Pergamon

Tetrahedron Letters 42 (2001) 6425–6428

TETRAHEDRON
LETTERS

Highly selective cross-metathesis with phenyl vinyl sulphone using the 'second generation' Grubbs' catalyst

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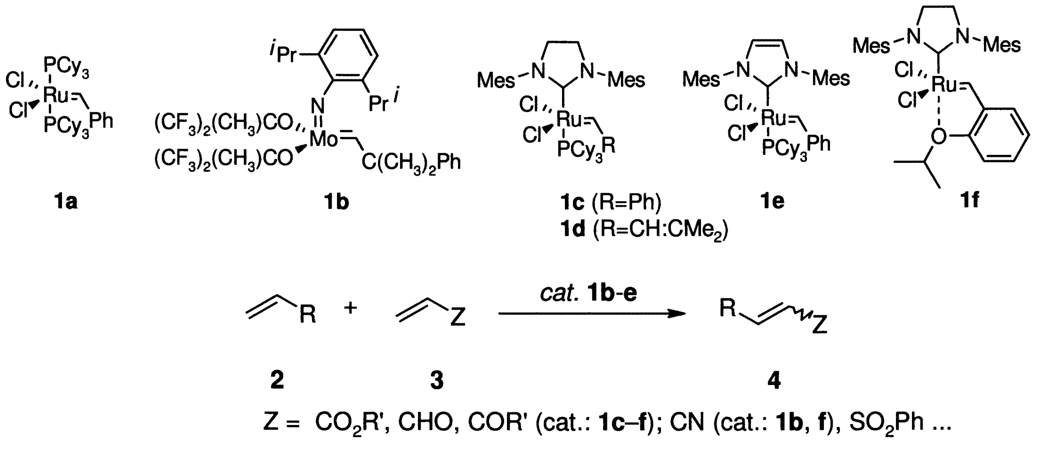
Received 30 May 2001; revised 5 July 2001; accepted 13 July 2001

Abstract—A cross-metathesis reaction was achieved between functionalised terminal olefins and phenyl vinyl sulfone by using the commercially available ruthenium catalyst **1c**. The cross-metathesis products were isolated in moderate to good yield with excellent (*E*)-stereoselectivity. © 2001 Elsevier Science Ltd. All rights reserved.

During recent years, olefin metathesis has gained a position of increasing significance.[1] The ruthenium carbene **1a** developed by Grubbs et al. constitutes a highly efficient metathesis pre-catalyst tolerating most functional groups. In spite of the generally superb application profile of the ruthenium carbene **1a**, its limited thermal stability and the low activity towards substituted double bonds are major drawbacks. Specifically, the preparation of substituted olefins with electron-withdrawing functionality, such as α,β-unsaturated carbonyl compounds, nitriles, etc., via cross metathesis with terminal alkenes (Scheme 1) remains a difficult task.[1]

Crowe and Goldberg[2] demonstrated that acrylonitrile, unreactive towards Grubbs' catalyst **1a**, readily participates in cross-metathesis reactions catalysed by the more active Schrock alkylidene **1b**.[1c] Other olefins, such as acrylic acid esters and enones also fail to react with **1a** and are not functional group compatible with the very sensitive catalyst **1b**.

The newly-introduced highly active ruthenium alkylidene complexes with sterically demanding *N*-heterocyclic carbene (NHC)[3] ligands have dramatically alleviated this limitation.[4] Complexes of type **1c**–**f** were found to catalyse efficiently reactions of previously metathesis-inactive substrates, including α,β-unsaturated carbonyl compounds.[5]



Scheme 1. Cross-metathesis with electron deficient olefins.

Keywords: carbene complex; olefin metathesis; sulfone; ruthenium; homogenous catalysis.

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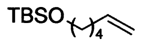
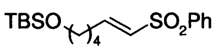
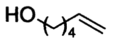
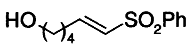
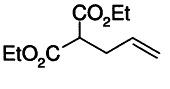
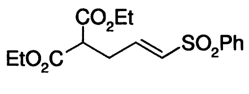
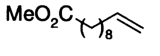
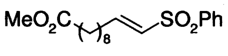
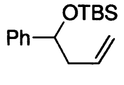
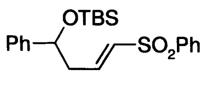
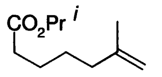
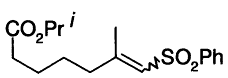
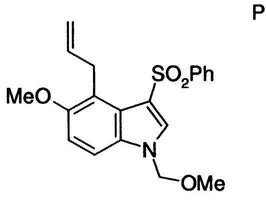
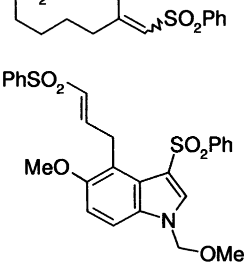
PII: S0040-4039(01)01269-2

Grubbs et al. have shown recently that the 'second generation' catalyst **1d**, which contains a 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ligand, readily promotes the cross-metathesis reaction of terminal olefins with α,β-unsaturated aldehydes, ketones and esters (Scheme 1).[5b] The authors have noted, however, that other electron deficient substrates, such as *vinyl sulfones* and *acrylonitriles*[6] are not reactive in cross-metathesis using **1d**.[5b] The compatibility of remote sulfone and sulfoxide functions in the standard metathesis reactions is well established,[7] but according to our best knowledge the successful metathesis of vinyl sulfones has not yet been reported.[8] Substituted α,β-unsaturated sulfones are generally well accepted as useful intermediates in organic synthesis. Thus, vinyl sulfones serve efficiently, e.g. as Michael acceptors and as 2π partners in cycloaddition reactions. In addition, the stability and ease of further transformation of the sulfonyl group via elimination or either reductive or alkylative desulfonylation renders further advantages to vinyl sulfones as synthetic intermediates.[9]

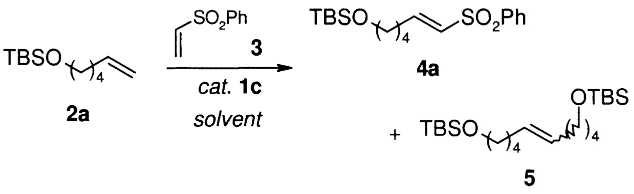
Therefore, we decided to investigate the cross-metathesis of readily available phenyl vinyl sulfone with terminal olefins. In this communication, we report the single-step synthesis of functionalised α,β-unsaturated sulfones catalysed by the commercially available[10] Grubbs' alkylidene **1c**.

Test reactions between olefin **2a** (1 equiv.), phenyl vinyl sulfone **3** (2 equiv.) and complexes **1a** and **1c** (0.10 equiv.) were performed under argon, at 45°C in dichloromethane. The 'classical' Grubbs' alkylidene **1a** did not react under these conditions. However, in the case of the NHC–ruthenium complex **1c**; the corresponding product **4a** was formed after 15 h in quantitative yield (>99%) and with excellent stereoselectivity as the (*E*)-isomer was the only product detected by GC and NMR. Under such conditions, we observed the initial formation of a small amount of the homodimer **5** which *decreased* during prolongation of the reaction time (Scheme 2). However, in the absence of vinyl sulfone **3**, the dimerisation product **5** was formed almost quantitatively instead.

Table 1. Cross-metathesis between olefins **2a**–**g** and phenyl vinyl sulfone **3**

Entry	Olefin 2	Product 4	Yield (%) [a]
a			85 [b]
b			81 [c]
c			74
d			76 [d]
e			55 [c]
f			0 [c, e]
g			33 [c, f]

a. Isolated yields of analytically pure compounds. All reactions were carried out with 5 mol.% of **1c** in refluxing CH_2Cl_2 for 3-24 h, unless stated otherwise; b. TBS = *tert*-butyldimethylsilyl; c. with 10 mol.% of **1c**; d. GC-yield e. 87% of **2f** was recovered after the reaction; f. 67% of unreacted **2g** was recovered.



Ratio (mol.) 2a	3	1c	Conditions	Yield (%) [a] 4a	5
1	2	0.10	PhMe; 50 °C	86	5
1	2	0.10	Et_2O; reflux	80 (90)	20 (10)
1	2	0.10	CH_2Cl_2; reflux	92 (>99)	8 (<1)
1	3	0.05	CH_2Cl_2; reflux	82	0
1	1	0.05	CH_2Cl_2; reflux	57	17
1	0	0.05	CH_2Cl_2; reflux	(0)	(>95)

a. Yields based on GC after 3 h of the reaction. Data in parentheses are the GC yields after 15 h of reaction.

Scheme 2. Selected results of the cross-metathesis of **2a**.

Using the model reaction of olefin **2a** we have further studied the effect of ratio of the reagents and conditions on this transformation (Scheme 2). We have found that the optimal conditions for the sulfone cross-metathesis are: ratio of the reagents **2**:**3**:**1c** as 1:2:0.05 in refluxing dichloromethane as the solvent.

Under such conditions the reaction of terminal alkenes **2a**–**e** with commercially available[10] sulfone **3** proceeds smoothly to give the corresponding products **4a**–**e** in moderate to good yields.[11,12] In all reported cases the (*E*)-alkene was the only isomer detected by GC/MS and NMR. Dimerisation products of the terminal olefin were observed in only trace amounts. Unprotected alcohol **2b** and highly C–H acidic malonic ester **2c** were converted in good yields. Somewhat lower yields were obtained from sterically crowded substrates such as **2e** and **g** (Table 1). The geminal disubstituted olefin (entry f) did not react, as ester **2f** was recovered after the reaction almost quantitatively (87%), suggesting that the cross-metathesis of phenyl vinyl sulfone is very sensitive to steric hindrance.

In conclusion, the use of the robust catalyst **1c** and readily available sulfone **3**[10] demonstrates the applicability of cross-metathesis for the preparation of synthetically useful, functionalised α,β-unsaturated sulfones with excellent stereoselectivity under mild conditions. Further studies in the field of cross-metathesis of substituted vinyl sulfones and sulfoxides are in progress in our laboratory.

Acknowledgements

M.B. thanks the Institute of Organic Chemistry for a scholarship. We thank Mr. Igor Prowotorow for the providing the sample of ester **2f** and Dr. Jacek Stalewski for the preparation of **2g**.[13]

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6. For a few examples of successful RCM of dienes containing an α-substituted α,β-unsaturated nitrile function catalysed by **1c**, see: Ref. 5c. However, according to the authors, the acrylonitrile itself does not react with terminal olefins in the presence of **1c**. The latter transformation is only possible when phosphine free complex **1f** is used instead. See: Refs. 5c,d.
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10. Catalyst **1c** is available from Strem Chemicals. Cf. also: *The Strem Chemiker* **2000**, *1*, 30; Sulfone **3** is available from Aldrich Chemical Co.
11. All described new compounds were characterised by ^{1}H and ^{13}C NMR, IR, MS and combustion or HRMS analysis.
12. General procedure for cross-metathesis reactions with phenyl vinyl sulfone: To a mixture of **2a** (53.6 mg, 0.25 mmol) and vinyl sulfone **3** (84.1 mg, 0.50 mmol) in dichloromethane (15 mL) was added a solution **1c** (10.6 mg, 5 mol%) in dichloromethane (5 mL). The resulting mixture was stirred at 45°C for 15 h. The solvent was removed under reduced pressure. Flash chromatography (*c*-hexane/EtOAc 8:2 v/v) of the crude brown residue gave 75.1 mg of **4a** (85%). Colourless oil: IR (film): 2952, 2931, 2858, 1447, 1321, 1148, 1088, 835 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.03 (s, 6H, $(CH_3)_2Si$), 0.88 (s, 9H, $(CH_3)_3C$), 1.46–1.60 (m, 4H, $(CH_2)_2$), 2.20–2.35 (m, 2H, CH_2), 3.53–3.62 (m, 2H, CH_2O), 6.32 (tt, $J=15.1$, 1.5 Hz, 1H, $CH=CHSO_2Ph$), 7.00 (tt, $J=15.1$, 6.8 Hz, 1H, $CH=CHSO_2Ph$), 7.47–7.67 and 7.83–7.93 (2m, 5H, Ph); ^{13}C NMR (50 MHz, $CDCl_3$): δ −5.37, 18.26, 24.02, 25.89, 31.22, 32.01, 62.49, 127.50, 129.18, 130.43, 133.16, 140.72, 147.00; MS (EI): *m*/*z* 339 (4, $[M-15]^+$), 297 (100), 217 (1), 199 (10), 135 (49), 125 (5), 81 (5), 79 (5), 75 (12), 61 (2), 55 (1); HRMS (LSIMS) calcd for $[M+H]^+$ ($C_{18}H_{31}O_3SSi$): 355.1763. Found: 355.1768.
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