Tetrahedron Letters, Vol.31, No.33, pp 4697-4698, 1990
Printed in Great Britain

0040-4039/90 \$3.00 + .00
Pergamon Press plc

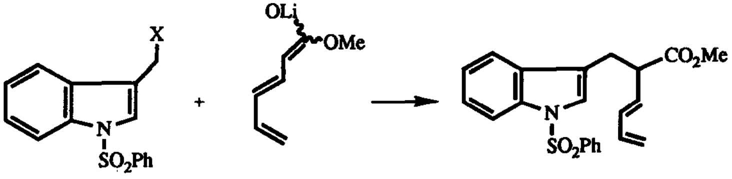
A Convenient Preparation of 1-Phenylsulfonyl-3-Iodomethylindole

Michito Sato[1] **and Michael Kahn**[2]
University of Illinois at Chicago
Department of Chemistry M/C 111
Box 4348
Chicago, Illinois 60680

Summary: A facile and efficient synthesis of the title compound is outlined.

As part of a synthesis of a conformationally restricted β-turn mimetic,[3] we required a convenient preparation of diene 1. A conceptually straightforward route to this intermediate is outlined in Scheme 1.[4] The success of this scenario is linked to a facile method of preparation of the requisite alkylating reagent 2 (1-phenylsulfonyl 3-iodomethylindole). Inspection of the literature demonstrates a paucity of reliable preparations of the title compound.[5] A facile and efficient synthesis of this alkylating reagent is outlined in Scheme 2, and is the subject of this letter.

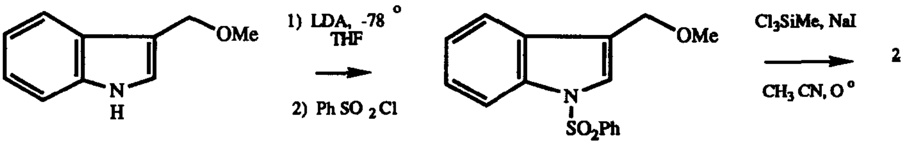
Scheme 1



2 X=I 5 1

3-Methoxymethylindole 3 in THF was reacted with LDA (1.5 equivalents) at -78°C. After thirty minutes, benzenesulfonyl chloride (1.1 equivalents) was added dropwise with stirring. Stirring was continued for an additional hour at -78°C at which time the reaction was quenched with saturated NH_4Cl, and extracted with ethyl acetate. Flash chromatography afforded a 92% yield of 1-phenylsulfonyl-3-methoxymethylindole 4. Treatment of 4 at 0° in acetonitrile with dichloroiodomethylsilane, prepared *in situ* from trichloromethylsilane and anhydrous sodium iodide,[6] for three hours effected cleavage of the methoxy group. The reaction was extracted with ethyl acetate, washed with saturated aqueous sodium bisulfite, water and brine, dried (Na_2SO_4) and the volatiles removed *in vacuo*. The

Scheme 2



3 92% 4 98%

benzene soluble portion of the residue was separated to provide a 98% yield of 2. The material so produced was reacted with the lithium enolate of methyl sorbate 5, to provide a 52% yield of the requisite intermediate 1 after chromatography.

In summary, a facile, convenient preparaton of a useful alkylating agent for introduction of an indole moiety has been described. Elaboration of diene 1 within the context of the synthesis of a β-turn mimetic of the insect neurohormone HTH is in progress and will be reported in due course.

Acknowledgements:

We gratefully acknowledge the generous financial support of the Camille and Henry Dreyfus Foundation, Searle Scholars Program/The Chicago Community Trust, the NIH GM 38260 O1A1, the NSF (PYI Award), Monsanto, Procter and Gamble, Schering, Searle and Syntex for matching funds and the American Cancer Society for a Junior Faculty Fellowship.

Notes

1. On leave from Lion Akzo Company, Tokyo, Japan.
2. Recipient of a Dreyfus Young Faculty Grant (1985-1990), Searle Scholars Award (1986-1989), Presidential Young Investigators Award (1987-1992), American Cancer Society Junior Faculty Fellowship (1987-1990), and an American Cyanamid Award (1989).
3. Kahn, M., Wilke, S., Chen, B. and Fujita, K. (1988) *J. Am. Chem. Soc.*, **110**, 1638; Kahn, M., Wilke, S., Chen, B., Fujita, K., Lee, Y.-H. and Johnson, M.E. (1988) *J. Mol. Recognition*, **1**, 75; Kahn, M. and Bertenshaw, S. (1989) *Tetrahedron Letters*, **30**, 2317.
4. This is conceptually identical to the well known reaction of gramine methiodide with malonic esters; unfortunately this reaction fails with less acidic partners, Snyder, H.R., Smith, C.W. and Stewart, J.M. (1944) *J. Am. Chem. Soc.*, **66**, 200.
5. a) For X=I, Sun, H. Weng, Z. and Owen, T-Y (1982) *Yaoxue Xuebao*, **17**, 275 (C.A., (1982) **97**, 92714 q)

   b) For X=Br, Suvorov, N.N., Eryshev, B.Ya. and Dubinin, A.G., U.S.S.R. 389, 093 (C.A. (1973) 789, 1263 obd)

   c) For X=Cl, Ahmad, M.V., Libbey, L.M. and Scanlan, R.A. *Food Addit. Contam.*, (1987) **4**,45 (C.A. (1987) **107**, 198714 e)
6. Olah, G.A., Husain, A., Singh, B.P. and Mehrotra, A.K. *J. Org. Chem* (1983) **48**, 3667.
7. Spectral data for:

   2 ^{1}H (400MHz, $CDCl_3$) δ7.30-8.01 (m, 10H), 4.52 (S, 2H)

   IR ($CHCl_3$) 3100, 1449, 1374

   MS M^+ - I 270.1

   1 ^{1}H (400MHz, $CDCl_3$) δ7.13-7.99 (m, 10H), 6.30 (ddd, 1H), J_a=10.3, J_b =10.3, J_c = 16.9 Hz), 6.11 (dd, 1H, J_a = 10.3, Jb = 15.3Hz), 5.72 (dd, 1H, J_a = 7.8Hz, J_{16} = 15.3Hz), 5.17 (d, 1H, J=16.9Hz), 5.11 (d, 1H, J=10.3Hz), 3.62 (S, 2H), 3.44 (1H, m), 3.19 (dd, 1H, J_a =7.8Hz, J_b =14.8Hz), 2.93 (dd, 1H, J_a = 7.8Hz, Jb =14.8Hz)

   IR $CHCl_3$ 1732, 1449, 1365

   MS M^+ 395.2

(Received in USA 20 December 1989; accepted 28 June 1990)