SYNTHETIC COMMUNICATIONS, 21(20), 1991-1998 (1991)

A Novel One-pot Synthesis of 2,4-Enynyl Amides

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Abstract: Silylated 2,4-enynyl amides can be synthesized by the reaction of 3-(trimethylsilyl)-2-propynylidenetriphenylarsorane, generated in situ from the corresponding arsonium salt and n-butyllithium, with α-bromoacetamides in 40-59% yields (two steps) and with high stereoselectivity.

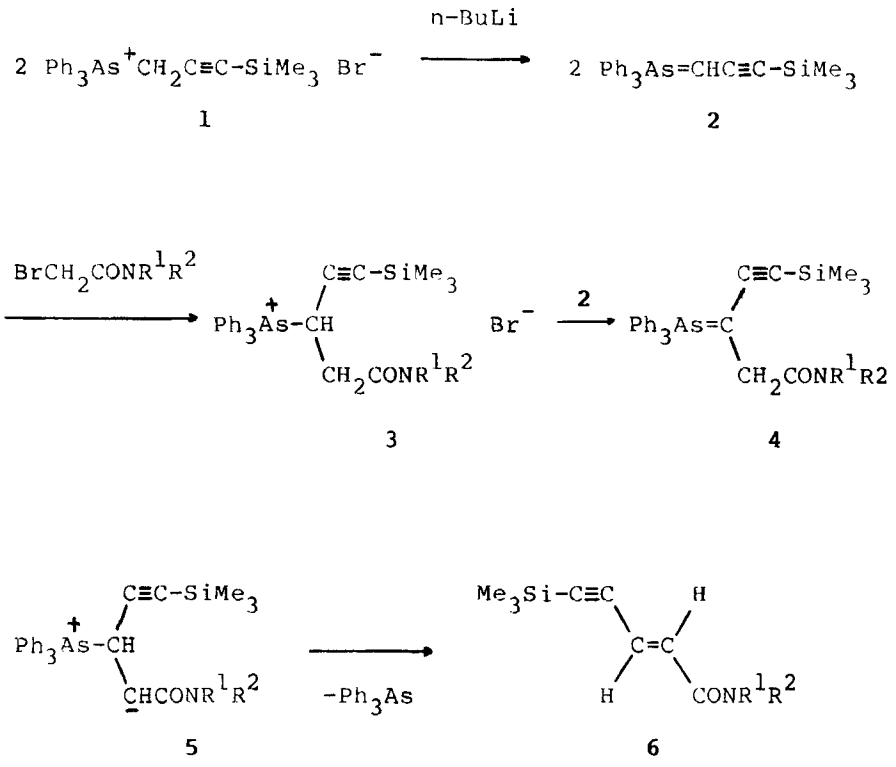
Some natural products with functionalized enyne groups have attracted much attention because of their biological properties.[1] They are also useful intermediates for the synthesis of various complex compounds[2] and capable of

undergoing many useful organic transformations.[3] Therefore to develop an effective method for their preparation would be valuable.

Recently we found that 3-(trimethylsily)-2-propynylidenetriphenylarsorane could react with ketones to give terminal trimethylsilyl enynes[4] and with chalcones to afford (trimethylsilyl-ethynyl) cyclopropanes.[5] In our continuing investigation to exploit the synthetic utility of this arsorane in organic synthesis, we wish to report a novel one-pot synthesis of 2,4-enynyl amides by the reaction of 3-(trimethylsilyl)-2-propynylidenetriphenylarsorane, generated in situ from the corresponding arsonium salt and n-butyllithium, with α-bromoacetamides in 40-59% yields (two steps) and with high stereoselectivity(Scheme 1).

The reaction was initiated by nucleophilic attack of arsorane **2** on the α-carbon atom of bromoacetamide to give arsonium salt **3**. **3** reacted with another molecule of **2** to give **4** which converted to **5** via hydrogen transfer, followed by elimination of triphenylarsine affording product **6**. It may be rationalized that **5** is more stable than **4** due to the negative charge can be stabilized by $CONR^1R^2$ group. The results are shown in Table 1.

This one-pot synthesis of silylated enynyl amides is quite convenient under mild conditions giving E-isomer exclusively and offers a wide scope since R^1 and R^2 may



Scheme 1

be alkyl, heterocyclic or alicyclic group. Thus, this reaction provides a new method for the preparation of the title compounds which would be useful for further elaboration of biologically active compounds.

Experimental

All boiling points were uncorrected. IR spectra of liquid products were obtained as films on a Shimadzu

Table 1.

Preparation of Silylated 2,4-Enynyl Amides **6.**

Product	R^1	R^2	Yield(%)
6a	$-(CH_2)_4-$		59
6b	$-(CH_2)_5-$		40
6c	$-(CH_2)_2-O-(CH_2)_2-$		51
6d	C_2H_5	C_2H_5	45
6e	C_3H_7-i	C_3H_7-i	40
6f	C_3H_7-n	C_3H_7-n	42
6g	C_4H_9-n	C_4H_9-n	44

IR-440 spectrometer. ^1H NMR spectra were recorded on a Varian XL-200 (200 MHz) spectrometer with $SiMe_4$ (positive for upfield shifts) as external references. Mass spectra were measured on a GC-MS-4021 spectrometer.

General procedure: n-butyllithium (4.0 mmol in 3 ml of hexane) was added dropwise over 30 min to a stirred suspension of 3-trimethylsilyl-2-propynyl triphenyl arsonium bromide (4 mmol) in dry THF (20 ml) at -78°C under nitrogen. The mixture was allowed to warm to 0°C, stirred for 30 min, cooled to -78°C and the α-bromoacetamide (2

mmol) was added. After stirring at 20°C for 2h, the product **3** was isolated by column chromatography on silica gel with light petroleum ether (b.p. 60-90°C)-ethyl acetate (8 2) as eluant.

6a: 59% yield; bp 104°C/2mmHg; IR(film) 2320, 2260, 1640, 1600 cm^{-1}; ^1H NMR($CDCl_3$/TMS): 0.21(9H,s), 1.87-1.95(4H, m), 3.44-3.52(4H, m), 6.60(1H, d, J=15.4Hz), 6.73(1H, d, J=15.4Hz); MS m/z: 221(M^+,64%), 206(M^+-CH_3,51%), 151($M^+-C_4H_8N$,52%), 70($C_4H_8N^+$,100%) (Found: C, 65.53; H, 8.68; N, 5.65. Calcd for $C_{12}H_{19}NOSi$: C, 65.15; H, 8.59; N, 6.33%)

6b: 40% yield; bp 99 °C/2mmHg; IR(film) 2300, 2200, 1640, 1600cm^{-1}; ^1H NMR($CDCl_3$/TMS): 0.21(9H,s), 1.57-1.62(6H,m), 3.51-3.59(4H,m), 6.70(1H,d,J=15.4Hz),6.82(1H,d,J=15.4Hz); MS m/z 235(M^+,37%), 220(M^+-CH_3,24%), 151($M^+-C_5H_{10}N$,15%), 84($C_5H_{10}N^+$,100%)(Found: C, 66.15; H, 9.59; N, 5.97. Calcd for $C_{13}H_{21}NOSi$: C, 66.38; H, 8.93; N, 5.95%)

6c: 51% yield; bp 106°C/2mmHg; IR(film) 2320, 2200, 1640, 1600cm^{-1}; ^1H NMR($CDCl_3$/TMS): 0.22(9H,s), 3.59-3.87(8H,m), 6.71(1H,d,J=15.4Hz), 6.78(1H,d,J=15.4Hz); MS m/z: 237(M^+, 31%), 222(M^+-CH_3, 30%), 151($M^+-C_4H_8NO$, 69%), 86($C_4H_8NO^+$, 100%) (Found: C, 60.06; H, 8.05; N, 5.68. Calcd for $C_{12}H_{19}NO_2Si$: C, 60.76; H, 8.01; N, 5.90%)

6d: 45% yield; bp 92°C/2mmHg; IR(film) 2320, 2200, 1640, 1600cm^{-1}; ^{1}H NMR($CDCl_3$/TMS): 0.22(9H,s), 1.20(3H, t,J= 6.8Hz), 1.23(3H,t,J=6.8Hz),3.40(2H,q,J=6.8Hz), 3.42(2H,q, J=6.8Hz), 6.68(1H,d,J=15.4Hz), 6.79(1H, d, J=15.4Hz); MS m/z: 223(M^+, 27%)), 208(M^+-CH_3, 71%), 151($M^+-C_4H_9N$,100%) (Found C, 64.26; H, 9.78; N, 6.17. Calcd for $C_{12}H_{21}NOSi$: C, 64.57; H, 9.41, N, 6.27%)

6e: 40% yield; bp 98°C/2mmHg; IR(film) 2320, 2220, 1640, 1600cm^{-1}; ^{1}H NMR($CDCl_3$/TMS): 0.19(9H, s), 1.26(6H, d,J= 6.0Hz), 1.32(6H,d,J=6.0Hz), 3.74(1H, hepta,J=6.0Hz), 4.02 (1H,hepta,J=6.0Hz), 6.60(1H,d,J=15.4Hz), 6.72(1H,d,J=15.4 Hz); MS m/z: 251(M^+, 10%), 236(M^+-CH_3,20%), 208($M^+-C_3H_7$, 78%), 151($M^+-C_6H_{14}N$,82%)(Found: C, 66.44; H, 10.65; N, 5.67. Calcd for $C_{14}H_{25}NOSi$: C, 66.93; H, 9.95; N, 5.57%)

6f: 42% yield; bp 92°C/2mmHg; IR(film) 2300, 2200, 1640, 1600cm^{-1}; ^{1}H NMR($CDCl_3$/TMS): 0.21(9H,s), 0.89(3H, t,J= 7.6Hz), 0.92(3H,t,J=7.6Hz), 1.52-1.66(4H, m), 3.27(2H, t, J=7.6Hz), 3.31(2H,t, J=7.6Hz), 6.67(1H, d,J=15.4Hz), 6.74 (1H,d,J=15.4Hz); MS m/z: 251(M^+, 11%), 236(M^+-CH_3,17%), 151($M^+-C_6H_{14}N$, 100%) (Found: C, 66.79; H, 10.24; N, 5.56. Calcd for $C_{14}H_{25}NOSi$: C, 66.93; H, 9.95; N, 5.57%)

6g: 44% yield; bp 96°c/2mmHg; IR(film) 2320, 2220, 1640, 1600cm^{-1}; ^{1}H NMR($CDCl_3$/TMS): 0.23(9H,s), 0.93(3H,t,J=8.0

Hz), 0.95(3H,t,J=8.0Hz), 1.26-1.41(4H,m),1.48-1.64(4H,m), 3.29(2H,t,J=8.0Hz), 3.37(2H,t,J=8.0Hz), 6.68(1H,d, J=15.4 Hz), 6.79(1H,d,J=15.4Hz); MS m/z: 279(M^+, 11%), 264(M^+ -CH_3,13%), 152(M^+-$C_8H_{18}N$,100%)(Found: C, 68.92; H, 10.56; N, 4.93. Calcd for $C_{16}H_{29}NOSi$: C, 68.81; H, 10.38; N, 5.01%)

Acknowledgement.

Financial support by the National Natural Science Foundation of China and Academia Sinica is gratefully appreciated.

References

1. K. Nakatani, K. Arai, N. Hirayama, F. Matsuda and S. Terashima, Tetrahedron Lett., 1990, **31**, 2323; F. Tellier and C. Descoins, Tetrahedron Lett., 1990, **31**, 2295.
2. M. Nikles, D. Bur and U. Sequin, Tetrahedron., 1990, **46**, 1569; T. Norin and C. R. Unelius, Acta. Chem. Scand., 1990, **44**, 106; C. R. Ziegler, J. Org. Chem., 1990, **55**, 2983.
3. K. Doyama, T. Joh, S. Takahashi and T. Shiohara, Tetrahedron Lett., 1986, **27**, 4497; J. Ohshita, K. Furumori, A. Matsuguchi and M. Ishikawa, J. Org. Chem., 1990, **55**, 3277.

4. Y.-C. Shen and Q.-M. Liao, J. Organomet. Chem., 1988, **346**, 181.

5. Y.-C. Shen and Q.-C. Liao, Synthesis., 1988, 321.

(Received in USA 16 May, 1991)