A New One-flask Ramberg–Bäcklund Reaction

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A refined verson of the Meyers' modification of the Ramberg–Bäcklund reaction employing the reagent alumina-supported KOH–CBr_2F_2–Bu^{t}OH allows α- and α′-hydrogen-bearing sulfones of various structural types to be converted into alkenes.

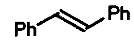
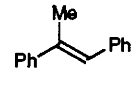
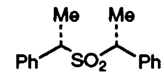
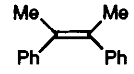
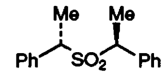
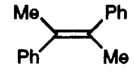
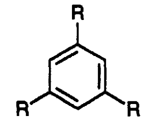
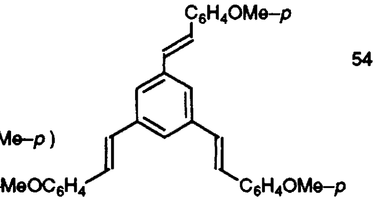
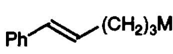
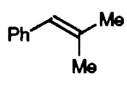
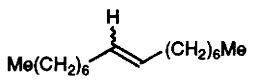
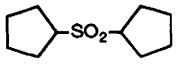
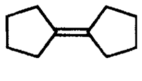
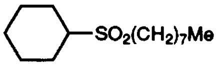
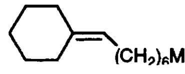
Because of its ability to convert sulfones into alkenes in one operation without recourse to the prior preparation of the α-halogenosulfones by a separate step, the Meyers' modification[1] of the Ramberg–Bäcklund reaction[2] has been used with considerable frequency in organic synthesis. However, as a method of olefination, the applicability of the Meyers' protocol, which entails the treatment of a sulfone bearing both α- and α′-hydrogens with pulverized KOH suspended in a mixture of CCl_4 and Bu^{t}OH, is rather limited to the construction of stilbenes from dibenzylic sulfones and of 1,1-diarylalkenes from benzhydryl alkyl sulfones.[1] Sulfones of other structural types behave differently under these conditons to yield other products[1]: diprimary-alkyl sulfones suffer serious α, α- and/or α, α′-dichlorination before base-induced 1,3-elimination to give almost exclusively the potassium salts of alkenesulfonates; benzyl primary-alkyl sulfones are beset by similar problems to give mixtures of β-alkylstyrenes, α-chloro-β-alkylstyrenes, and potassium alkenesulfonates; di-*sec*-alkyl sulfones give predominantly tetraalkyl *gem*-dichlorocyclopropanes arising from the assault of the initially formed tetrasubstituted alkenes by dichlorocarbene which is the remnant of CCl_4 in the wake of chlorine transfer. Thus, while the Meyers' modification was a step forward in providing a direct conduit for sulfones to be transformed into alkenes without the necessity of isolating the α-halogenosulfones, there was clearly room for improvement in the scope of its applicability. We report herein our findings that the aforementioned difficulties encountered in the Meyers' procedure can be completely overcome by simply replacing powdered-KOH–CCl_4–Bu^{t}OH by alumina-supported KOH–CBr_2F_2–Bu^{t}OH, so that α- and α′-hydrogen-bearing sulfones, regardless of structural types, can now be uniformly converted into alkenes in good yields [eqn. (1)].

$$R^1R^2CHSO_2CHR^3R^4 \xrightarrow[CBr_2F_2,\ Bu^tOH]{KOH/Al_2O_3} R^1R^2C{=}CR^3R^4 \qquad (1)$$

Although the intrusion of dichlorocarbene to the alkene products under the conditions of the Meyers' procedure can be suppressed by the inclusion of a carbene scavenger in the reaction mixture,[1] the need to separate the trapped adducts creates an additional step in the workup. We felt that a more direct way to address this problem would be to substitute CCl_4 with an alternate halogen source from which only a relatively unreactive carbenic species, if any at all, could evolve. Towards this end, attention was first focussed on the conversion of dicyclopentyl sulfone into bicyclopentylidene, which was plagued by a particularly serious *gem*-dichlorocyclopropanation problem in the Meyers' reaction. After some experimentation with a number of positive halogen sources, CBr_2F_2 was found to be the best substitute for CCl_4 in bringing about a clean reaction to afford bicyclopentylidene as the only isolable product in 85% yield *versus* a mixture consisting of bicyclopentylidene (33%) and its dichlorocarbene adduct (67%) using the Meyers' method.[1a,c] The most attractive feature in the reaction of dicyclopentyl sulfone with pulverized KOH–CBr_2F_2–Bu^{t}OH is the absence of any detectable amount of carbene addition byproduct as shown by the NMR spectrum of the crude product. We are uncertain at this stage as to whether difluorocarbene is indeed generated under these reaction conditions, but even if it were, its relatively low reactivity towards alkenes[3] would probably direct its course of destruction *via* reaction with the KOH–Bu^{t}OH system rather than with the alkene being formed.

However, with the above adjustment in the halogenating agent alone, the problem of dihalogenation persisted for diprimary-alkyl sulfones as indicated by the formation of only 10–15% of hexadec-8-ene together with 20–25% of 8-bromohexadec-8-ene in the reaction of di-*n*-octyl sulfone with the reagent pulverized-KOH–CBr_2F_2–Bu^{t}OH. In an attempt to

Table 1 The conversion of α, α′-hydrogen-containing sulfones into alkenes by treatment with KOH/Al_2O_3–CBr_2F_2–Bu^{t}OH

Entry	Sulfone	Alkene	Yield[a] (%)
1	$PhCH_2SO_2CH_2Ph$		96
2	$PhCHMeSO_2CH_2Ph$		85
3		 (Z) : (E) = 95 : 5	90
4		 (Z) : (E) = 10 : 90	92
5	 (R = $CH_2SO_2CH_2C_6H_4OMe$-*p*)		54
6	$PhCH_2SO_2(CH_2)_4Me$		92
7	$PhCH_2SO_2CHMe_2$		90
8	$Me(CH_2)_7SO_2(CH_2)_7Me$	 (Z) : (E) = 30 : 70	75
9			90
10			82

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[a] Isolated yield.

suppress dibromination, our attention was turned to the enhancement of the efficacy of the base in the reaction. Since KOH and Bu^{t}OH had been firmly established to be the optimum base-solvent pair in the Meyers' reaction,[1] there was little room for manipulation except for the manner in which KOH was to be dispersed in the reaction mixture. To our great delight, when di-*n*-octyl sulfone was treated with CBr_2F_2 and Bu^{t}OH in the presence of alumina-supported KOH, hexadec-8-ene was formed in 75% yield.

The serendipitous discovery of the ability of alumina-supported KOH in subduing dihalogenation prior to 1,3-elimination has become a valuable asset in the present study, for not only does this simply assembled catalyst, in conjunction with CBr_2F_2 and Bu^{t}OH, enable the one-flask Ramberg–Bäcklund reaction of diprimary-alkyl sulfones to proceed smoothly to give alkenes in good yields but also provides uniformly better yields of alkenes from all other types of sulfones than those obtained in the corresponding reactions employing pulverized but unsupported KOH. The efficacy of alumina-supported KOH is apparently a consequence of a large increase in the surface area of the catalyst and perhaps also the activating effects produced by the alumina surface.[4] The catalyst used in our study can be routinely prepared by thorough stirring at room temperature of three parts in weight of neutral alumina (E. Merck, grade 1, 70–230 mesh) in a methanolic solution of one part in weight of commercial KOH pellets followed by rotaevaporation at 40–60 °C until a free-flowing powder of constant weight is obtained. When kept in a stoppered container, this material sustains a long shelf-life of several months.

The results from the reaction of representative sulfones with the new one-flask Ramberg–Bäcklund reagent KOH/Al_2O_3–CBr_2F_2–Bu^{t}OH are summarized in Table 1. In all reactions, good to high yields of alkenes are obtained. A high degree of stereoselectivity of the resultant double bonds is observed for benzylic sulfones although mixtures of geometric alkenes are formed from diprimary sulfones. The most significant result remains that all α- and α′-hydrogen-bearing sulfones, independent of structural type, yield predominantly alkenes as products.

The typical experimental procedure for benzylic sulfones is as follows: to a vigorously stirred mixture of the sulfone (10 mmol), the above described alumina-supported KOH (20 g) and Bu^{t}OH (40 ml)† kept at 5–10 °C is added dropwise CBr_2F_2‡ (40 mmol) over 2–3 min. The reaction mixture is stirred at room temperature for an additional 1–2 h after which the solid catalyst is removed by suction filtration through a pad of Celite. The filtrate is rotaevaporated to remove most of solvent; the filter cake is washed thoroughly with C_6H_{14} or CH_2Cl_2 and the washes are combined with the residue from the first filtrate. The resultant organic solution is washed with brine and water, dried and rotaevaporated to give the crude alkene which is purified by flash column chromatography.

Higher temperatures are generally needed for non-benzylic sulfones. The reaction is best carried out by flashing CBr_2F_2 onto a stirred mixture of the sulfone, the KOH catalyst and Bu^{t}OH which is preheated to 60–80 °C.

In summary, we have developed an efficient one-flask Ramberg–Bäcklund reaction of general applicability. Since α- and α′-hydrogen-bearing sulfones can often be assembled with ease in various manners, their attractiveness as precursors of alkenes is now considerably enhanced by this experimentally simple procedure.

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Footnote

† For those sulfones having low solubilities in Bu^{t}OH, an appropriate volume of CH_2Cl_2 may be added.

‡ For convenience of handling, CBr_2F_2 is best precooled to below 0 °C before use.

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