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"EFFICIENT CONVERSION OF SULFIDES INTO ESTER-STABILIZED YLIDS; ALKENE SYNTHESIS VIA YLID FRAGMENTATION"

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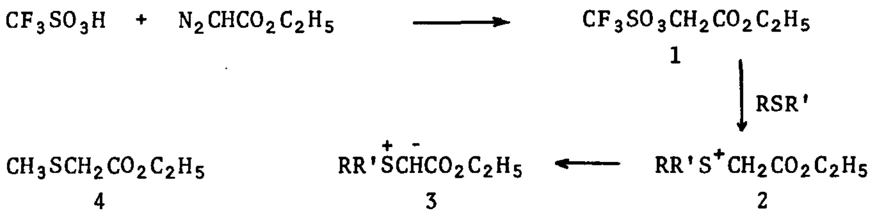
During our work on sulfur ylid ring expansions[1], we needed to prepare ester-stabilized ylids from dialkyl sulfides. The obvious approach of sulfide alkylation with ethyl bromoacetate and subsequent deprotonation failed repeatedly due to nucleophilic cleavage of the desired sulfonium salts by bromide ion.[2,3] To avoid this complication, we have resorted to the triflate 1, easily prepared from ethyl diazoacetate and trifluoromethane sulfonic acid.[4] This new reagent alkylates a variety of sulfides in 85-98% yield at room temperature in acetonitrile. Reaction times for the alkylation step range from a few minutes for dialkyl sulfides to several days for hindered and inductively deactivated systems (see Table). Deprotonation of the resulting sulfonium salts 2 with 1,5-diazabicyclo [5.4.0]undec-5-ene (DBU) is rapid and efficient. Thus, various ester-stabilized sulfur ylids 3 become available for study.



$$\begin{tikzcd}
CF_3SO_3H + N_2CHCO_2C_2H_5 \arrow[rr] & & CF_3SO_3CH_2CO_2C_2H_5 \ \mathbf{1} \arrow[d, "RSR'"] \\
CH_3SCH_2CO_2C_2H_5 \ \mathbf{4} & RR'\overset{+}{S}\overset{-}{C}HCO_2C_2H_5 \ \mathbf{3} & RR'S^{+}CH_2CO_2C_2H_5 \ \mathbf{2} \arrow[l]
\end{tikzcd}$$

In the case of simple alkyl derivatives such as 3a-3d, the ylids can be observed in acetonitrile solution by nmr. However, the ylids 3e-3j fragment rapidly at room temperature to afford α,β-unsaturated esters or lactones and ethyl α-methylsulfenylacetate 4 (Table 2). The overall isolated yield of elimination products is 70-90% from starting sulfide for the two step (one pot) sequence. This procedure can be recommended as a useful, low-temperature alternative to sulfide elimination via pyrolysis of α-methylsulfinyl esters and lactones which requires temperatures above 100°[5]. Furthermore, sulfoxide pyrolysis generates a potentially reactive (transient) sulfenic acid while ylid fragmentation results in the relatively innocuous ethyl α-methylsulfenyl acetate in addition to the olefin.

Table 1; Ylids Generated From Dialkylsulfides

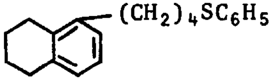
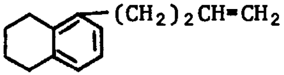
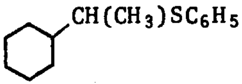
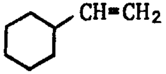
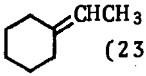
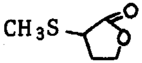
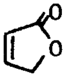
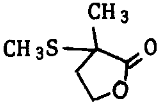
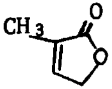
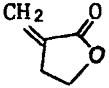
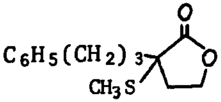
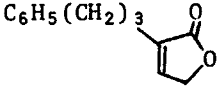
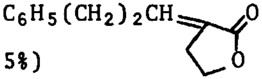
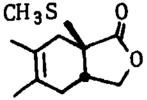
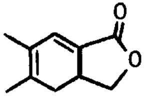
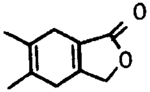
Sulfide	Alkylation Time[a]	Ylide	Elimination Time (50°, DMF)	Products (Overall Yield)
$C_6H_5(CH_2)_3SC_6H_5$	3 hrs.	**3a**	3 hrs.	$C_6H_5CH_2CH{=}CH_2$ (69%)[b]
$C_6H_5(CH_2)_2CH(CH_3)SC_6H_5$	9 hrs.	**3b**	3 hrs.	$C_6H_5(CH_2)_2CH{=}CH_2$ (50%), $C_6H_5CH_2CH{=}CHCH_3$ (31%, 2:1 trans:cis)
	4 hrs.	**3c**	3 hrs.	 (89%)
	11 hrs.	**3d**	1.5 hrs.	 (57%)  (23%)

Table 2; Ylids From α-Sulfenyl Esters and Lactones

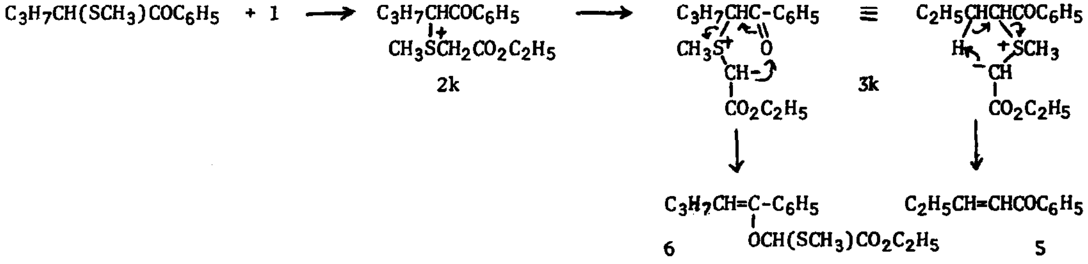
Sulfide	Alkylation Time[a]	Ylide	Elimination Time (50°, DMF)	Products (Overall Yield)
$C_5H_{11}CH(SCH_3)CO_2CH_3$	5 hrs.	**3e**	c	$C_4H_9CH{=}CHCO_2CH_3$ (88%)
$C_6H_5CH_2CH(SCH_3)CO_2C_2H_5$	8 hrs.	**3f**	c	$C_6H_5CH{=}CHCO_2C_2H_5$ (76%)
	2 days	**3g**	c	 (94%)[b]
	2 days	**3h**	c	 (40%)  (47%)
	10 days	**3i**	c	 (45%)  (42%)
	8 hrs.	**3j**	c	 (39%)  (31%)

a) All alkylations in CH_3CN, 25°, 1.1 eq. triflate 1 b) Nonisolated yield, based on internal standard
c) Reaction complete by nmr within 10 min. at 25° in CH_3CN

Synthetically useful yields of alkenes can also be obtained by elimination of the simple alkyl sulfide-derived ylids 3a-3d. Elimination is complete after 2-3 days at 25° or ca. 3 hours at 50°. The results in Table 1 refer to eliminations using DMF as the solvent for ylid generation. Acetonitrile may also be used, but the fragmentation step is somewhat slower.

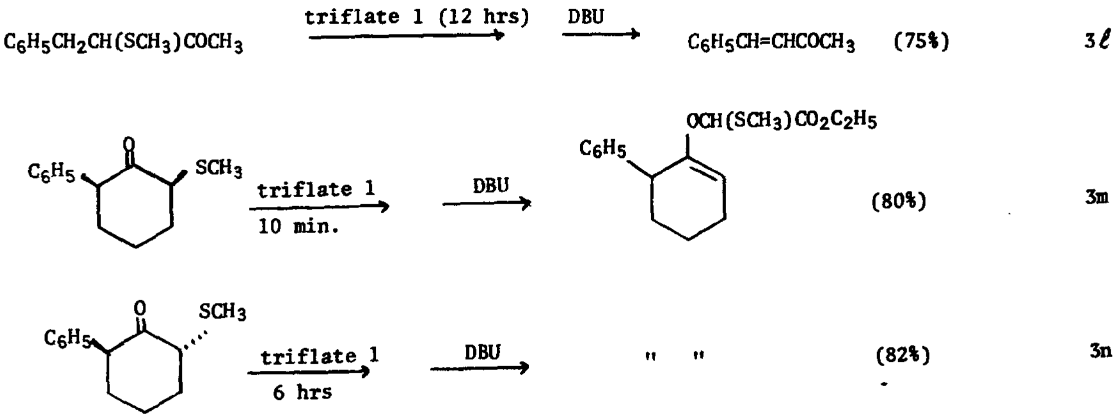
Conversion of α-sulfenyl ketones into ester-stabilized ylids can be accomplished as before by alkylation with triflate 1 and DBU deprotonation.[6] However, the resulting ylids have available a second reaction path which competes with fragmentation to the enone. Thus, treatment of salt 2k with DBU results in rapid conversion to 3k and spontaneous formation of enone 5 (52% based on sulfide) and the enol ether 6 (43%) (Scheme 1).

Scheme 1



Scheme 2

(α-Sulfenylketone-derived ylids)



As summarized in Scheme 2, changes in the substitution pattern of the α-sulfenyl ketone can favor either the elimination pathway to enone (3ℓ) or cause exclusive rearrangement (formally, a 2,3 shift) to enol ether (3m, 3n). Enol ether formation has been observed previously in analogous systems.[7]

The literature contains several reports of alkene formation by the fragmentation of sulfur ylids.[8,9] A concerted 5-center mechanism is generally proposed for these reactions, and this has been confirmed in one case involving a nonstabilized ylid.[9] There are also several examples where the fragmentation of ester-stabilized ylids was inferred although the alkene was not isolated.[10,11] Thus, decomposition of ethyl diazoacetate in sulfides of the formula C_2H_5SR gives low yields of $RSCH_2CO_2C_2H_5$, a plausible ylid fragmentation product.[10]

Our results establish a superior method for ester-stabilized ylid generation, and demonstrate unambiguously that such ylids fragment to alkenes. The procedure is especially useful for the mild conversion of α-sulfenyl esters and lactones into the α,β-unsaturated compounds. We also note that typical α-sulfenyl carbonyl compounds are most conveniently prepared by enolate sulfenylation by thiolsulfonates ($CH_3SSO_2CH_3$, $ArSSO_2Ar$)[12,13]. Yields are consistently excellent in our experience, and the byproduct is the water soluble and odorless sulfinate anion.

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References

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4. Preparation of the triflate 1: Ethyl dizaoacetate (4.56g) is added to trifluoromethanesulfonic acid (6g) in liquid SO_2 (100 ml) over 20 minutes at -78°. After an additional hour, the Dry Ice bath is removed. The residue after SO_2 evaporation is cooled to -78° and treated with ice (10g) and extracted with hexane. After drying (Na_2SO_4) and evaporation (aspirator) the yellow oil is dissolved in hexane, (150 ml), the hexane is decanted from any residue and cooled to -78°. The oily-crystalline product is allowed to redissolve and a layer of insoluble yellow oil is withdrawn by pipette from the bottom of the flask. The process is repeated if necessary to remove the insoluble oily byproducts, and the solution is then stored in the freezer to crystallize pure 1 as long colorless needles. The cold hexane is decanted from the product to leave 6.9g (73%) of 1 (lachrymator)M.P. 22-3°. The reaction can also be done in ether solution, but the yield is only 30-40%.
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