethers[2] can be replaced by electrophiles. Silyl substituted ynamines undergo substitution only with powerful electrophiles in highly polar solvents,[1b] while with silyl ynethers only addition reactions are observed.[3]

The stannylated alkoxyacetylenes I react with acid halides in acetonitrile to give mainly the alkoxyethynyl ketones II;[4] some new representatives of II are described in the Table.

$$ROC{\equiv}CSnMe_3 + R'COCl \longrightarrow ROC{\equiv}C\overset{O}{\overset{\|}{C}}R'$$

I II

a) R = Me, R' = $CHCl_2$
b) R = Me, R' = CCl_3
c) R = Me, R' = $C(Br)Me_2$
d) R = Me, R' = $CH{=}CMe_2$
e) R = Me, R' = CH(OAc)Ph
f) R = Et, R' = CCl_3
g) R = Et, R' = CH_2Br
h) R = Et, R' = $C(Br)Me_2$
i) R = Et, R' = CMe_3

In view of the synthetic importance of these previously little known substances,[5,6] we invested some effort into our new synthesis in order to improve the reaction conditions and to determine the best isolation methods. At room temperature, the alkoxyethynyl ketones II are oils, sensitive to acids and bases, which cannot be distilled without partial decomposition. The first method for purification involves column chromatography of

the reaction mixture over carefully dried silica gel using dried solvents (method A in Experimental Section). Although this method furnished only moderate yields,[2] it had to be used in all cases where some by-products may be present in the reaction mixture.

TABLE. New Alkoxyethynyl Ketones

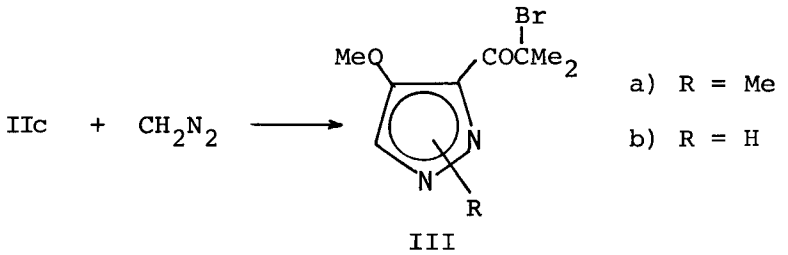
Cmpd	Time[a] (hr)	Yield[b] (%)	Spectral Data	
			IR(cm^{-1}, film)	^{1}H-NMR[c]
IIa	1.0	79(B)	2246, 2220, 1676	5.87(s, 1H), 4.20(s, 3H)
IIb	1.0	98(B)	2246, 2226, 1701	4.24(s, 3H)
IIc	1.0	87(B)	2230, 2200, 1660	4.15(s, 3H), 1.87(s, 6H)
IId	0.5	34(A)	2228, 1650	6.05(m, 1H), 4.06(s, 3H) 1.88, 2.17(2d, 3H each)[d]
IIe	3.0	34(A)	2235, 1744 1682	5.98(s, 1H), 3.98(s, 3H), 2.17(s, 3H)
IIf	0.5	12(A) 80(B)[e]	2231, 1704	4.51(q, 2H), 1.54(t, 3H)
IIg[f]	1.0	53(A) 76(B)	2227, 1678, 1662	4.40(q, 2H), 3.96(s, 2H), 1.50(t, 3H)
IIh	1.0	82(B)	2230, 1662	4.40(q, 2H), 1.87(s, 6H), 1.48(t, 3H)
IIi	0.5[g]	16(A)	2227, 1658	4.33(q, 2H), 1.47(t, 3H), 1.16(s, 9H)

a. Temperature is 20° unless otherwise noted. b. (A) refers to method A and (B) refers to method B. c. Run in $CDCl_3$ and reported in δ values; J ≃ 7 Hz (OEt). d. J ≃ 1.2 Hz. e. Small amount of impurities present (1760, 1730 cm^{-1}). f. MS(70eV), m/e: 164(6, M-C_2H_4), 123 (3), 97(35, M-CH_2Br), 95 (5), 69 (100, M-$COCH_2Br$); ^{13}C-NMR($CDCl_3$): δ = 178.70 (s, CO), 106.49 (s, OC≡), 78.34 (t, OCH_2), 43.13 (s, ≡C-), 36.12 (t, CH_2Br), 14.46 (q, CH_3). g. Temperature 80°.

Although we subsequently developed an improved procedure (method B), it is, however, applicable only when the formation of the acylated ynether II is practically complete; in these cases only the removal of chlo-

ro (or bromo) trimethylstannane by-product by extraction needs to be carried out. In order to achieve this separation, the reaction mixture was shaken with several portions of buffer solution (pH = 7), thereby causing hydrolysis of the halogenostannane to the trimethyltin hydroxide and hydrogen halide; the former is soluble in aqueous solution while the latter is removed by the buffer system.

Both methods gave the alkoxyethynyl ketones II as crude oils.[7] However the existence of these products was unequivocally established by their spectroscopic data (see Table), by an osmotic determination of the molecular weight of one product and by the transformation of II into stable and analyzable products; thus the ynethers could be hydrolyzed to the β-ketoesters (one example is given in the Experimental Section) and IIc was treated with diazomethane to give the pyrazoles IIIa and IIIb.[8]



III

EXPERIMENTAL SECTION

(Trimethylstannylethynyl) ethyl ether is described in literature.[9]

(Trimethylstannylethynyl) methyl ether.- Ethynyl methyl ether[10] (11.2 g, 0.2 mol) in ether (40 ml) was added at -30° to a mixture of butyllithium (0.24 mol, 150 ml of a 15% solution in hexane) and ether (150 ml). After 30 min. at room temperature, a solution of chlorotrimethylstannane (39.8 g, 0.2 mol) in ether (50 ml) was added dropwise (∿ 10 min) without cooling. After stirring for 90 min. at room temperature, the precipitate was removed by centrifugation. Removal of the solvent and fractionation of the residu-

al oil provided 33 g (76%) of the acetylenic ether, bp. 52-54°/12 mm. ^{1}H-NMR ($CDCl_3$): δ 3.85 (s, 3H, OMe), 0.22 (s, 9H, $SnMe_3$). IR(film): 2160 (C≡C), 774 ($SnMe_3$) cm^{-1}.

Anal. Calcd. for $C_6H_{12}OSn$: C, 32.93; H, 5.53. Found: C, 32.50; H, 5.46.

Alkoxyethynyl Ketones II. General Procedure.- The appropriate acid chloride (or acid bromide, used for example in the preparation of IIc, IIg and IIh, 5 mmol) was added to a solution of the stannylated ynether I (5 mmol) in acetonitrile (10 ml). The mixture was stirred at room temperature or heated under reflux (see Table). The isolation of the products II can be effected by two different methods discussed below.

A) Isolation by Column Chromatography (*Method A*).- After removal of the solvent, the residue was chromatographed over silica gel (65 g; Woelm, 0.063-0.2 mm, dried at 180° for 5 hrs in a vacuum drying oven) and eluted with chloroform (300 ml) and then with chloroform/ether (9:1, 300 ml). By evaporation of the eluent the alkoxyethynyl ketone II was obtained as a crude oil.

B) Treatment by Buffer Solution (*Method B*).- The reaction mixture was diluted by ether (50 ml), washed three times with 30 ml of buffer solution (pH = 7) and dried over Na_2SO_4. Removal of the solvent in vacuo gave the crude alkoxyethynyl ketone II.

Hydrolysis of IIa.- To a solution of crude 1,1-dichloro-4-methoxy-3-butyne-2-one (IIa) (0.5 g, 3.0 mmol) in acetone (5 ml) was added concentrated HCl (0.5 ml). The mixture was stirred for 1 hr at room temperature and then refluxed for 45 min. Kugelrohr distillation yielded methyl 4,4-dichloroacetoacetate (0.15 g, 27%) as a colourless liquid, bp. 130°/0.2 mm. IR (film): 1755, 1734, 1662 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.03 (s, 1H, $CHCl_2$), 3.87 (s, 2H, CH_2), 3.77 (s, 3H, OCH_3).

Anal. Calcd. for $C_5H_6Cl_2O_3$: C, 32.46; H, 3.27. Found: C, 32.30; H, 3.16

Pyrazoles III.- A mixture of crude 4-bromo-1-methoxy-4-methyl-1-butyne-3-one (IIc) (0.82 g, 4 mmol) and diazomethane (prepared from 1 g N-methyl-N-nitrosourea) in ether (10 ml) was stirred for 6 days at room temperature. Column chromatography of the reaction mixture on silica gel gave 0.26 g. (25%) of:

3(5)-(2-bromo-2-methylpropanoyl)-4-methoxy-1-methylpyrazole (IIIa)[8] as a colourless oil, bp. 160°/0.08 mm. IR(film): 1655, 1547 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.27 (s, 1H, CH), 4.02, 3.90 (2s, 3H each, OMe, NMe), 2.00 (s, 6H, CMe_2); MS, m/e(%): 262 (3, M^+), 139 (100, M-CMe_2Br).

Anal. Calcd. for $C_9H_{13}BrN_2O_2$: C, 41.40; H, 5.02; N, 10.73.
Found: C, 41.30; H, 4.96; N, 10.50

and 0.14 g. (15%) of 3-(2-bromo-2-methylpropanoyl)-4-methoxypyrazole (IIIb) as colourless crystals, mp. 153-154°. IR(KBr): 1656, 1568 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 11.10 (s, 1H, NH), 7.44 (s, 1H, CH), 3.94 (s, 3H, OMe), 2.04 (s, 6H, CMe_2); MS, m/e(%): 248 (5, M^+), 125 (100, M-CMe_2Br).

Anal. Calcd. for $C_8H_{11}BrN_2O_2$: C, 38.89; H, 4.49; N, 11.34
Found: C, 38.10; H, 4.38; N, 11.00

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