Pergamon

Tetrahedron Letters 40 (1999) 4857–4860

TETRAHEDRON
LETTERS

A Novel Sulfinylation of Alkenes by Tosyl Cyanide with Titanium(IV) Chloride.

Paul E. Morgan, Ray McCague[§] and Andrew Whiting[*].

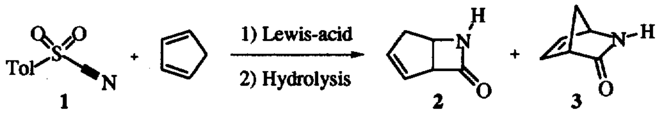
Department of Chemistry, Faraday Building, U.M.I.S.T., P.O. Box 88, Manchester M60 1QD, U.K.
[§]Chiroscience Ltd., Cambridge Science Park, Milton Road, Cambridge CB4 4WE, U.K.

Received 8 March 1999; accepted 6 May 1999

***Abstract** Tosyl cyanide is activated by titanium(IV) chloride to generate a tolylsulfinyl chloride equivalent, which readily stereo- and regio-specifically adds to certain alkenes to provide β-chlorosulfoxides. These chlorides rapidly hydrolyse on silica gel to provide β-hydroxysulfoxides in stereocontrolled manner.* © 1999 Elsevier Science Ltd. All rights reserved.

Tosyl cyanide **1** is a reactive heterodienophile in Diels-Alder reactions and has been used, for example, the construction of pyridine and hydropyridine analogues.[1] During the course of recent mechanistic studies on the cycloaddition chemistry of tosyl cyanide **1** with cyclopentadiene,[2] we had reason to investigate Lewis-acid catalysis of this cycloaddition. Unexpectedly, under certain Lewis-acid conditions, low yields, after hydrolysis, of β-lactam **2** were obtained resulting from [2+2]-addition, instead of the γ-lactam **3** from [4+2]-addition (**Equation 1**).[3] While [2+2]-addition is well known for chlorosulfonyl isocyanate[4] it is unknown for tosyl cyanide **1**. This result prompted us to examine the behaviour of **1** with unconjugated olefins.

Equation 1.



In preliminary studies, a range of simple alkenes did not react with tosyl cyanide **1** under either thermal conditions or in the presence of several Lewis-acids. However, a marked exception was with titanium(IV) chloride and in this communication we report the potentially useful sulfinylated products that are then obtained.

We have thus discovered that various simple mono- and di-substituted alkenes **4** react with tosyl cyanide **1** and stoichiometric titanium(VI) chloride to provide hydrolytically unstable β-chlorosulfoxides **5** (**Scheme 1, Table 1**). These β-chlorosulfoxides **5**, upon silica gel chromatography, provided the corresponding *trans*-β-hydroxysulfoxides **6** (**Scheme 1, Table 1**) as single diastereoisomers (n.m.r.).[5] In the case of styrene and vinyl acetate, the reactions displayed complete regiocontrol, providing solely β-chloro and β-hydroxy adducts **5a** and **5b**, and **6a** and **6b** respectively.

0040-4039/99/$ - see front matter
PII: S0040-4039(99)00894-1

Scheme 1.

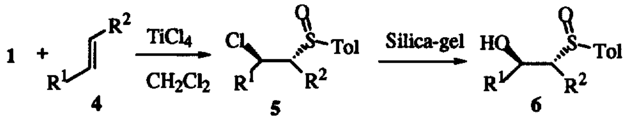


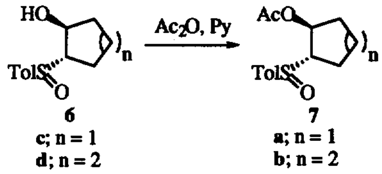
Table 1.

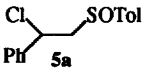
Entry	Alkene **4**	Time (h)	Conversion to **5**^{a} (%)	Isolated yields of **6** (%)^b
1	Cyclopentene	8	96	95
2	Cyclohexene	12	72	98
3	4-Methyl-cyclohexene	24	65	89
4	Cyclooctene	24	46	76
5	Styrene	24	45	94
6	Oct-1-ene	24	67	78
7	Vinyl acetate	24	59	35

^{a}Degree of conversion determined by ^{1}H nmr. ^{b}For typical procedure, see ref. 5.

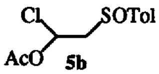
Acetylation of the β-hydroxysulfoxide adducts derived from cyclopentene and cyclohexene provided evidence for the stereochemistry of these products (**Equation 2**) being as shown (the sulfoxide stereochemistry is undefined, though appears as a single diastereoisomer by n.m.r.) and retaining the original α-chlorosulfoxide stereochemistry.[5]

Equation 2.

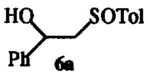




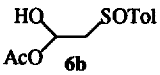
5a



5b



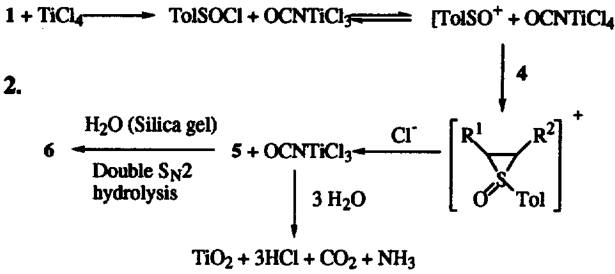
6a



6b

Both the regiospecificity[6] (shown by adducts **5a** and **b**, and **6a** and **b**) and the stereospecificity (shown by acetates **7**), point to a simple mechanistic explanation whereby the reaction of titanium(IV) chloride with tosyl cyanide results in the formation of a new reagent, that is (formally) a tolylsulfinyl electrophile equivalent (possibly a trichloro titanium(IV) isocyanate complex[7]), as shown in **Scheme 2**. Attack of this species on the alkenes **4** and trapping of the incipient carbenium ion equivalent with chloride ion, can give adducts **5**. Subsequent exposure to silica gel results in double S_N2 hydrolysis *via* anchimeric assistance from the sulfoxide function, which would then provide *trans*-hydroxy products **6**. This is supported by isolation of the *trans*-acetates **7**. A possible explanation for these events is shown in **Scheme 2**. Interestingly, overall the product has four-valent sulfur, while that of tosyl cyanide is six-valent. This is also a feature of the cycloaddition chemistry and may be a characteristic feature of the reactivity of tosyl cyanide.

Scheme 2.



Consistent with the above mechanism are the few reports of the Lewis-acid catalysed addition of (aryl) sulfinyl halides to alkenes.[8] Significantly, in all those procedures, the generation of an air-sensitive sulfinyl chloride was required. It appears from the results presented here, that *in situ* generation of an aryl sulfinyl chloride equivalent, by the activation of tosyl cyanide with titanium(IV) chloride, is a convenient alternative to existing methods. Subsequent addition to alkenes allows clean conversion to β-chloro and β-hydroxysulfoxides. It is also worth noting that this reaction can generate up to three new chiral centres (including the sulfoxide centre) and perhaps could be adapted to an asymmetric process with judicious choice of asymmetric catalyst. Endeavours along this line of approach are underway.

Acknowledgements.

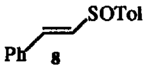
We thank the EPSRC for a studentship (to P.E.M.) and Chiroscience for additional funding.

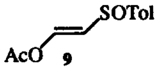
References.

1. a) "Hetero Diels-Alder Methodology in Organic Synthesis", Boger, D.L.; and Weinreb, S.M.; Organic Chemistry Monographs; Vol. 47, Academic Press, San Diego, 1987; b) Meyers, A.I.; in "The chemistry of the cyano group", Patai, S.; and Rappoport, Z.; Interscience, London, 1970, 356; c) Rüffer, U.; and Breitmair, E.; *Synth.*, **1989**, 623; d) Weinreb, S.M.; and Smith, R.R.; *Tetrahedron*, **1982**, *38*, 3087; e) Pews, P.G.; Nyquist, E.B.; and Corson, F.P.; *J. Org. Chem.*, **1970**, *35*, 4096; f) Jagt, J.C.; and Van Leusen, A.M.; *Recl. Trav. Chim. Pays-Bas*, **1973**, *82*, 1343; g) *idem*, *J. Org. Chem.*, **1974**, *39*, 564; h) Daluge, S.; and Vince, R.; *J. Org. Chem.*, **1978**, *43*, 2311.
2. Morgan, P.E.; McCague, R.; and Whiting, A.; *J. Chem. Soc., Chem. Commun.*, **1996**, 1811.
3. In the presence of Et_2AlCl and racemic binaphthol, a 20 % yield of the [2+2]-adduct **2** was obtained, but none of the normal product **3**: Morgan, P.E.; McCague, R.; and Whiting, A.; unpublished results.
4. Malpass, J.R.; and Tweddle, N.J.; *J. Chem. Soc., Perkin Trans. 1*, **1977**, 874.
5. Procedure: $TiCl_4$ (1 eq.) was added to a stirred solution of **4** (1.1 eq.) and **1** (1 eq.) in CH_2Cl_2, at 0°C. After 8-24 h, the mixture was quenched with H_2O, separated, dried ($MgSO_4$) and evaporated to give **5** as pale yellow oils. Conversion of the tosyl cyanide was determined by the comparison of the tolyl methylene signal at δ 2.24 in the ^1H nmr. Silica gel chromatography of the crude α-chlorosulfoxide **5**

(EtOAc:hexanes, 4:6 as eluant) resulted in isolation of the corresponding α-hydroxysulfoxide **6**. All compounds had satisfactory analytical and spectroscopic data, complimentary with the structures shown, particularly, *all* chlorides showed clean molecular ions which correctly measured accurate masses. Selected ^{1}H n.m.r. data, δ: **5** (from cyclopentene) 3.75 (1H, m, CH.SO), 4.20 (1H, dt, *J* 8 and 3 Hz, CH.Cl); **5** (from cyclohexene) 3.65 (1H, m, CH.SO), 4.12 (1H, dt, *J* 5 and 10 Hz, CH.Cl); **6c** 3.32 (1H, dt, *J* 7 and 4 Hz, CH.SO), 4.08 (1H, m, CH.OH); **6d** 2.59 (1H, dt, *J* 5 and 10 Hz, CH.SO), 3.19 (1H, dt, *J* 5 and 10 Hz, CH.OH); **7a** 3.50-3.56 (1H, m, CH.SO), 5.03 (1H, dt, *J* 6 and 3 Hz, CH.OAc); **7b** 3.04 (1H, dt, *J* 9 and 4 Hz, CH.SO), 4.75 (1H, dt, *J* 9 and 4 Hz, CH.OAc).

6. The regiospecific formation of **5a** and **5b** is indicated by the fact that direct elimination (NaOH) results of clean unambiguous formation of the corresponding *E*-vinylsulfoxides **8** and **9** respectively: Morgan, P.E.; McCague, R.; and Whiting, A.; unpublished results.


8


9

7. Quenching of the TsCN/TiCl$_4$/alkene reaction with water results in effervescencent formation of CO$_2$, which supports the idea of formation of a titanium(IV) isocyanate complex.
8. a) Vorob'eva, I.S.; and Stadnichuk, M.D.; *Zh. Obsch. Khim.*, **1984**, *54*, 2064; b) Glaros, G.; and Sullivan, S.; *Synth. Commun.*, **1976**, *6*, 495.