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α-HALOALKANESULFONYL BROMIDES IN ORGANIC SYNTHESIS. 4. REGIOSELECTIVE γ-DEPROTONATION OF α,β-UNSATURATED SULFONES. A SIMPLE SYNTHESIS OF 2-ALKYL-1,3-BUTADIENES.[1]

Eric Block*, Venkatachalam Eswarakrishnan, and Kassu Gebreyes

Department of Chemistry, State University of New York at Albany, Albany, New York 12222

Abstract: A simple method for converting 2-methyl-1-alkenes into 2-alkyl-1,3-butadienes is described. Evidence for complexation of lithium cations by sulfonyl groups in the course of reactions of α,β-unsaturated sulfones with LiO*t*-Bu is presented.

Conjugated dienes may be conveniently synthesized via addition of bromomethanesulfonyl bromide, **1**, $BrCH_2SO_2Br$, to olefins followed by treatment of the adduct with base, typically triethylamine and then potassium *tert*-butoxide (e.g., eq 1, R=H).[2] α,β-Unsaturated bromomethyl sulfones such as **3a** could undergo vinylogous Ramberg-Bäcklund reaction[2] by deprotonation *syn* (γ) and/or *anti* (γ') to the sulfonyl group. In unsymmetrical systems this could give mixtures of products. In practice we find that good regioselectivity may be realized in the deprotonation of various unsymmetrical analogues of **3a**, that the regioselectivity may be altered by changing from potassium to lithium *tert*-butoxide and that the regioselectivity provides the basis for a simple synthesis of 2-alkyl-1,3-butadienes from 2-methyl-1-alkenes.

Addition[2] of **1** to 3-methyl-1-methylenecyclohexane[3] (**2b**) followed by dehydrobromination with triethylamine gave a 1:1 mixture of **3b** and **3b'**[4] in 94% overall yield. Fractional recrystallization of the mixture from CCl_4 afforded **3b**, mp 79-80°, homogeneous by capillary GC and HPLC. The structure of **3b** was established by X-ray crystallography, as shown in Figure 1.[5] Preparative HPLC (99% hexane, 1% isopropanol) of the mother liquor from the above recrystallization afforded **3b'**, chromatographically and spectroscopically different from **3b**. Separate treatment of **3b** with KO*t*-Bu and **3b'** with LiO*t*-Bu in *t*-BuOH/THF gave, respectively, 5-methyl-1-vinyl-1-cyclohexene, **4b**, and 3-methyl-1-vinyl-1-cyclohexene, **4b'**,[6] in each case regiospecifically in 77-78% yield.[7] Reaction of **3b'** with LiO*t*-Bu and excess 12-crown-4 gave a 4:1 mixture of **4b'**:**4b** while KO*t*-Bu gave a 62:38 mixture of **4b'**:**4b**.

Treatment of 2-methyl-1-octene (**5**, eq 2) with **1** followed by triethylamine gave in 87% yield a 2.8:1 mixture of **6a** and **6a'**[4] which could be separated into pure compounds by HPLC (99.5% hexane, 0.5% isopropanol). Compounds **6a** and **6a'**, showing ^1H NMR methyl resonances at δ 2.21 and 2.01 ppm, respectively, can be characterized as (*E*)- and (*Z*)-2-methyl-1-octenyl bromomethyl sulfone, respectively, based on the known deshielding of alkyl groups syn to the sulfonyl group in α,β-ethylenic sulfones.[8] Treatment of **6a** with KO*t*-Bu or LiO*t*-Bu led regiospecifically to 2-*n*-hexyl-1,3-butadiene, **7**,[4] while **6a'** gave mixtures of **7** and (*E*,*Z*)-3-methyl-1,3-nonadiene, **8**, in ratios varying from 7:93 (LiO*t*-Bu), to 13:87 (LiO*t*-Am-C_6H_6) to 29:71 (LiO*t*-Bu, 12-Crown-4) to 68:32 (KO*t*-Bu). For synthetic purposes, the crude mixture of isomers **6a**,**a'** may be used to prepare **7**. Thus a 0.25 M solution of mixed isomers in 7:1 *t*-BuOH-THF is added to 3 equiv. of KO*t*-Bu in 5:2 *t*-BuOH-THF (0.8 M) at -23° C and the mixture is warmed to 25° C, diluted with water and extracted with pentane, which is washed with water to remove THF. Distillation of the dried pentane extract affords **7** (84% yield, 91% purity). Additional examples of syntheses of 2-alkyl-1,3-butadienes by this route are given in the Table. Entry 3 is of interest because it demonstrates the preference of reagent **1** for addition to the terminal rather than internal double bond while entry 6 demonstrates that deprotonation can be regiospecific in particularly hindered cases.

The above observations on the regioselective deprotonation of bromomethyl sulfones **3b**, **b'** and **6a**,**a'** can be rationalized as follows: 1) Steric factors should favor deprotonation of compounds **3b**,**b'** and **6a**,**a'** with *tert*-alkoxides at the less hindered positions (remote from the R group) giving **4b** and **7**, in accord with earlier studies on enolate generation in analogous systems.[7] 2) Coordination of the cations of alkali *t*-butoxides by sulfonyl oxygen should favor deprotonation *syn* to the sulfonyl group. In particular we suggest that the lithium cation of LiO*t*-Bu coordinates to the sulfonyl oxygen in **3b'** and **6a'** promoting removal of the γ-proton despite steric hindrance at that position.[9,10] The X-ray structure of **3b** indicates that the sulfonyl oxygen is within 2.51Å of the closest ring hydrogen, a value within the sum of the van der Waals radii of O and H, which should facilitate the type of coordination depicted in Figure 2. When the extent of coordination is diminished by substituting the "softer" (HSAB terminology) potassium for lithium or by complexing lithium with 12-crown-4, the relative proportion of γ-deprotonation decreases.[11]

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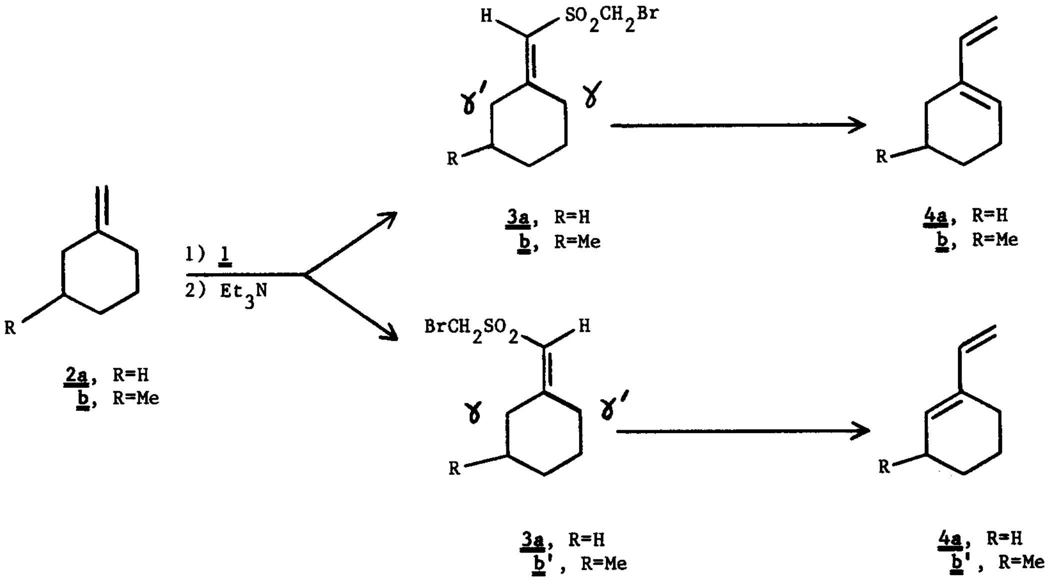
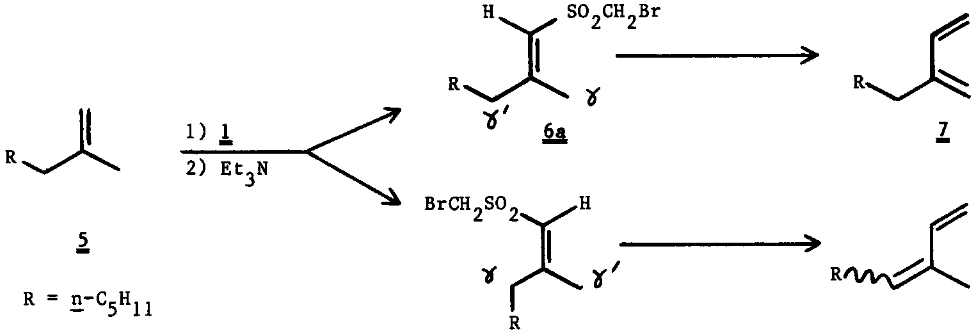


(1)



6a' **8** (2)

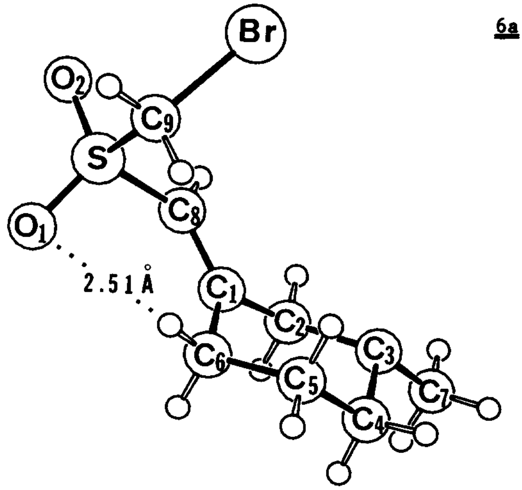


Figure 1

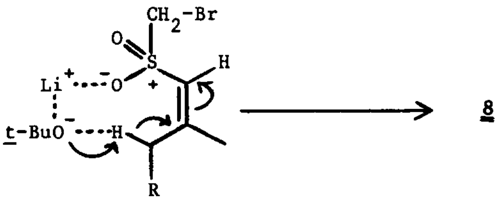


Figure 2

TABLE I. Synthesis of 2-Alkyl-1,3-butadienes from 2-Methyl-1-alkenes.

Entry	R in CH_2=$CRCH_3$ and CH_2=CRCH=CH_2	Overall Distilled Yield of Diene[4] (%)	Purity
1	*n*-C_5H_{11}	79	91%[a]
2	*n*-C_6H_{13}	73	91%[b]
3	$(CH_3)_2C$=$CHCH_2CH_2$	65	89%[c]
4	$(CH_3)_2CHCH_2CH_2$	63	92%[d]
5	*n*-C_9H_{19}	55	92%[e]
6	*c*-C_6H_{11}	62	100%

a) 9% 3-methyl-1,3-octadiene. b) 9% 3-methyl-1,3-nonadiene. c) 11% 3,7-dimethyl-1,3,6-octatriene. d) 8% 3,6-dimethyl-1,3-heptadiene. e) 8% 3-methyl-1,3-dodecadiene.

References and Notes

*Fellow of the John Simon Guggenheim Foundation, 1984-1985.

1. Part 3: E. Block, M. Aslam, R. Iyer and J. Hutchinson, *J. Org. Chem.*, in press.
2. E. Block and M. Aslam, *J. Amer. Chem. Soc.*, **105**, 6164 (1983); E. Block, M. Aslam, V. Eswarakrishnan, and A. Wall, *ibid.*, **105**, 6165 (1983); E. Block and M. Aslam, procedure submitted to *Organic Synthesis*.
3. Olefins were conveniently prepared via reaction of the respective ketones with CH_2Br_2-$TiCl_4$-Zn: L. Lombardo, *Tetrahedron Lett.*, **23**, 4293 (1982).
4. All new compounds were fully characterized as will be detailed in the full report.
5. Crystal data: $C_9H_{14}O_2SBr$, monoclinic space group $P2_1/c$, a = 7.910(2)Å, b = 14.599(3)Å, c = 9.833(3)Å, β = 94.88(1); V = 1131.4(10)Å^3 for Z=4 to give D_c = 1.56 g cm^{-3}; 636 reflections were used of 1103 collected (Mo-K_α radiation, current R value 0.077). Bond lengths and angles are unexceptional and will be given in the full report: C1-C8, 1.32(1)Å; Br-C9, 1.891(8)Å; S-C9, 1.784(10)Å; O1···H2B, 2.51Å.
6. Compound **4b** with a gc retention time of 8.02 min (70° C) and compound **4b'** with a retention time of 7.90 min can be identified by the ^{1}H NMR triplet at δ 5.66 in **4b** due to the ring CH_2<u>C</u>H=C and the doublet at δ 5.59 in **4b'** due to the ring $CH(CH_3)$C<u>H</u>=C.
7. Note the 82:18 kinetic ratio of the 3-methyl to 5-methyl enolate of 3-methylcyclohexanone using trityllithium as base: A. Anthony and T. Maloney, *J. Org. Chem.*, **37**, 1055 (1972); also see E.J. Corey and A.W. Gross, *Tetrahedron Lett.*, **25**, 495 (1984) for related work.
8. C.Y. Meyers and I. Sataty, *Tetrahedron Lett.*, 4323 (1972); I. Sataty, *Ph.D. Thesis*, Southern Illinois University, 1970; W.E. Truce and M.J. Lusch, *J. Org. Chem.*, **43**, 2252 (1978); also note M. Mikolajczyk, S. Grzejzczak, and A. Zatorski, *J. Org. Chem.*, **40**, 1979 (1975).
9. The greater kinetic acidity of syn vs. anti methyl groups in α,β-ethylenic sulfones has been noted: J.J. Eisch and J.E. Galle, *J. Org. Chem.*, **44**, 3279 (1979); note chelation in α-lithio sulfones: S.Wolfe, L.A.LaJohn, D.F.Weaver, *Tetrahedron Lett.*, **25**, 2863 (1984).
10. It has recently been found that α,β-unsaturated esters also undergo regioselective deprotonation by LDA on β-alkyl groups *syn* to the ester function via lithium-carbonyl group coordination: F.L. Harris and L. Weiler, *Tetrahedron Lett.*, **25**, 1333 (1984).
11. Address inquiries on the X-ray crystallography studies to Jon Zubieta at SUNY-Albany.

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