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α-Sulfinyl Carbanions as A New Source of Olefins

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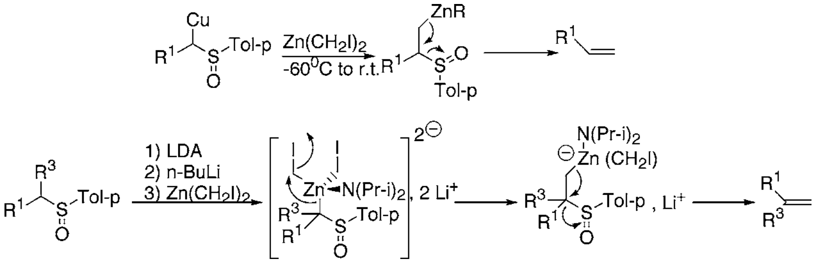
ABSTRACT



Secondary α-lithiosulfinyl carbanions react either intermolecularly, after transmetalation into an organocopper derivative in an S_N2-type process with zinc carbenoid, or intramolecularly via higher-order zincate to give, through a tandem zinc homologation–β-elimination reaction the corresponding alkenes. α,α-Disubstituted alkenes are only formed from tertiary α-lithiosulfinyl carbanions via the 1,2-metalate rearrangement.

Chiral sulfoxides are very efficient chiral auxiliaries that are inducing important asymmetric transformations. Therefore, the past decades have witnessed an exponential use of these chiral auxiliaries in asymmetric synthesis, establishing the chiral sulfinyl group as one of the most efficient and versatile chiral controllers in carbon−carbon bond formations.[1] In this context, we have recently reported the use of chiral sulfoxides in a four-component condensation reaction for the creation of chiral quaternary centers.[2] However, in most of the applications, sulfoxides are only chiral synthetic tools and must be disposed of at the end of the sequence.[3] As a potentially very interesting transformation, we have reported the first preparation of organometallic derivatives from vinyl sulfoxides and it was found to be synthetically very useful since further functionalization easily increases the complexity of the carbon skeleton.[4] On the other hand, the thermal syn-β-elimination reaction between hydrogen and sulfoxide is a well-known process and has been found to be a powerful route to chiral alkenes.[5] Similarly, the β-elimination reaction of sulfinyl radicals (estimated to be a very fast process, ca. 10^9 s^{-1}) for arylsulfoxide borne by a Csp^3 center[6] or a Csp^2 center[7] was recently used. In parallel, we have also shown that vinylic sulfoxides can be easily eliminated when organometallics are situated in a β-position[8] to lead to the corresponding allenes.[9] Therefore, in this three-component condensation reaction, namely, the carbocupration reaction of alkynyl sulfoxides with the organocopper **1** followed first by a zinc homologation reaction of the resulting vinylic organometallic **2** with the primary zinc carbenoid **3** and finally by a spontaneous syn-β-elimination, the corresponding allene **5** is obtained in a single-pot operation and in excellent overall yields (see Scheme 1). This strategy was recently applied to the preparation of chiral allenes.[10]

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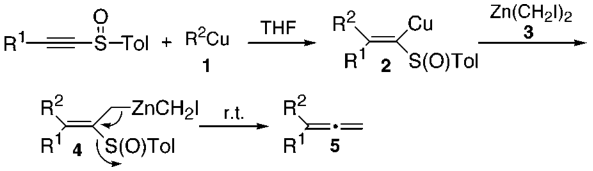
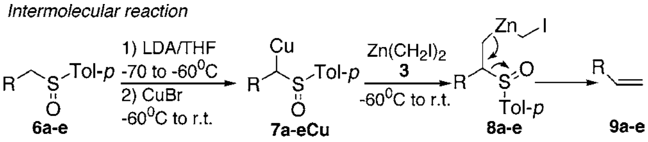
Scheme 1



The question of the fate of sp^3 α-sulfinyl carbanions for the zinc homologation followed by β-elimination reactions as a new source of olefins was then logically raised,[11] because this conversion (alkyl sulfoxides into polysubstituted olefins) would be an interesting synthetic transformation. To answer this appealing question, **6a**−**e** were first metalated with LDA[12] and transmetalated with CuBr to lead to the α-sulfinyl organocopper derivatives **7a**−**e** (Table 1). Primary zinc carbenoid, namely, bis(iodomethyl)zinc carbenoid[13] **3** (prepared by treatment of Et_2Zn with CH_2I_2 in THF) was then added, and via the tandem intermolecular nucleophilic substitution followed by β-elimination reaction, olefins **9a**−**e** were obtained in good overall yields as described in Table 1. Aliphatic as well as aromatic olefins can be easily prepared (Table 1, entries 1−5).

Table 1. α-Sulfinyl Carbanions into Monosubstituted Alkenes

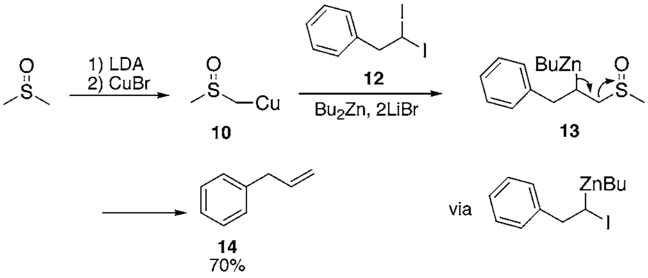


entry	compounds	R	products	yield (%)[a]
1	**6a**	$C_{11}H_{23}$	**9a**	77
2	**6b**	$PhCH_2CH_2CH_2$	**9b**	70
3	**6c**	C_6H_5	**9c**	50[b]
4	**6d**	p-$MeOC_6H_4$	**9d**	65
5	**6e**	p-MeC_6H_4	**9e**	65

[a] Yield of isolated pure products after purification on column chromatography. [b] Styrene **9c** is a volatile product, and therefore this yield is lower.

Dimethyl sulfoxide (DMSO) can also be used in this reaction as a source of terminal olefin as described in Scheme 2.

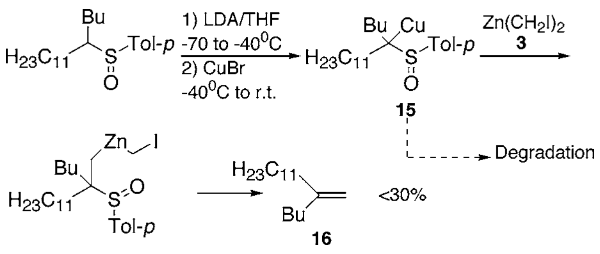
Scheme 2



After metalation−transmetalation, the formed dimsyl copper[14] **10** is treated with the in situ-prepared secondary zinc carbenoid[15] **11** (formed by treatment of 1,1-bisiodoalkane[16] **12** with Bu_2Zn, 2 LiBr) to give the zinc homologated product **13**, which spontaneously undergoes a β-elimination reaction to lead to the corresponding allylbenzene **14** in 70% overall yield.

However, this olefination reaction from α-sulfinyl carbanion does not proceed in satisfactory yield when the tertiary metalated sulfoxide **15** is used. Indeed, the resulting organocopper was found to be thermally unstable[17] and therefore no homologated product was obtained (Scheme 3).

Scheme 3



With the idea to solve this problem, we turned our attention to the intramolecular zinc homologation reaction via the 1,2-zincate rearrangement.[18] We first tested the behavior of primary sulfoxides such as **6a** in this new experimental condition. When **6a** was successively metalated with LDA, followed by the addition of a second equivalent of *n*-BuLi

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[11] Transformation of alkyl sulfones into olefins is known and successfully used in natural product synthesis, see: (a) De Lima, C.; Julia, M.; Verpeaux, J.-N. *Synlett* **1992**, 133. (b) Smith, A. B., III; Minbiole, K. P.; Verhoest, P. R.; Beauchamp, T. J. *Org. Lett.* **1999**, *1*, 913. (c) Romo, D,; Meyer, S. D.; Johnson, D. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 7906. (d) Charreau, P.; Julia, M.; Verpeaux, J.-N. *J. Organomet. Chem.* **1989**, *379*, 201. (e) Smith, A. B., III.; Zhuang, L.; Brook, C. S.; Boldi, A. M.; McBriar, M. D.; Moser, W. H.; Murase, N.; Nakayama, K.; Verhoest, P. R.; Lin, Q. *Tetrahedron Lett.* **1997**, *38*, 8667. (f) Alonso, D. A.; Falvello, L. R.; Mancheno, B.; Najera, C.; Tomas, M. *J. Org. Chem.* **1996**, *61*, 5004. (g) Alonso, D. A.; Alonso, E.; Najera, C.; Ramon, D. J.; Yus, M. *Tetrahedron* **1997**, *53*, 4835 (h) Alonso, D. A.; Costa, A.; Mancheno, B.; Najera, C. *Tetrahedron* **1997**, *53*, 4791.

[12] Corey, E. J.; Weigel, L. O.; Chamberlin, A. R.; Cho, H.; Hua, H. C. *J. Am. Chem. Soc.* **1980**, *102*, 6613.

[13] For a detailed study on the structure of halomethylzinc reagents, see: (a) Charette, A. B.; Marcoux, J. F.; Molinaro, C.; Beauchemin, A.; Brochu, C.; Isabel, E. *J. Am. Chem. Soc.* **2000**, *122*, 4508. (b) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592. (c) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 3390. (d) Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974.

[14] Lipshutz, B. H. *Synlett* **1990**, 119.

[15] For preparation of secondary zinc carbenoid via bismetalated species, see: Chemla, F.; Marek, I.; Normant, J. F. *Synlett* **1993**, 665. For the preparation from 1,1-bisiodoalkanes, see: (b) Shibli, A.; Varghese, J. P.; Knochel, P.; Marek, I. *Synlett* **2001**, 818. (c) Charette, A. B.; Lemay, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1090.

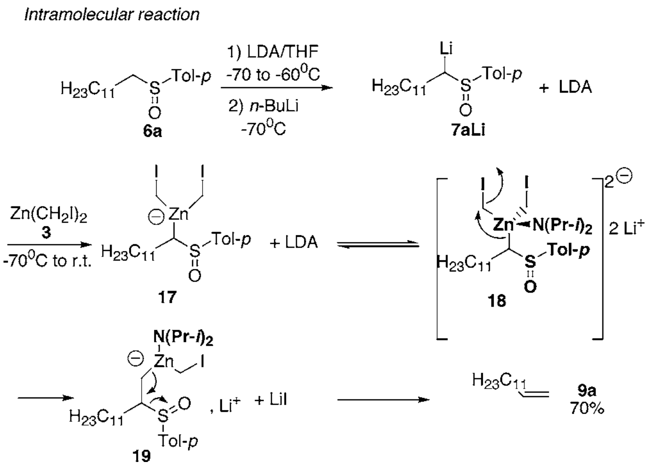
[16] Aufauvre, L.; Knochel, P.; Marek, I. *Chem. Commun.* **1999**, 2207.

[17] Tertiary organocopper **15** already decomposes at −50 °C.

[18] (a) Marek, I. *Tetrahedron* **2002**, *58*, 9463. (b) Harada, T.; Katsuhira, T.; Hara, D.; Kotani, Y.; Maejima, K.; Kaji, R.; Oku, A. *J. Org. Chem.* **1993**, *58*, 4897. (c) Harada, T.; Chiba, M.; Oku, A. *J. Org. Chem.* **1999**, *64*, 8210.

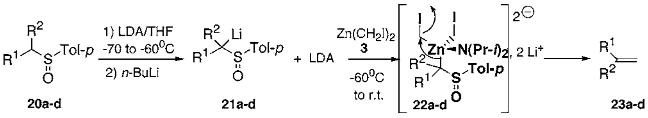
to regenerate the LDA, and then with the bis(iodomethyl)zinc carbenoid **3**, the olefin **9a** was isolated in 70% yield (Scheme 4).

Scheme 4



The regeneration of LDA is fundamental for the reaction to proceed (without adding this second equivalent of BuLi, no transformation of alkyl sulfoxide into olefin was observed). This result can be interpreted by the necessity to reach the "higher order zincate" **18** as a reactive intermediate (Scheme 4).[19] Higher order cuprate[20] and zincate[21] derivatives have already been described for the 1,2-metalate rearrangement.[22] Based on these observations, the preparation of α,α-disubstituted alkenes was reinvestigated through the 1,2-metalate rearrangement of higher order zincate as described in Table 2.

Table 2. α-Lithiocarbanions into α,α-Disubstituted Alkenes



entry	R^1	R^2	products	yield (%)[a]
1	$C_{11}H_{23}$	C_4H_9	**23a**	65
2	C_4H_9	C_6H_5	**23b**	68
3	C_4H_9	$CH_2CH{=}CH_2$	**23c**	66
4	C_6H_5	$CH_2CH{=}CH_2$	**23d**	67

[a] Yield of isolated pure product after column chromatography.

By using these new conditions for the intramolecular 1,2-metalate rearrangement, α,α-disubstituted olefins are obtained in good overall yield from the corresponding α-sulfinyl carbanions in an easy and straightforward manner. It should be emphasized that the reaction does not require an excess of reagents; 1 equiv of zinc carbenoid **3** for 1 equiv of disubstituted sulfoxide **20** and 1 equiv of LDA are used. Moreover, these mild conditions allow the exclusive preparation of nonconjugated dienes such as **23c**,**d** (Table 2, entries 3 and 4).

In conclusion, α-mono- and α,α-disubstituted alkenes are easily prepared from α-lithiosulfinyl carbanions via two different mechanisms: (1) an intermolecular S_N2-type process between an organocopper and the zinc carbenoid and (2) intramolecular reaction via a higher order zincate and subsequent 1,2-metalate rearrangement.

In both cases, the tandem zinc homologation−β-elimination reaction leads to the expected olefins in an easy and straightforward manner.

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Supporting Information Available: Experimental procedures with a description of ^1H and ^{13}C NMR data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) If the in situ-generated $HN(i\text{-}Pr)_2$ protonates the organozincate **17**, two different carbon−carbon bonds of **17** can be cleaved. (a) The Zn−CH_2I bond leads to a new $RCH(SOTol)ZnCH_2I$ combined with CH_3I and $LiN(i\text{-}Pr)_2$. The reaction between the first and the latter compounds may lead to the new heterozincate $RCH(SOTol)Zn(i\text{-}Pr)_2NCH_2I$, Li^+. However, no zinc homologation was observed. (b) If the Zn−CH(SOTol)R bond is cleaved, $Zn(CH_2I)_2$, RCH_2SOTol, and $LiN(i\text{-}Pr)_2$ are formed. Heterozincate $Zn(CH_2I)_2N(i\text{-}Pr)_2$ can result from the combination of the two anionic species, but no zinc homologation of alkyl sulfoxides $RCH_2(SOTol)$ can be expected.

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(22) Mc Williams, J. C.; Amstrong, J. D., III; Zheng, N.; Bhupathy, M.; Volante, R. P.; Reider, P. J. *J. Am. Chem. Soc.* **1996**, *118*, 11970.