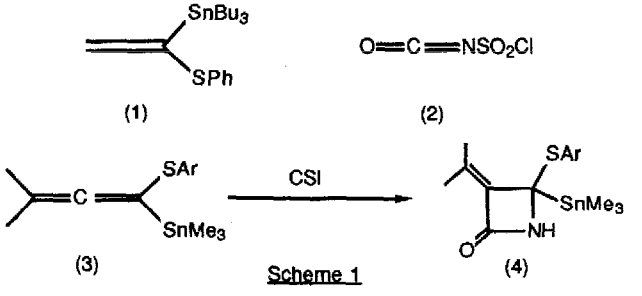
Tetrahedron Letters,Vol.30,No.20,pp 2689-2692,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

A FACILE PREPARATION OF ß-(TRI-N-BUTYLTIN)ACRYLAMIDES

Hussein Imanieh, Donald MacLeod and Peter Quayle*
Department of Chemistry
Victoria University Of Manchester
Manchester M13 9PL. UK.
and
Gareth M. Davies
ICI Pharmaceuticals
Alderley Park
Macclesfield SK10 4TG. UK.

Reaction of phenyl 1-(tri-n-butylstannyl)vinyl thioether and related compounds with reactive isocyanates provides rapid access to β-(tri-n-butylstannyl)acrylamides which themselves serve as useful precursors for the generation of the synthetically versatile β-lithioacrylamide anions.

In connection with a programme of work related to the development of novel strategies for the synthesis of functionalised bi-cyclic ß-lactams, we had occasion to investigate the reaction between the vinylstannane (1) and chlorosulphonyl isocyanate,[1] CSI (2). Whereas the reaction between CSI (and reactive isocyanates) and enol ethers and esters has been the focus of much recent attention,[2a] the analogous reaction with functionalised thioenol ethers has been largely left unexplored.[2b] In this regard, we were encouraged by Buynaks observation[3] that functionalised allenes (3) underwent relatively clean cycloaddition reactions with reactive isocyanates to afford the ß-lactams (4) in moderate yields (Scheme 1).

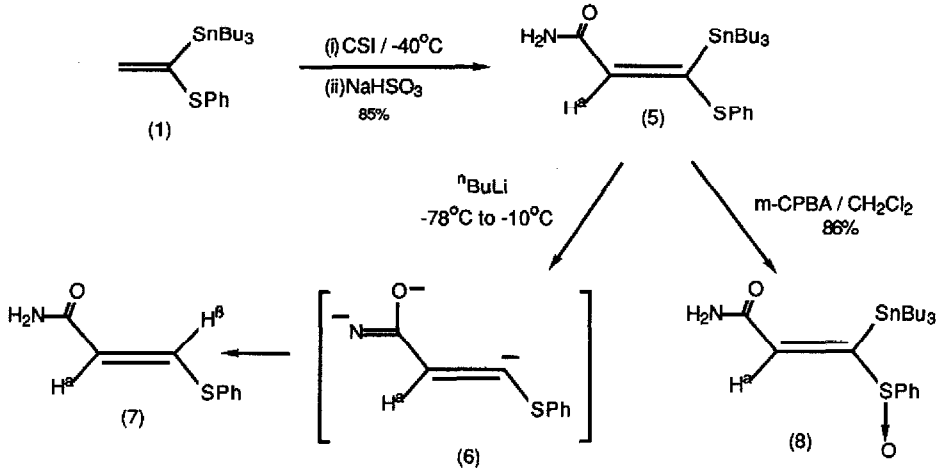


(1) (2) (3) (4)

Scheme 1

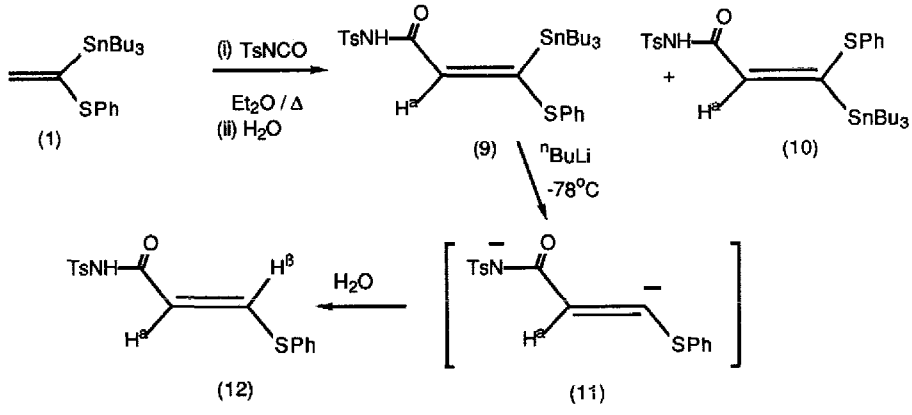
In contrast, we have observed that reaction of the readily available[4a] vinylstannane (5) with CSI in ethereal solvents at low temperature (-78 °C) followed by reductive removal of the chlorosulphonyl residue cleanly afforded the unsaturated amide[4b] (5) in high yield (85%) (Scheme 2). Of interest was the observation that the reaction is both highly chemoselective and stereoselective, producing the *Z*-isomer (5) with >95:1 selectivity .

The double bond geometry in (5) was initially inferred as being *Z*- from the relatively large[5] coupling constant between Ha and the tin residue at C-3 (J 117/119 Sn- Ha = 80, 84 Hz). Subsequent chemical investigations indeed confirmed this assumption. Hence, treatment of the amide (5) with a slight excess of n-BuLi (3.3-4.0 equivalents) at low temperature (-78 °C to -10°C) cleanly lead to transmetallation, presumably *via* the tri-anion[6] (6), which upon protonation at -70°C led to the isolation of the acrylamide derivative (7) in 84% yield. Again, this process was highly stereoselective affording the acrylamide (7) in an isomerically pure form, as judged by an examination of its ^{1}H nmr spectrum (J Ha - Hß = 15 Hz). Alternatively, reaction of the amide (5) with MCPBA (1 equivalent, RT, CH_2Cl_2) yielded the sulphoxide (8) in excellent isolated yield (86%), in which the proton Ha had experienced a downfield shift from 5.65 to 7.5 ppm (J 117/119Sn - Ha = 70, 74 Hz), indicative of a *cis* - relationship between the sulphur residue at C-3 and the hydrogen at C-2 (Scheme 2).

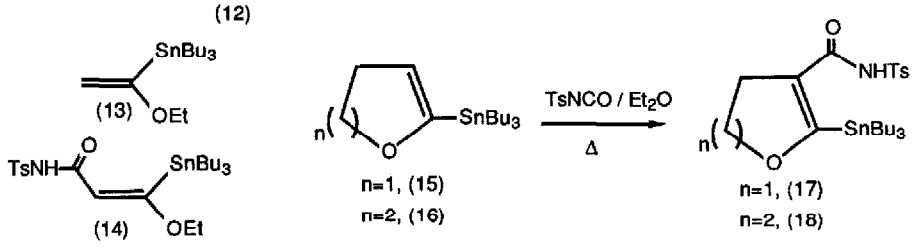


Scheme 2

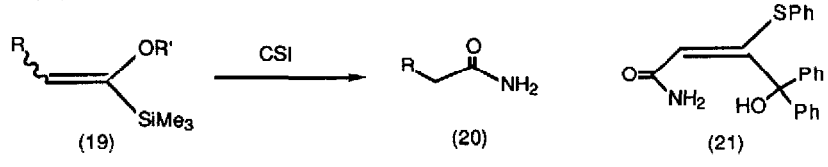
Reaction of the stannane (1) with the less reactive tosyl isocyanate (2 equivalents, ether, reflux) for 24 hours led to the formation of two isomeric amides. The major (61%) product being the *Z* - amide (9) (J 117/119 Sn - Ha = 72, 76 Hz) and the minor product (<10%) being the the *E* - isomer (10) (J 117/119Sn - Ha = 45 Hz). Again, reaction of the major isomer (9) with a slight excess of n-BuLi at low temperature produced a stable di-anion (11) which on protonation at -78°C (acetate buffer, pH 5) afforded the tosamide (12) (J Ha-Hß= 15 Hz) in 60% yield after chromatography. Similarly, reaction of the enol ether (13) with tosyl isocyanate resulted in the isolation of the tosamide (14) in 86% yield (> 95% *Z* - isomer).



Whereas, reaction of the heterocyclic stannanes (15) and (16) with CSI merely resulted in the formation of complex reaction mixtures, the analogous reactions with tosyl isocyanate (1 equivalent, ether, reflux, 24 hours) cleanly afforded the tosamides (17) and (18) in moderate yields (65% and 55% respectively). Surprisingly, 4-methoxyphenyl isocyanate was completely unreactive under identical reaction conditions.



Of synthetic importance is the observation that the above reactions are highly chemoselective[7] providing a rapid, steroselective high yielding route to functionalised vinylstannanes.[8] Interestingly, the outcome in these rections is at variance with the recent results reported by Page[9] in which reaction of the functionalised silanes (19) with CSI afforded the amides (20). Clearly the nature of the substituent has a pronounced effect upon the exact course of the reaction of heterofunctionalised alkenes with reactive isocyanates.



It should be noted that both the tri-anion (6) and the di-anion (11) are stable species,[10] even at 0°C, and that reaction of such species with a variety of electrophiles could lead to the facile preparation of functionalised acrylates. For example, reaction of the tri-anion (6) with benzophenone (2 equivalents) at -78°C, followed by an aqueous quench led to the isolation of the hydroxy-amide (21) in 62% yield. The use of these intermediates in natural product synthesis is currently under investigation and the results of these studies will be reported elsewhere.[11]

Acknowledgements.

One of us (D. M.) thanks the SERC for the provision of a CASE award; we thank ICI Pharmaceuticals for generous support of our work.

References and notes.

(1) For a recent review see A. Kamal and R. S. Sattur, Heterocycles, 1987, 26, 105.
(2a) e.g. F. Effenberger and R. Gleiter, Chem. Ber., 1964, 97, 1576; K. Clauß, D. Grimm and G. Prossel, Liebigs Ann. Chem. 1974, 539; J. K. Rasmussen and A. Hassner, Chem. Rev., 1976, 76, 389; A. G. M. Barrett, A. Fenwick, and M. J. Betts, J. Chem. Soc., Chem. Commun., 1983, 299; S. Michel, Aldrichimica Acta, 1985, 18, 95; M. Chmielewski, Z. Kaluza, W. Abramski, J. Grodner, C Belzecki, and P. Sedmera, Tetrahedron, 1989, 45, 233 and refs. therein.
(2b) c.f. K. Hirai, H. Matsuda, and Y. Kishida, Chem. Pharm. Bull. Jpn., 1973, 21, 1090; M. S. Manhas, D. R. Wagle, J. Chiang, and A. K. Bose, Heterocycles, 1988, 27, 1755 and refs. therein.
(3) J. D. Buynak, M. N. Rao, R. Y. Chandrasekaran, E. Haley, P. de Meester, and S. C. Chu, Terahedron Letters, 1985, 26, 5001.
(4a) B. Harichian and P. Magnus, J. Chem. Soc., Chem. Commun., 1977, 522.
(4b) All new compounds were fully characterised by 'Hnmr, ir and high res. mass spectroscopy or microanalysis. Typical procedure:- To a mixture of the thioenol ether (1) 3.73 g, 8.8 mmol) in anhydrous THF (10 ml) at -40°C under an atmosphere of nitrogen was slowly added CSI (1.87 g, 1.15 ml, 13.2 mmol). The resulting mixture was stirred at -40°C for 30 minutes and then poured onto a mixture of di-potassium hydrogen orthophosphate (5.15g), sodium hydrogen sulphite (1.8 g), water (50 ml) and ether (50) ml maintained at 0°C. The mixture was then extracted with ether and the organic extracts dried and concentrated *in vacuo*. Flash chromatography of the residue afforded the acrylamide (5) as a white solid m.pt. 54-56°C (ex. ethyl acetate/hexane). Yield 3.52 g (85%). ^{1}Hnmr (300 MHz) ∂ 0.9 (9H, tr., J = 7 Hz), 1.1 (6H, tr., J = 7 Hz), 1.35 (6H, m), 5.0 (2H, brd. s., exch.), 5.55 (1H, s., J_{Sn-H} = 80, 84 Hz), 7.4 - 7.5 (5H, m); IR, ν max 3472, 3371, 3346, 3175, 1651, 1625 cm^{-1}; $C_{21}H_{35}NOSn$ requires C, 53.85; H, 7.55; N 3.00; S,6.85 %. Found C, 54.0; H, 7.85; N,2.9; S, 7.0 %.
(5) c.f. E. Piers, J. M. Chong and H. E. Morton, Tetrahedron Letters, 1981, 22, 4905, Tetrahedron, 1989, 45, 413; A. J. Leusink, H. A. Budding and J. W. Marsman, J. Organometal. Chem., 1967, 9, 285.
(6) For alternative preparation of similar species see R. R. Schmidt and R. Hirsenkorn, Tetrahedron, 1983, 39, 2043; N. C. Barua and R. R. Schmidt, Synthesis, 1986, 891.
(7) Vinylstannanes are observed to undergo facile *ipso* - substitution reactions with acyl halides c.f. A. A. Alvanipour, C. Eaborn, and D. R. M. Walton, J. Organometal. Chem., 1980, 201, 233; see also D. Zhai, W. Zhai, and R. M. Williams, J. Amer. Chem. Soc., 1988, 110, 2501 for similar reactions of alkynylstannanes.
(8) Vinylstannanes are versatile synthetic intermediates, e.g. R. F. Heck in " Palladium reagents in Organic Synthesis", Academic Press.1985; J. K. Stille, Angew. Chem., Int. Ed. Engl., 1986, 25, 508 J. K. Stille and B. L. Groh, J. Amer. Chem. Soc., 1987, 109, 813; A. M. Echavarren and J. K. Stille, J. Amer. Chem. Soc., 1988, 110, 1557; M. Pereyre, J.-P. Quintard and A. Rahm in "Tin in Organic Synthesis", Butterworths.1987; E. Piers and Skerlj, J. Chem. Soc., Chem. Commun., 1987, 1025; E. Piers, Pure and Applied Chemistry, 1988, 60, 107; W. J. Scott and J. E. McMurry, Acc. Chem. Res., 1988, 21, 47.
(9) P. C. B. Page, S. Rosenthal and R. V. Williams, Synthesis, 1988, 621.
(10) The preparation of ß-acyl vinyl anions *via* alternative procedures is sometimes hampered by unwanted side reactions/anion instability e.g. R. R. Schmidt and J. Talbiersky, Angew. Chem., Int. Ed. Engl., 1978, 17, 204.
(11) H. Immanieh, D. MacLeod, P. Quayle and G. M. Davies, unpublished results.

(Received in UK 4 April 1989)