Reaction of Arylsulfonylhydrazones of Aldehydes with α-Magnesio Sulfones. A Novel Olefin Synthesis

Alicja Kurek-Tyrlik, Stanislaw Marczak, Karol Michalak, Jerzy Wicha,* and Andrzej Zarecki

Institute of Organic Chemistry, Polish Academy of Sciences, ul. Kasprzaka 44, 01-224 Warsaw, Poland

jwicha@icho.edu.pl

Received April 20, 2001

Reactions of representative tosylhydrazones of aldehydes and ketones with α-metalated sulfones were examined in order to develop a practical olefination method. Treatment of aldehyde tosylhydrazone **2** with an excess of α-lithiated methyl phenyl or dimethyl sulfones yielded **3a**. The reaction of **2** with sterically unhindered lithiated alkyl sulfones gave mixtures of the respective olefination products **3b**−**d** along with the Shapiro fragmentation product **4**. Sterically hindered lithiated sulfones afforded Shapiro products exclusively. In contrast, aldehyde tosylhydrazones **2** or **6** in reactions with a variety of α-magnesio primary or secondary alkyl sulfones gave olefination products **3a**−**j** and **7a**−**c** in high yields (Tables 1 and 2). *β*-Branched alkyl sulfones afforded predominantly (*E*)-alkenes, whereas unhindered primary sulfones gave mixtures of (*E*)- and (*Z*)-alkenes with low selectivity. Reaction of the 2,4,6-triisopropylbenzenesulfonylhydrazone (trisylhydrazone) of cyclodecanone **11c** with α-magnesio methyl phenyl sulfone afforded the methylidene derivative **12a** contaminated with the Shapiro product **13**. Tosylhydrazone **2** resisted reaction with *i*-PrMgCl and gave only a small amount of the addition product in reaction with Bu_2Mg. Some mechanistic aspects of the reaction of tosylhydrazones with organomagnesium compounds are discussed.

Introduction

A number of useful synthetic methods have emerged from reactions of arylsulfonylhydrazones of aldehydes or ketones with organometallic reagents. Most notably, alkyllithium acts as a base, inducing fragmentation of arylsulfonylhydrazones of ketones bearing a proton in the *β* position i (Scheme 1, route a, the Shapiro reaction) to afford the corresponding vinyllithium derivatives iv, which can be protonated or used as synthetic intermediates.[1−4] The reaction involves exchange of the sulfamidic proton with Li^+ to give ii, followed by 1,4-elimination of lithium arylsulfinate and then nitrogen expulsion from the intermediate iii. Some previous reports have indicated that Shapiro fragmentation of ketone tosylhydrazones may be accompanied by reductive alkylation reaction in certain cases [5−9] (Scheme 1, route b). It has been shown[10] that reductive alkylation products (viii, $R^2 = H$) are typically generated in reactions of aldehyde tosylhydrazones (i, $R^2 = H$) with alkyllithiums. Improved synthetic procedures for reductive alkylation, involving initial N-silylation of arylsulfonylhydrazones of aldehydes, have been developed.[11,12] With regard to stabilized organolithium reagents, Vedejs and co-workers[13] have discovered that arylsulfonylhydrazones of aldehydes react with sterically unhindered α-lithio sulfones to afford the corresponding olefins (Scheme 2, route a). However, this olefination reaction was inefficient when branched sulfones were used, owing to competing Shapiro fragmentation.

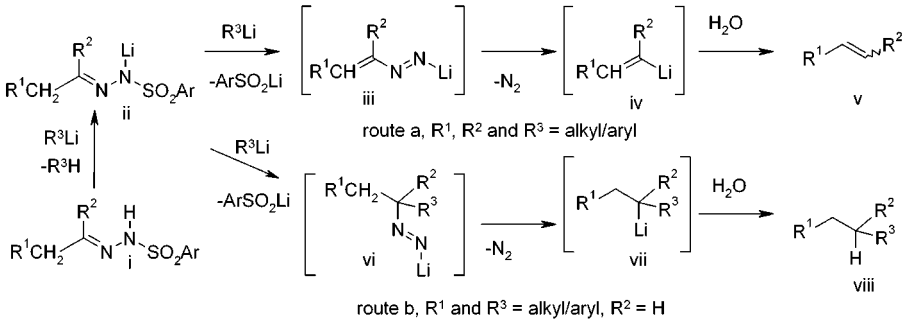
In contrast to plentiful literature on transformations of arylsulfonylhydrazones by organolithium reagents (reactions of lithium cuprates have also been examined[14]), the corresponding organomagnesium reagents have received little attention. Only recently, it was reported that some tosylhydrazones, bearing a leaving group such as an alkoxy or an amino group in the α-position, react with Grignard reagents to yield the corresponding alkenes,[15−18] in a reaction pathway analogous to that with organolithiums.[16,18,19] On the other hand, it was noted that organomagnesium reagents do not react—or react very slowly—with N-silylated tosylhydrazones.[11]

The purpose of this work was to explore the reaction of arylsulfonylhydrazones of aldehydes and, possibly, of

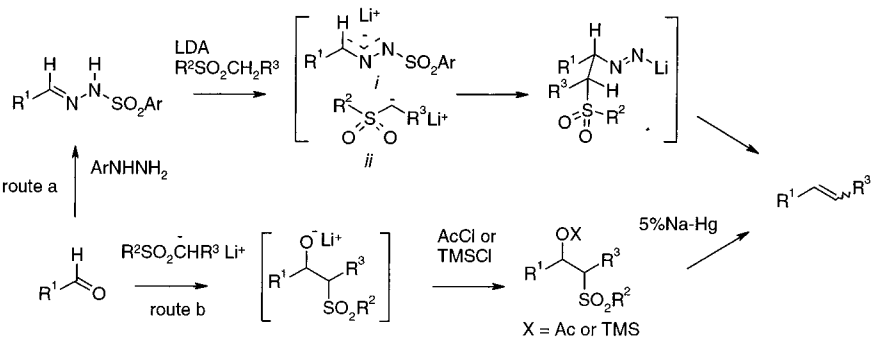
(1) Chamberlin, A. R.; Bloom, S. H. *Org. React. (N.Y.)* **1990**, *39*, 1.
(2) Addlington, R. M.; Barrett, A. G. M. *Acc. Chem. Res.* **1983**, *16*, 55.
(3) Shapiro, R. H. *Org. React. (N.Y.)* **1976**, *23*, 405.
(4) Shapiro, R. H.; Heath, M. J. *J. Am. Chem. Soc.* **1967**, *89*, 5734−5735.
(5) Danieli, B.; Lesma, G.; Mauro, M.; Palmisano, G. *Tetrahedron* **1994**, *50*, 8837−8852.
(6) Srebnik, M.; Mechoulam, R. *Tetrahedron* **1984**, *40*, 3839−3843.
(7) Herz, J. E.; Ortiz, C. V. *J. Chem. Soc. C* **1971**, 2294−2295.
(8) Bessiere-Chretien, Y.; Bras, J.-P. *C. R. Acad. Sc. Paris, Ser. C* **1969**, 221−2224.
(9) Meinwald, J.; Uno, F. *J. Am. Chem. Soc.* **1968**, *90*, 800.
(10) Vedejs, E.; Stolle, W. T. *Tetraheron Lett.* **1977**, 135−138.
(11) Myers, A. G.; Movassaghi, M. *J. Am. Chem. Soc.* **1998**, *120*, 8891−8892.
(12) Myers, A. G.; Kukkola, P. J. *J. Am. Chem. Soc.* **1990**, *112*, 8208−8210.
(13) Vedejs, E.; Dolphin, J. M.; Stolle, W. T. *J. Am. Chem. Soc.* **1979**, *101*, 249−251.
(14) Bertz, S. H. *Tetraheron Lett.* **1980**, *21*, 3151−3154.
(15) Chandrasekhar, S.; Reddy, M. V.; G., R. *Tetrahedron Lett.* **2000**, *41*, 10131−10134.
(16) Yadav, J. S.; Chandrasekhar, S.; Sasmal, P. K. *Tetraheron Lett.* **1997**, *38*, 8765−8768.
(17) Chandrasekhar, S.; Takhi, M.; Yadav, J. S. *Tetraheron Lett.* **1995**, *36*, 307−310.
(18) Chandrasekhar, S.; Takhi, M.; Yadav, J. S. *Tetraheron Lett.* **1995**, *36*, 5071−5074.
(19) Schneider, C.; Kazmaier, U. *Synthesis* **1998**, 1314−1320.

10.1021/jo015699l CCC: $20.00
Published on Web 09/19/2001

Scheme 1



Scheme 2



ketones with α-metalated sulfones.[20] It was expected that conversion of a carbonyl compound into its arylsulfonylhydrazone and the reaction of the latter with α-metalated sulfone might provide a useful alternative to the classical Julia olefination reaction sequence[21−23] (Scheme 2, routes a and b). The same easily accessible starting materials are used in both cases, but the arylsulfonylhydrazone route is shorter and avoids harsh reagents (some modifications of the reduction steps are noteworthy[24−26]). In particular, we were interested in examining the reaction of arysulfonylhydrazones with organomagnesium reagents that are less basic than their lithium counterparts[27] and consequently less prone to indusing the Shapiro fragmentation. On mechanistic grounds, the addition of a metalated sulfone (ii, Scheme 2) to an N-metalated tosylhydrazone (i) bears some resemblance to the carbon−carbon bond-forming sulfonyl anion−sulfonyl anion coupling reaction[28−30] and other anion−anion reactions that have attracted considerable attention recently.[31−36]

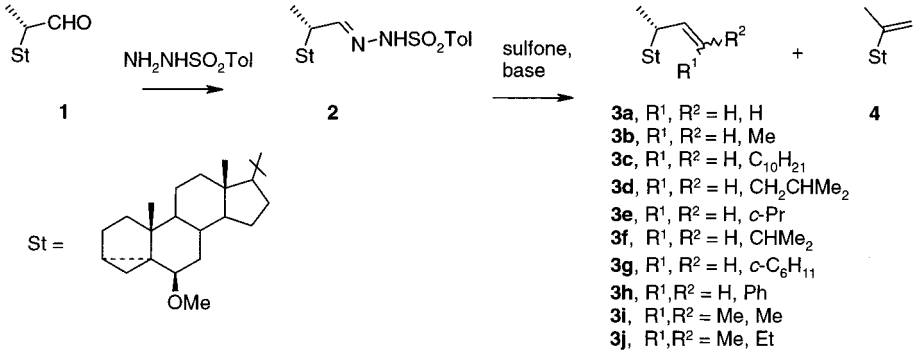
Results and Discussion

The olefination reaction was examined using aldehyde tosylhydrazones **2** (Scheme 3) and **6** (Scheme 4) and a variety of sulfones. The derivative **2** was prepared from aldehyde **1** (several procedures for preparation of this compound are available[37−40]), which is readily accessible from stigmasterol via *i*-stigmasteryl methyl ether.[41] It was crystalline and could be stored for several weeks without decomposition. Tosylhydrazone **6** was prepared from commercially available 3*β*-acetoxychol-5-en-24-oic acid via aldehyde **5**.[42] The derivative **6** was unstable and was used immediately after preparation. Tosylhydrazone **2** was obtained as the pure *E* isomer,[43] whereas compound **6** was obtained as a mixture of geometric isomers in a ratio of 3:1 as evidenced by its ^{1}H and ^{13}C NMR spectra. The C=N bond in **2** is sterically rather hindered, owing to chain branching and the proximity of the cyclic system, whereas that in **6** is unhindered.

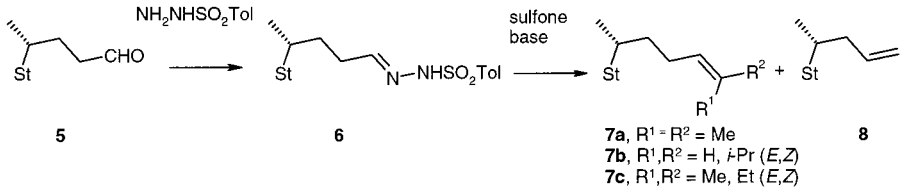
Reaction of Arylsulfonylhydrazones with α-Lithiated Sulfones. The reaction of tosylhydrazones **2** and **6** with selected lithiated sulfones was first examined under the conditions analogous to those described by Vedejs and co-workers.[13] Treatment of **2** with an excess of lithiated

(20) Preliminary communication: Kurek-Tyrlik, A.; Marczak, S.; Michalak, K.; Wicha, J. *Synlett* **2000**, 547−549.
(21) Julia, M.; Paris, J.-M. *Tetrahedron Lett.* **1973**, 4833−4836.
(22) Kocienski, P. J.; Lythgoe, B.; Ruston, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1290−1293.
(23) For new sulfone-based olefination reactions, see: Blakemore, P. R.; Cole, W. J.; Kocienski, P. J.; Morley, A. *Synlett* **1998**, 26−28.
(24) Kende, A. S.; Mendoza, J. S. *Tetrahedron Lett.* **1990**, *31*, 7105−7108.
(25) Barton, D. H. R.; Jaszberenyi, J. C.; Tachdjian, C. *Tetrahedron Lett.* **1991**, *32*, 2703−2706.
(26) Lee, G. H.; Lee, H. K.; Choi, E. B.; Kim, B. T.; Pak, C. S. *Tetrahedron Lett.* **1995**, *36*, 5607−5608.
(27) Wakefield, B. J. *Organomagnesium Methods in Organic Chemistry*; Academic Press: San Diego, 1995.
(28) Daub, I.; Hebermann, A.-K.; Hobert, A.; Julia, M. *Eur. J. Org. Chem.* **1999**, 163−165.
(29) Gai, Y.; Julia, M.; Verpeaux, J.-N. *Bull. Soc. Chim. Fr.* **1996**, *133*, 805−816.
(30) Engman, L. *J. Org. Chem.* **1984**, *49*, 3559−3563.
(31) Hoffmann, R. W.; Knopff, O.; Kusche, A. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 1462−1464.
(32) Nakamura, E.; Kubota, K.; Sakata, G. *J. Am. Chem. Soc.* **1997**, *119*, 5457−5458.
(33) Habermann, A.-K.; Julia, M.; Verpeaux, J.-N.; Zhang, D. *Bull. Soc. Chim. Fr.* **1994**, *131*, 965−972.
(34) Lima, C. D.; Julia, M.; Verpeaux, J.-N. *Synlett* **1992**, 133−134.
(35) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933−1940.
(36) Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1986**, *27*, 1039−1043.
(37) Hutchins, R. F. N.; Thompson, M. J.; Svoboda, J. A. *Steroids* **1970**, *15*, 113−130.
(38) Jung, M. E.; Johnson, T. W. *Tetrahedron* **2001**, *57*, 1449−1481.
(39) Nagano, H.; Matsuda, M.; Yajima, T. *J. Chem. Soc., Perkin Trans. 1* **2001**, 174−182.
(40) Spencer, T. A.; Li, D.; Russel, J. S. *J. Org. Chem.* **2000**, *65*, 1919−1923.
(41) Steele, J. A.; Mosettig, E. *J. Org. Chem.* **1963**, *28*, 571−572.
(42) Wechter, W. J. U.S Patent 3,152,152; *Chem. Abstr.* **1964**, *61*, 16135g.
(43) Structure of **2** has been confirmed by X-ray analysis; details will be published elsewhere.

Scheme 3



Scheme 4



dimethyl sulfone or lithiated methyl phenyl sulfone afforded the expected olefination product **3a** (Table 1, entries 1 and 2). However, even a slight increase in the sulfone steric bulk resulted in concomitant formation of addition and fragmentation products. Thus, the reaction of **2** with lithium derivatives of diethyl sulfone or ethyl phenyl sulfone gave **3b** along with ca. 10% of **4** (Table 1, entries 3 and 7). In the reactions of **2** with lithium derivatives of phenyl undecyl sulfone and 3-methylbutyl phenyl sulfone, the fragmentation product **4** predominated (Table 1, entries 10 and 12). Treatment of **2** with lithiated phenyl isopropyl sulfone afforded compound **4** in a 95% yield (Table 1, entry 20). The reaction of less hindered tosylhydrazone **6** (Scheme 4) with lithium derivatives of diisopropyl or phenyl isopropyl sulfones consistently afforded a mixture of addition and fragmentation products **7a** and **8**, respectively (Table 2, entries 1 and 4). It is noteworthy that the reaction of tosylhydrazone **2** with butyllithium (THF−hexane, −20 °C) proceeds almost instantly to give the reductive alkylation product **9** (86% yield, Scheme 5).

Reaction of Arylsulfonylhydrazones with Organomagnesium Reagents. We commenced our studies with an evaluation of relative reactivity of a Grignard reagent, dialkylmagnesium, and α-magnesio sulfones toward tosylhydrazones. Tosylhydrazone **2** in THF at room temperature was treated with 3 molar equiv of *i*-PrMgCl. After 24 h, the reagent excess was destroyed, and organic material was isolated and shown to comprise unchanged **2** (70%) and a newly formed product (14% yield), which was assigned as the nitrile **10**[44] (Scheme 5). Base-induced transformation of an aldehyde tosylhydrazone into the corresponding nitrile has previously been recorded.[10,13] The treatment of **2** in THF−hexane with Bu_2Mg at room temperature for 22 h gave the reductive alkylation product **9** (Scheme 5) in a 28% yield along with starting material (48% yield). Remarkably, when *i*-PrMgCl (3 molar equiv) was added to a mixture of tosylhydrazone **2** and diethyl sulfone (3 molar equiv), the olefination products **3b** could be detected (TLC) almost instantly. After the reaction was complete, **3b** was obtained in a 86% yield.

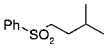
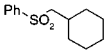
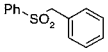
The foregoing experiments revealed important differences in the reaction of tosylhydrazones with the organometallic reagents: α-magnesio sulfones undergo smooth olefination in those cases where the α-lithio sulfones induce fragmentation. Moreover, the high reactivity of tosylhydrazones toward α-magnesio sulfones contrasts sharply with the sluggishness of their reaction with alkylmagnesiums.

In the course of further investigations, Bu_2Mg or *i*-PrMgCl was used to generate magnesium derivatives of sulfones. Deuterium labeling experiments indicated that primary sulfone metalation occurs in 30−45 min at room temperature when Bu_2Mg is used (1 molar equiv) and in 1−1.5 h with *i*-PrMgCl (1 molar equiv). In all reactions, an excess of a metalated sulfone was used to account for an exchange of the tosylhydrazone proton for the metal cation. Preliminary experiments showed that an excess of sulfone is needed to achieve complete consumption of arylsulfonylhydrazone. The best results were obtained when an arylsulfonylhydrazone was treated in THF at room temperature with a sulfonyl anion prepared from 3 molar equiv of a sulfone and 3 molar equiv of Bu_2Mg. Under these conditions, the reaction of tosylhydrazone **2** with unhindered sulfones was typically completed within 4 h. Upon generation of the sulfonyl anion with 0.5 molar equiv of Bu_2Mg, lower yields of alkylation products were obtained and the reaction was slower (approximately 16 h were needed for consumption of the tosylhydrazone). Alternatively, the sulfonyl anion was generated from a sulfone and 3 molar equiv of *i*-PrMgCl. The reactions of **2** with diethyl sulfone (Table 1, entries 4−6) are illustrative for various methods of anion generation.

The reactions of tosylhydrazone **2** with magnesium derivatives of representative sulfones were examined. Unbranched primary alkyl sulfones and the γ-branched sulfone afforded uniformly excellent yields of the respective olefination products (Table 1, entries 4−6, 8, 9, 11, and 13). Phenyl cyclopropylmethyl sulfone afforded the product **3e** in 94% or 89% yields (Table 1, entries 14 and

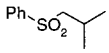
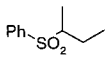
(44) Khripach, V. A.; Zhabinskii, V. N.; Kotyatkina, A. I. *Zh. Org. Khim.* **1993**, *29*, 1569−1572.

Table 1. Reaction of Tosylhydrazone 2 with α-Metalo Sulfones[a] According to Scheme 3

	Sulfone	Base	Product(s)	Yield (%)	2/3 ratio	*E*/*Z* ratio[b]
1		BuLi	**3a**	93	-	-
2		BuLi	**3a**	93	-	-
3		BuLi	**3b/4**	88	9:1	**3b**, 4:1
4		Bu_2Mg	**3b**	87	-	**3b**, 1:2
5		Bu_2Mg[c]	**3b**	77	-	**3b**, 1:2
6		*i*-PrMgCl	**3b**	86	-	**3b**, 1:2
7		BuLi	**3b/4**	88	9:1	**3b**, 4:1
8		Bu_2Mg	**3b**	94	-	**3b**, 1:2
9		*i*-PrMgCl	**3b**	96	-	**3b**, 1:2
10		BuLi	**3c/4**	85	1:9	**3c**, 1:1
11		Bu_2Mg	**3c**	90	-	**3c**, 1:1[d]
12		BuLi	**3d/3**	90	1:4	**3d**, 1:1[d]
13		Bu_2Mg	**3d**	80	-	**3d**, 1:1
14		Bu_2Mg	**3e**	94	-	**3e**, 1:3
15		*i*-PrMgCl	**3e**	89	-	**3e**, 1:1.2
16		Bu_2Mg	**3f**	85	-	**3f**, 7:1
17		Bu_2Mg	**3g**	68	-	**3g**, 12:1
18		Bu_2Mg	**3h**	60	-	**3h**, 2:1
19		Bu_2Mg	**3i**	80	-	-
20		BuLi	**4**	95	-	-
21		Bu_2Mg	**3i**	85	-	-
22		Bu_2Mg	**3j**	50	-	**3j**, 4:1

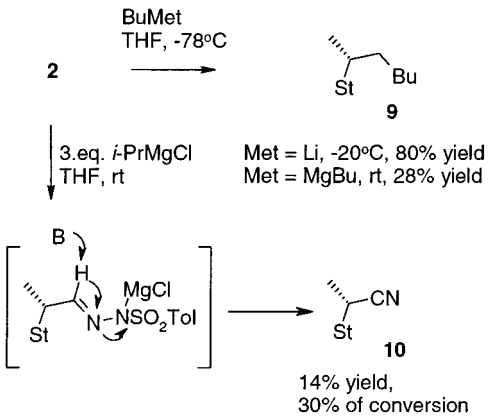
[a] α-Metalo sulfones were generated from sulfones and 1 molar equiv of butyllithium or the alkylmagnesium regents. [b] Isomer ratios were determined by GC, except where otherwise indicated. [c] 0.5 molar equiv of dibutylmagnesium was used. [d] Isomer ratio was determined from ^{1}H NMR spectra.

Table 2. Reaction of Tosylhydrazone 6 with α-Metalo Sulfones[a] According to Scheme 4 (Procedure A, with Isolation of 6; Procedure B, without Isolation of 6, Yields from Aldehyde 5)

	Sulfone	Base	Procedure	Product(s)	Yield(%)	**7**, *E*/*Z* ratio
1		BuLi	A	**7a/8**, 4:1	78	-
2		Bu_2Mg	A	**7a**	81	-
3		*i*-PrMgCl	A	**7a**	85	-
4		BuLi	A	**7a/8**, 2.3:1	80	-
5		Bu_2Mg	A	**7a**	84	-
6		*i*-PrMgCl	A	**7a**	89	-
7		Bu_2Mg	B	**7a**	94	-
8		Bu_2Mg	A	**7b**	81	1.5:1[b]
		i-PrMgCl	A	**7b**	75	1:1.2
9		Bu_2Mg	B	**7b**	85	1.5:1
10		Bu_2Mg	A	**7c**	61	1.7:1
11		*i*-PrMgCl	A	**7c**	57	2:1
12		Bu_2Mg	B	**7c**	68	1.8:1

[a] α-Metalo sulfones were generated from sulfones and 1 molar equiv of butyllithium or the alkylmagnesium regents. [b] Isomer ratios were determined by GC, first is given isomer with shorter t_R.

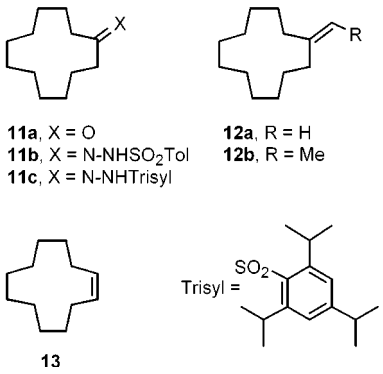
Scheme 5



15). The reactions of **2** with β-branched sulfones were markedly slower, requiring 16 h for consumption of the starting material. Nevertheless, when the reaction was carried out with strict preclusion of air and using freshly distilled isobutyl phenyl sulfone, product **3f** was obtained in an 85% yield (Table 1, entry 16). Cyclohexylmethyl phenyl sulfone gave **3g** in a 68% yield (Table 1, entry 17). The reaction of **2** with benzyl phenyl sulfone gave the derivative **3h** in 60% yield (Table 1, entry 18). Lower yields of alkenes **3f**, **3g**, and **3j** presumably reflect the combined effect of steric hindrance in both reactants, the respective sulfone and the tosylhydrazone **2**. Indeed, reaction of the magnesium derivative of isobutyl phenyl sulfone with unhindered tosylhydrazone **6** was completed within 4 h to afford olefin **7b** in 81% yield (Table 2, entry 8). Reactions of tosylhydrazones **2** or **6** with isopropyl sulfones proceeded smoothly to give the corresponding trisubstituted olefins **3i** or **7a** (Table 1, entries 19 and 21; Table 2, entries 2, 3 5).

The foregoing observations on the relative rates of the reaction of isopropyl sulfone and isobutyl sulfone were verified in a competition experiment. Thus, a mixture of isopropyl and isobutyl phenyl sulfones, 0.3 mmol of each, in THF was treated with 0.6 mmol of Bu_2Mg in hexane, followed by tosylhydrazone **2** (ca. 0.1 mmol). A mixture of products **3f** and **3i** was obtained in a ratio of 1:20 (by GC), respectively. An analogous experiment with tosylhydrazone **6** yielded olefins **7a** and **7b** in a ratio of 10:1. These experiments suggest that branching in the α-position of the sulfone has less effect on the reaction (cf. Table 1, entries 8 and 21) than branching in the β-position (cf. Table 1, entries 11 and 16). The reaction of **2** with *sec*-butyl phenyl sulfone afforded **3j** in a 50% yield (Table 1, entry 22).

Scheme 6



The olefination procedure, as described above, involves two steps: transformation of an aldehyde into the corresponding tosylhydrazone and the reaction of the latter with α-magnesio sulfones. In principle, condensation of an aldehyde with arylsulfonyl hydrazide should provide the product quantitatively. However, sterically unhindered tosylhydrazones such as **6** are often isolated in rather low yields, due to their instability.[45] A one-pot olefination procedure omitting tosylhydrazone isolation would present an advantage in such cases. To this end, it was found that the treatment of aldehyde **5** in THF at room temperature with 1 molar equiv of *p*-toluenesulfonyl hydrazide followed (after 45 min) by treatment with the reagent prepared from isopropyl phenyl sulfone (3 molar equiv) and dibutylmagnesium (3 molar equiv) afforded alkene **7a** in a 94% yield (Table 2, entry 7). Under similar conditions, **5** was transformed into alkenes **7b** or **7c** in 85% and 68% yields, respectively (Table 2, entries 9 and 12), without isolation of **6**. It is noteworthy that water generated in the condensation step had no effect on the overall outcome of the reaction.

The results presented above allow for some comments on the stereochemistry of the alkenylation reaction. The differences in the reactions of lithio and magnesio sulfones with tosylhydrazone **2** are apparent: the lithium derivative of diethyl and ethyl phenyl sulfones gave predominantly *E* products (although in low yields, Table 1, entries 3 and 7), whereas magnesium derivatives favor formation of *Z*-products (Table 1, entries 4, 5, 8, and 9). Magnesio sulfones with a longer unbranched alkyl chain or a side chain branched in the β position (Table 1, entries 11 and 13) gave mixtures of (*E*)- and (*Z*)-alkenes with low selectivity. Branching at the β-position resulted in predominant formation of an (*E*)-alkene (only one example was examined; Table 1, entry 22). The highest *E*-selectivity was observed for sulfones in which the alkyl group was branched at the β position (Table 1, entries 16 and 17). However, cyclopropylmethyl phenyl sulfone afforded a product consisting of *E*- and *Z*-isomers in a ratio of 1:3 with Bu_2Mg (Table 1, entry 14) and in a ratio of 1:1.2 with *i*-PrMgCl (Table 1, entry 15). Reactions of hydrazone **6** (*E*- and *Z*-isomers, 3:1) afforded olefins as mixtures of geometric isomers with low selectivity.

The results obtained in olefination of aldehydes via their tosylhydrazones prompted us to examine olefination of ketones in an analogous way. Cyclododecanone **11a** (Scheme 6) was chosen as a model. The reaction of cyclodecanone tosylhydrazone **11b** with the reagent generated from Bu_2Mg and dimethyl sulfone was slow and yielded mixtures of olefination and fragmentation products **12a** and **13** (a mixture of *E* and *Z* isomers, Table 3, entry 1). Since 2,4,6-triisopropylbenzenesulfonylhydrazones show higher reactivity than the corresponding tosylhydrazones,[46−48] it was of interest to compare the reaction outcome for the trisylhydrazone **11c**. The reaction of **11c** with the reagents prepared from dimethyl sulfone or methyl phenyl sulfone and *i*-PrMgCl afforded the olefination product **12a** in high yield, contaminated with only a small amount of fragmentation product **13** (Table 3, enties 4−6). However, the magnesio derivative of ethyl phenyl sulfone gave a mixture of **12b** and **13**, in which the latter was the predominant product (Table 3, entry 7).

Table 3. Reactions of Arylsulfonylhydrazones 11b or 11c with α-Magnesio Sulfones Generated from 3 Molar Equiv of Sulfone and 3 Molar Equiv of Organomagnesium Reagent

	hydrazone	sulfone	base	products	yield (%)	ratio[a]
1	**11b**	Me_2SO_2	Bu_2Mg	**12a/13**	50−60[b]	2:1
4	**11c**	Me_2SO_2	Bu_2Mg	**12a/13**	91	9:1
5	**11c**	Me_2SO_2	*i*-PrMgCl	**12a/13**	92	30:1
6	**11c**	$PhSO_2Me$	*i*-PrMgCl	**12a/13**	89	9:1
7	**11c**	$PhSO_2Et$	*i*-PrMgCl	**12b/13**	76	1:4

[a] Determined by GC. [b] 20% of unreacted **11b** was recovered.

The pattern of higher reactivity for α-magnesio sulfones than Bu_2Mg, in addition to the tosylhydrazone C=N bond, contradicts the expectations based upon reactivity of the C=O bond. One possible explanation of the observed discrepancy is illustrated in Scheme 7. The reaction of tosylhydrazone i with dibutylmagnesium affords the proton−metal exchange product ii (for clarity of drawings Mg is localized on the sulfamidic nitrogen). The addition of an external nucleophile to the C=N bond in intermediate ii providing iii is retarded. On the other hand, the reaction of i and α-magnesio sulfone may generate two derivatives, ii and v. The latter may undergo a 1,4-metalate rearrangement, which is facilitated by charge stabilization in the migrating group (CH_2-SO_2R) and concomitant fragmentation of the intermediate vi.

In conclusion, a novel and efficient synthesis of olefins from aldehydes and sulfones based upon the reaction of aldehyde tosylhydrazone with α-magnesio sulfone has been developed. The utility of this method stems from its operational simplicity (one or two step procedures), mildness of the reaction conditions, and use of a phenylsulfonyl group that by virtue of inertness is easy to handle in syntheses of polyfunctional subunits. Reactions involving β-branched primary sulfones afford (*E*)-alkenes with significant stereoselectivity.

Experimental Section[49]

(*E*)-Tosylhydrazone of 3α,5-Cyclo-23,24-dinor-6β-methoxy-5α-cholan-24-al 2. To a stirred solution of **1** (2.24 g, 6.5 mmol) in 96% EtOH (20 mL) was added *p*-toluenesulfonyl hydrazide (1.21 g, 6.5 mmol) at 0 °C. The mixture was set aside at room temperature for 4 h, and then solid K_2CO_3 (2 g) was

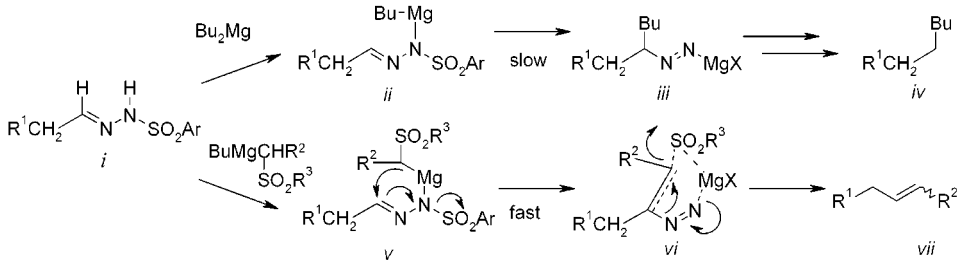
(45) Bertz, S. H.; Dabbagh, G. *J. Org. Chem.* **1983**, *48*, 116−119.

(46) Cusack, N. J.; Reese, C. B.; Risius, A. C.; Roozpeikar, B. *Tetrahedron* **1976**, *32*, 2157−2162.

(47) Jiricny, J.; Orere, D. M.; Reese, C. B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1487−1492.

(48) Chamberlin, A. R. *J. Org. Chem.* **1978**, *43*, 147−154.

Scheme 7



added and stirring was continued for 2 h. The solid was filtered off, and the solvent was evaporated. The residue was chromatographed on SiO_2 (90 g, hexane−EtOAc, 8:2) to give **2** (2.94 g, 91%) as a crystalline mass. A sample was recrystallized from CH_2Cl_2−hexane: mp 162−164 °C; FTIR (KBr) 3193 (NH) cm^{-1}; ^1H NMR 7.79 (d, J = 8.2 Hz, 2H), 7.71 (s, 1H, N*H*), 7.27 (d, J = 8.2 Hz, 2H), 6.98 (d, J = 7.3 Hz, 1H), 3.29 (s, 3H), 2.74 (t, J = 2.6 Hz, 1H), 2.40 (s, 3H) overlapping 2.42−2.20 (m, 1H), 0.98 (s, 3H), 0.98 (d, J = 6.6 Hz, 3H), 0.61 (s, 3H), 0.41 (dd, J = 7.9, 5.1 Hz, 1H)(in other spectra of this compound the N*H* signal appeared between 8.1 and 7.3 ppm); ^{13}C NMR 157.7, 143.9, 135.2, 129.4, 127.9, 82.2, 56.5, 56.1, 53.5, 47.9, 43.3, 42.9, 39.8, 39.5, 35.1, 35.0, 33.3, 30.3, 27.1, 24.8, 24.1, 22.6, 21.5, 21.4, 19.2, 17.3, 13.0, 12.4; HRMS calcd for $C_{30}H_{45}O_3N_2S$ 513.31509 (M^+), found 513.31749.

(*E*)- and (*Z*)-Tosylhydrazones of 3α,5-Cyclo-6*β*-methoxy-5α-cholan-24-al 6. To a stirred solution of methyl 3α,5-cyclo-6*β*-methoxy-5α-cholan-24-oate[42] (250 mg, 0.62 mmol) in toluene (1.5 mL) was added DIBALH (1.2 M in toluene, 0.62 mL, 0.74 mmol) dropwise at −78 °C. The mixture was stirred −78 °C for 45 min, and then the reaction was quenched with a mixture of Et_2O−AcOH−H_2O (10:4:1, 0.35 mL). The product was isolated with Et_2O and chromatographed on SiO_2. Aldehyde **5**[42] was obtained (214 mg, 92% yield): ^1H NMR 9.77 (s, 1H), 3.32 (s, 3H), 2.79 (m, 1H), 2.41 (m, 2H), 1.02 (s, 3H), 0.94 (d, J = 6.1 Hz, 3H), 0.72 (s, 3H). To a stirred solution of the aldehyde **5** (742 mg, 2.00 mmol) in 96% EtOH (20 mL) was added *p*-toluenesulfonyl hydrazide (459 mg, 2.47 mmol) at −20 °C. The mixture was allowed to warm to room temperature over 2 h and then set aside for 4 h. Solid K_2CO_3 (0.5 g) was added; the suspension was stirred for 2 h and filtered. The solvent was evaporated at room temperature, and the residue was chromatographed on SiO_2 (45 g, hexane−EtOAc, 8:2) to give **6** as a foam (1.05 g, 90% yield): ^1H NMR, major isomer, 7.88−7.76 (m, 2H), 7.5 (br. s, 1H, NH), 7.36−7.27 (m, 2H), 7.14 (t, J = 5.6 Hz, 1H, CH=N), 3.32 (s, 3H), 2.77 (t, J = 2.8 Hz, 1H), 2.43 (s, 3H), 1.02 (s, 3H), 0.85 (d, J = 6.6 Hz, 3H), 0.65 (s, 3H), 0.43 (dd, J = 8.1, 5.1 Hz, 1H); minor isomer 7.64 (br s, 1H), 6.70 (t, J = 5.2 Hz, 1H, CH=N), 0.68 (s, 3H); ^{13}C NMR (major isomer, diagnostic signals) 153.3, 143.7, 129.4, 127.7. Isomer ratio 3:1 was determined from C*H*=N signals in the ^1H NMR spectrum. This product was further used immediately after preparation.

3,5-Cyclo-6*β*-methoxy-27-nor-5α-cholestane 9. a. Reaction of 2 with BuLi. To a solution of **2** (45 mg, 0.09 mmol) in THF (3 mL) was added BuLi (2.25 M in hexane, 0.12 mL, 0.27 mmol) at −20 °C. After 10 min, the starting material was consumed (TLC). The reaction was quenched with MeOH (0.1 mL). The product was isolated with hexane and chromatographed on SiO_2 (5 g, hexane−EtOAc, 98:2) to give **9** (29 mg, 86%).

b. Reaction of 2 with Bu_2Mg. To a solution of **2** (100 mg, 0.195 mmol) in THF (0.5 mL) was added Bu_2Mg (1 M in heptane, 0.5 mL, 0.5 mmol) at room temperature. The mixture was stirred for 22 h, and the reaction was quenched with aqueous NH_4Cl. The product was isolated with ether and chromatographed on SiO_2 to give **9** (21 mg, 28%) and unchanged **2** (49 mg, 49%).

9: ^1H NMR 3.31 (s, 3H), 2.76 (br t, J = 2.7 Hz, 1H), 1.01 (s, 3H), 0.91−0.82 m, 6H), 0.71 (s, 3H); ^{13}C NMR 82.43, 56.52, 56.31, 48.03, 43.37, 42.75, 40.29, 35.91, 35.76, 35.29, 35.04, 33.35, 32.40, 30.47, 28.31, 25.79, 24.97, 24.18, 22.77, 21.50, 19.29, 18.69, 14.15, 13.06, 12.25; HRMS calcd for $C_{27}H_{46}O$ 386.35487 (M^+), found 386.35442.

Reaction of 2 with *i*-PrMgCl. 20(*S*)-6*β*-Methoxy-3,5-cyclo-5α-pregnane-20-carbonitrile 10. To a solution of **2** (205 mg, 0.4 mmol) in THF (1.4 mL) was added *i*-PrMgCl (2M in THF, 0.6 mL, 1.2 mmol), and the mixture was stirred at room temperature for 24 h. The reagent excess was quenched with aqueous NH_4Cl. The product was isolated with Et_2O and chromatographed on SiO_2 to give unchanged **2** (143 mg, 70%) and nitrile **10** (19 mg, 14%): FTIR (film) 2237 cm^{-1}; ^1H NMR 0.78 (s, 3H), 1.03 (s, 3H), 1.35 (d, J = 7.1 Hz, 3H), 2.65 (quintet, J = 7.1 Hz, 1H), 2.78 (m, 1H), 3.33 (s, 3H); MS *m/e* 341 (M^+); in agreement with those reported.[44]

General Procedure for Reaction of Tosylhydrazone 2 with Metalated Sulfones. a. With Use of BuLi. To a solution of sulfone (0.53 mmol) in THF (3 mL), stirred under argon at 0 °C, was added BuLi (2.2 M in hexane, 0.26 mL, 0.572 mmol). The cooling bath was removed, and after 15 min, a solution of tosylhydrazone **2** (90 mg, 0.176 mmol) in THF (1 mL) was added dropwise. The mixture was set aside for 16 h, and then saturated aqueous NH_4Cl (3 mL) was added. The product was extracted with Et_2O. The organic extract was dried with Na_2SO_4, and the solvent was evaporated. The residue was chromatographed on a silica gel column. Yields of the products are given in Table 1.

b. With Use of Bu_2Mg. To a solution of sulfone (0.53 mmol) in THF (3 mL), stirred under argon at room temperature, was added Bu_2Mg (1.0 M in heptane, 0.55 mL, 0.55 mmol). After 45 min, a solution of tosylhydrazone **2** (90 mg, 0.176 mmol) in THF (1 mL) was added dropwise. Progress of the reaction was monitored by TLC. After consumption of the hydrazone (ca. 1.5 h with unbranched sulfones and ca. 16 h with *β* branched ones), saturated aqueous NH_4Cl (3 mL) was added. The product was isolated with Et_2O. Yields are given in Table 1.

c. With Use of *i*-PrMgCl. To a solution of sulfone (0.53 mmol) in THF (3 mL), stirred under argon at room temperature was added *i*-PrMgCl (1.9 M in THF, 0.289 mL, 0.55 mmol). After 1 h, a solution of tosylhydrazone **2** (90 mg, 0.176 mmol) in THF (1 mL) was added dropwise. The mixture was set aside for 16 h, and then saturated aqueous NH_4Cl (3 mL) was added. The product was isolated with Et_2O. Yields are given in Table 1.

Product Identification. ^1H NMR spectra were in agreement with those reported, and HRMS confirmed the structures for the following compounds: 6*β*-methoxy-3,5-cyclo-24-nor-5α-

(49) General experimental conditions are described elsewhere.[50] NMR spectra were recorded at 200 MHz (^1H) and 50 MHz (^{13}C) unless otherwise indicated. Dibutylmagnesium (1 M in heptane), isopropylmagnesium chloride (2 M in THF), and butyllithium (2.2 M in hexane) were purchased from Aldrich. Concentrations of these solutions were determined by titration with *s*-butanol using 1,10-phenanthroline[51] or *N*-phenyl-1-naphthylamine[52] as an indicator. Sulfones were obtained from commercial suppliers or prepared by the usual methods, commercial reagents were distilled before the use. Olefination reactions were carried out under argon containing less than 0.5 ppm of oxygen and less than 1.4 ppm of water. 3α,5-Cyclo-23,24-dinor-6*β*-methoxy-5α-cholane-24-al[37] **1** was prepared from stigmasterol following the literature procedures. Methyl 3α,5-cyclo-6*β*-methoxy-5α-cholane-24-oate was prepared from methyl 3*β*-hydroxy-chol-5-en-24-oate using reported method.[42] GC were performed in a GC−MS unit, with Hewlett-Packard HP-5MS column at programmed temperature 70−300 °C.

chol-22-ene **3a**,[53] (*E*)- and (*Z*)-6*β*-methoxy-3,5-cyclo-5α-cholest-22-ene **3d**,[54] and 6*β*-methoxy-20-methylene-3,5-cyclo-5α-pregnane **4**.[55]

(*E*)- and (*Z*)-6*β*-methoxy-3,5-cyclo-5α-chol-22-ene 3b: isomers *E*/*Z* in a ratio of 4:1 or 1:2 by GC; ^{1}H NMR, selected signals, *E*-isomer (from the mixture) 5.42−5.05 (m), 3.32 (s, 3H), 2.76 (t, *J* = 2.8 Hz, 1H), 1.60 (d, *J* = 4.8 Hz, 3H), 1.02 (s, 3H), 0.98 (d, *J* = 6.6 Hz), 0.72 (s, 3H), 0.64 (m), 0.42 (dd, *J* = 5.0, 8.0 Hz); *Z*-isomer 5.45−5.05 (m), 0.95 (d, *J* = 6.6 Hz), 0.76 (s); decoupling experiment: at irradiation at d 1.6 ppm, multiplet at 5.45−5.05 ppm collapsed to q AB, 5.32, 5.21 ppm, *J* = 16 Hz, overlapping d 5.28 ppm, *J* = 10.3 Hz, and dd 5.16 ppm, *J* = 10.3 and 9.4 Hz; ^{13}C NMR, *E*-isomer 138.04, 121,67, 82.39, 56.60, 56.55, 56.09, 48.07, 43.40, 42.68, 40.19, 40.01, 35.32, 35.04, 33.38, 30.49, 28.63, 24.99, 24.17, 22,79, 21.54, 20.66, 19.33, 17.89, 13.10, 12.45; *Z*-isomer, selected signals, 137.60, 120.22; GC−MS *E*-isomer, t_R 42.21 min, *Z*-isomer, t_R 42.32 min; HRMS calcd for $C_{25}H_{40}O$ 356.30792, found 356.30780.

(*E*)- and (*Z*)-24-nonyl-6*β*-methoxy-3,5-cyclo-5α-chol-22-ene 3c: isomers *E*/*Z* in a ratio of 1:1 by ^{1}H NMR, selected signals, 5.35−5.05 (m, 2H), 3.32 (s, 3H), 2.76 (t, *J* = 2.5 Hz, 1H), 1.02 (s, 3H), 0.97 (d, *J* = 6.6 Hz, 1.5 H), 0.95 (d, *J* = 6.6 Hz, 1.5 H), 0.88 (t, *J* = 6.7 Hz, 3H), 0.75 (s, 1.5 H), 0.72 (s, 1.5 H); ^{13}C NMR, selected signals, 136.87, 136.56, 127.55, 126.64; HRMS calcd for $C_{34}H_{58}O$ 482.44877, found 482.44700.

(*E*)- and (*Z*)-23-cyclopropyl-6*β*-methoxy-3,5-cyclo-24-nor-5α-chol-22-ene 3e: isomers *E*/*Z* in a ratio of 1:3 or 1:1.2 by GC; ^{1}H NMR, selected signals, *E*-isomer (from the mixture) 5.31 (dd, *J* = 15.3, 8.4 Hz, 1H), 4.86 (dd, *J* = 15.3, 8.6 Hz, 1H), 3.317 (s, 3H), 2.76 (t, *J* = 2.8 Hz, 1H), 1.01 (s, 3H) overlapping 0.99 (d, *J* = 6.6 Hz, 3H), 0.71 (s, 3H), 0.32−0.22 (m, 2H); *Z*-isomer 5.06 (t, *J* = 10.5 Hz, 1H), 4.54 (t, *J* = 10.5 Hz), 3.322 (s, 3H), 1.03 (s, 3H) overlapping 1.01 (d, *J* = 6.6 Hz), 0.77 (s, 3H); ^{13}C NMR, selected signals, *E*-isomer 134.65, 130.85, *Z* 135.12, 130.64; GC−MS *E*-isomer, t_R 46.91 min, *Z*-isomer, t_R 46.61 min; HRMS calcd for $C_{27}H_{42}O$ 382.32357, found 382.32362.

(*E*)- and (*Z*)-6*β*-methoxy-24,24-dimethyl-5α-chol-22-ene 3f: isomers *E*/*Z* in a ratio of 7:1 by GC; ^{1}H NMR, *E*-isomer (from the mixture) 5.26 (part A of ABXY system, *J* = 15.3, 6.0 Hz, 1H), 5.16 (part B, 15.3, 7.5 Hz, 1H), 3.32 (s, 3H), 2.75 (t, *J* = 2.6 Hz, 1H), 1.02 (s, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.94 (d, 6.8 Hz, 6H), 0.72 (s, 3H), 0.64 (m, 1H), 0.42 (dd, *J* = 8.0, 5.0 Hz, 1H); ^{13}C NMR, selected signals *E*-isomer 134.72, 133.63; GC−MS *E*-isomer, t_R 43.61 min, *Z*-isomer, t_R 43.26 min; HRMS calcd for $C_{27}H_{44}O$ 384.33922, found 384.33939.

(*E*)- and (*Z*)-23-cyclohexyl-6*β*-methoxy-24-nor-5α-chol-22-ene 3g: isomers *E*/*Z* in a ratio of 12:1 by GC; ^{1}H NMR, *E*-isomer (from the mixture) 5.26 (part A of an ABXY system, *J* = 15.4, 5.8 Hz, 1H), 5.16 (part B, 15.4, 7.2 Hz, 1H), 3.32 (s, 3H), 2.75 (t, *J* = 2.6 Hz, 1H), 1.02 (s, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.72 (s, 3H), 0.64 (m, 1H), 0.42 (dd, *J* = 8.0, 5.0 Hz); ^{13}C NMR, *E*-isomer, selected signals 134.22, 133.58; GC−MS *E*-isomer, t_R 52.11 min, *Z*-isomer, t_R 51.14 min; HRMS calcd for $C_{30}H_{48}O$ 424.37052, found 424.36978.

(*E*)- and (*Z*)-6*β*-methoxy-23-phenyl-3,5-cyclo-24-nor-5α-chol-22-ene 3h: isomers *E*/*Z* in a ratio of 2:1 by GC; ^{1}H NMR (500 MHz) *E*-isomer (from the mixture) 7.36−7.15 (m, 5H), 6.33 (d, *J* = 15.8 Hz, 1H), 6.10 (dd, *J* = 15.8, 8.7 Hz, 1H), 3.35 (s, 3H), 2.79 (t, *J* = 2.8 Hz, 1H), 1.15 (d, *J* = 6.6 Hz, 3H), 1.06 (s, 3H), 0.81 (s, 3H), 0.64 (m, 1H), 0.42 (dd, *J* = 8.0, 5.0 Hz, 1H); *Z*-isomer, selected signals 6.28 (d, 11.7 Hz), 5.47 (dd, *J* = 11.7, 10.6 Hz), 3.33 (s), 1.14 (d, *J* = 6.6 Hz), 1.04 (s), 0.69 (s); GC−MS *E*-isomer, t_R 54.04 min, *Z*-isomer, t_R 51.76 min; HRMS calcd for $C_{30}H_{42}O$ 418.32357, found 418.324598.

6*β*-Methoxy-23-methyl-3,5-cyclo-5α-chol-22-ene 3i: ^{1}H NMR 4.89 (br d, *J* = 9.8 Hz), 3.32 (s, 3H), 2.78 (t, *J* = 2.8 Hz, 1H), 1.64 (d, *J* = 1.1 Hz, 3H), 1.60 (d, *J* = 1.1 Hz, 3H), 1.02 (s, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.75 (s, 3H), 0.66 (m, 1H), 0.42 (dd, *J* = 8.0, 5.0 Hz, 1H); ^{13}C NMR, 132.01, 127.49, 82.42, 56.86, 56.60, 56.54, 48.09, 43.39, 42.62, 40.21, 35.29, 35.05 (2C), 33,35, 30.47, 28.10, 25.77, 24.96, 24.12, 22.77, 21,50, 20.69, 19.30, 18.11, 13.07, 12.53; HRMS calcd for $C_{26}H_{42}O$ 370.32357, found 370.32256.

(*E*)- and (*Z*)-23,24-dimethyl-6*β*-methoxy-3,5-cyclo-5α-chol-22-ene 3j: isomers *E*/*Z* in a ratio of 4:1 by ^{1}H NMR, ^{1}H NMR (500 MHz) *E*-isomer (from the mixture) 4.89 (dq, *J* = 9.7, 1.3 Hz, 1H), 3.32 (s, 3H), 2.76 (t, *J* = 2.8 Hz, 1H), 1.60 (d, *J* = 1.4 Hz, 3H), 1.03 (s, 3H), 0.962 (t, *J* = 7.5 Hz, 3H), 0.932 (d, *J* = 6.6 Hz, 3H), 0.752 (s, 3H), 0.65 (m, 1H), 0.43 (dd, *J* = 8.0, 5.0 Hz, 1H); *Z*-isomer, selected signals 4.86 (br d, *J* = 9.5 Hz), 1.63 (d, *J* = 1.3 Hz), 0.966 (t, *J* = 7.5 Hz), 0.937 (d, *J* = 6.6 Hz), 0.747 (s) NOE measurements: at irradiation at d 1.60 ppm (the major isomer signal) increase of integration of the signal 2.5 ppm (assigned to C-20 by a COSY experiment) and no increase of integration of the vinylic proton signal at 4.89 ppm was recorded; at irradiation at *δ* 1.63 ppm increase of integration of the signals at 4.86 ppm was observed. These measurements indicate trans relationship of the vinylic methyl group and the vinylic proton in the major isomer (*E* configuration of the double bond). ^{13}C NMR, selected signals *E*-isomer 133.04, 130.51; *Z*-isomer 133.16; 131.76; HRMS calcd for $C_{27}H_{44}O$ 384.33922, found 384.34103.

General Procedure for Reaction of Tosylhydrazone 6 with Metalated Sulfones. Reactions were carried out as described above for **2**, using a sulfone (0.26 mmol) in THF (1.5 mL), BuLi (2.0 M in hexane, 0.15 mL, 0.30 mmol), or Bu_2Mg (1 M in heptane, 0.3 mL, 0.30 mmol) and tosylhydrazone **6** (47 mg, 0.087 mmol) in THF (0.5 mL). Yields are given in Table 2.

Olefination Reactions Involving in Situ Preparation of Tosylhydrazone 6. To a solution of aldehyde **5** (0.33 mmol) in THF (0.5 mL) was added *p*-toluenesulfonyl hydrazide (0.33 mmol) in THF (0.5 mL) (solution A). In parallel, a solution of sulfone (1 mmol) in THF (4 mL) was treated with Bu_2Mg (1 M in heptane, 1 mL, 1 mmol) (solution B). After 45 min, solution A was carefully added to solution B. Progress of the reaction was monitored by TLC. After consumption of the hydrazone (ca. 1.5 h with unbranched sulfones and ca. 16 h with *β* branched ones) saturated aqueous NH_4Cl (3 mL) was added, and the product was isolated with Et_2O. Yields are given in Table 2.

Product Identification. 6*β*-Methoxy-3,5-cyclo-5α-cholest-24-ene 7a: mp 62−64 °C (acetone); ^{1}H NMR 5.51 (tt, *J* = 5.7, 2.7 Hz, 1H), 3.32 (s, 3H), 2.76 (t, *J* = 2.7 Hz, 1H), 1.68 (s, 3H), 1.59 (s, 3H), 1.02 (s, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.71 (s, 3H), 0.66−0.62 (m, 1H), 0.45−0.39 (m, 1H), in agreement with that reported.[57]

6*β*-Methoxy-3,5-cyclo-5α-chol-23-ene 8: ^{1}H NMR (diagnostic signals from mixture **7** and **8**) 5.16−4.90, 3.31, 2.76, 1.01, 0.92, 0.71.

(*E*)- and (*Z*)-6*β*-methoxy-3,5-cyclo-24-homo-5α-cholest-24(24a)-ene 7b: isomers *E*/*Z* in a ratio of 1.5:1 by GC; ^{1}H NMR (500 MHz) *E*-isomer (from the mixture) 5.32−5.23 (m, 8 lines, 2H), 3.25 (s, 3H), 2.70 (t, *J* = 2.6 Hz), 2.15 (m, 1H), 0.95 (s, 3H), 0.89 (d, *J* = 6.8 Hz, 6H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.643 (s, 3H), 0.58 (m, 1H), 0.36 (dd, *J* = 8, 5 Hz); *Z*-isomer, selected signals, 5.17−5.06 (m, 2H), 2.52 (m, 1H), 0.88 (d, 6.8 Hz, 6H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.649 (s, 3H); ^{13}C NMR (125 MHz), *E*-isomer, selected signals, 137.27, 127.69; *Z*-137.29, 127.87; ^{1}H NMR in C_6D_6 (500 MHz) selected signals, *E*-isomer, 5.52−5.43 (m), *Z*-isomer 5.41−5.35 (m, 1H), 5.33−5.28 (m, 1H); Signals of the *E*-and *Z*-isomers were assigned from the

(50) Marczak, S.; Michalak, K.; Urbanczyk-Lipkowska, Z.; Wicha, J. *J. Org. Chem.* **1998**, *63*, 2218−2223.
(51) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165−168.
(52) Bergbreiter, D. E.; Pendegrass, E. *J. Org. Chem.* **1981**, *46*, 219−220.
(53) Posner, J. P.; Ourisson, G. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2061−2066.
(54) Lang, R. W.; Djerassi, C. *J. Org. Chem.* **1982**, *47*, 625−633.
(55) Dasgupta, S. K.; Gut, M. *J. Org. Chem.* **1975**, *40*, 1475−1477.
(56) Dasgupta, S. K.; Crump, D. R.; Gut, M. *J. Org. Chem.* **1974**, *39*, 1658−1662.
(57) Giner, J. L.; Margot, C.; Djerassi, C. *J. Org. Chem.* **1989**, *54*, 2117−2125.

decoupling experiment: at irradiation at d 2.1 ppm (C-23 H according to the COSY spectrum) multiplet 5.33−5.28 ppm collapsed to 5.34 (dd, J = 10.8, 7.9 Hz), multiplet 5.41−5.35 collapsed to 5.42 (dt, J = 10.8, 2.2 Hz) and multiplet 5.52−5.43 collapsed to distorted AB quartet, 5.51 (J = 15.5 Hz); GC−MS *E*- 47.56 min and *Z*- 47.42 min; HRMS calcd for $C_{29}H_{48}O$ 412.37052, found 412.37095.

(*E*)- and (*Z*)-6*β*-methoxy-26-methyl-3,5-cyclo-5α-cholest-24-ene 7c: isomers *E*/*Z* in a ratio of 1.7:1 by GC; ^{1}H NMR *E*-isomer (from the mixture) 5.20−5.00 (m, 1H), 3.32 (s, 3H), 2.75 (t, J = 2.6 Hz), 1.59 (br s, 3H), 1.02 (s, 3H), 0.98 (t, J = 7 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H), 0.71 (s, 3H), 0.64 (m, 1H), 0.42 (dd, J = 8, 5 Hz); *Z*-isomer, selected signals, 1.67 (d, J = 1 Hz, 3H); ^{13}C NMR, *E*-isomer, selected signals, 136.34, 123.59; *Z*-136.59, 124.78; *E*/*Z* assignments were based upon chemical shifts of vinylic methyl group signals, with that of the isomer *E*- occurring at higher field, cf. reported values for the respective 3-hydroxy-5-enes[58] and spectra of **3j**; GC−MS *E*-isomer 47.74 min and *Z*-isomer 47.53 min; HRMS calcd for $C_{29}H_{48}O$ 412.37052, found 412.37075.

Reaction of Tosylhydrazones 2 or 6 with a Mixture of Isobutyl- and Isopropyl Phenyl Sulfones. To a solution of isopropyl phenyl sulfone (48 mg, 0.3 mmol) and isobutyl phenyl sulfone (53 mg, 0.3 mmol) in THF (2 mL) was added Bu_2Mg (1 M in hexane, 0.6 mL, 0.6 mmol). The mixture was stirred at room temperature for 1 h, tosylhydrazone **2** (0.09 mmol) or **6** (0.09 mmol) in (THF, 1 mL) was added, and stirring was continued for 16 h. The reaction was quenched with water. The product was isolated with Et_2O and purified by chromatography on SiO_2 (hexane, hexane−EtOAc, 97:3). The composition of the mixture was determined by GC.

Reaction with tosylhydrazone **2**: crude product 31 mg, **3f**/**3i** = 1:20.

Reaction with tosylhydrazone **6**: crude product 33 mg, **7a**/**7b** = 10:1.

Tosylohydrazone of Cyclododecanone 11b. A mixture of cyclododecanone **11a** (1.02 g, 5.6 mmol), *p*-toluenesulfonyl hydrazide (1.10 g, 5.9 mmol), and anhydrous ethanol (10 mL) was heated under reflux for 2 h and then set aside at room temperature for 6 h. Crystalline material was filtered off, washed with ethanol, and dried to give **11b**: 1.76 g (90%); mp 160−161 °C dec; ^{1}H NMR 7.82 (d, J = 8.3 Hz, 2H), 7.74 (br.s, 1H), 7.26 (d, J = 8.3 Hz, 2H), 2.38 (s, 3H), 2.24−2.07 (m, 4H), 1.72−0.70 (m, 18H); ^{13}C NMR 159.35, 143.80, 135.42, 129.48 (2C), 125.12, 31.28, 28.76, 25.93, 25.84, 23.67, 23.14, 22.87, 22.64, 22.60, 21.75, 21.50, 21.44. Anal. Calcd for $C_{19}H_{30}N_2O_2S$ (350.53): C, 65.11; H, 8.63; N, 7.99; S, 9.15. Found: C,65.12; H, 8.80; N, 8.02; S, 9.16.

Trisylhydrazone of Cyclodecanone 11c. A mixture of **11a** (0.91 mg, 5 mmol), 2,4,6-triisopropylbenzenesulfonyl hydrazide[47] (1.19 g, 5 mmol), and Et_2O (25 mL) was stirred at room temperature for 16 h. The solvent was evaporated in a stream of dry nitrogen to ca. 1/3 of the mixture volume. The remainder was set aside at −20 °C for 1.5 h, and crystalline material was filtered off and washed with cold Et_2O. Trisylhydrazone **11c** was obtained: 1.60 g (69%); mp 136−138 °C dec; ^{1}H NMR 7.34 (br. s, 1H), 7.16 (s, 2H), 4.19 (sept., J = 6.6 Hz, 2H), 2.90 (sept., J = 7.0 Hz), 2.28−2.08 (m, 4H), 1.65−1.47 (m, 4 H), 1.32−1.05 (m, 14H) overlapping 1.27 (d, J = 6.6 Hz, 12H), 1.25 (d, J = 7.0 Hz, 6H); ^{13}C NMR 158.9, 153.0, 131.3, 123.4, 34.2, 31.8, 30.1, 28.2, 25.7, 25.6, 24.9, 24.6, 23.6, 23.3, 23.1, 23.0, 22.7, 22.6, 22.2. Anal. Calcd for $C_{27}H_{46}N_2O_2S$ (462.74) C, 70.08; H, 10.02; N, 6.05; S, 6.92. Found: C, 70.05; H, 10.19; N, 6.02; S, 7.06.

A General Procedure for Reaction of 11b or 11c with α-Magnesio Sulfones. To a solution of freshly distilled sulfone in THF (4 mL), stirred at room temperature, was added a solution of Bu_2Mg (1 M in heptane) or *i*-PrMgCl (2 M in THF). After 30 min, a solution of **11b** or **11c** (0.33 mmol) in THF (2 mL) was added. The mixture was stirred for 18 h, and then aqueous NH_4Cl and water were added. The product was isolated with CH_2Cl_2 and chromatographed on a SiO_2 (4 g). The olefins were eluted with hexane, and then the column was washed with hexane−acetone, 9:1, to recover unchanged hydrazones. The olefin **12**/**13** ratio was determined by GC. Yields and product composition are give in Table 3.

Product Identification. methylene−cyclodecane **12a**: ^{1}H NMR 4.80 (t, J = 1.0 Hz, 2H), 2.06 (t, J = 5.9 Hz, 4H), 1.59−1.44 (m, 4H), 1.37−1.27 (m, 14H); ^{13}C NMR 147.46, 110.32, 33.07 (2C), 24.47 (2C), 24.15 (2C), 23.73 (2C), 23.28 (2C), 22.63, in agreement with those reported.

Ethylidenecyclodecane **12b**: ^{1}H NMR from a mixture with **13**, 5.40−5.20 (m), 2.20−1.90 (m), 1.60 (d, J = 6.7 Hz), 1.50−1.10 (m); ^{13}C NMR 138.36, 118.81 ppm (diagnostic signals); *E*/*Z* **13**: ^{13}C NMR 130.35 ppm (diagnostic signal).

Acknowledgment. We thank Professor Philip J. Kocienski of the University of Leeds for helpful discussions, Professor James R. Bull of the University of Cape Town for assistance in idiomatic English, and Professor Zofia Urbanczyk-Lipkowska for the X-ray structure of compound **2**. Financial support from the State Committee for Scientific Research, Grant No. 3 T09A 134 18, is gratefully acknowledged.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **3b**,**c**,**e**−**j** and **7b**,**c** and ^{1}H NMR spectrum of compound **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO015699L

(58) Fukuzawa, S.; Mutoh, K.; Tsuchimoto, T.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 5400−5405.