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CONVENIENT SYNTHESIS OF VINYL KETONES *VIA* A NEW THREE CARBON HOMOLOGATING AGENT

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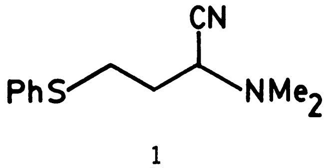
Syntheses of vinyl ketones and the himachalene skeleton from 4-phenylthio-N,N -dimethylaminobutyronitrile were demonstrated.

Much attention has been devoted to the development of a 3-carbon fragment as β-acylvinyl anion and homoenolated anion equivalents.1) Several applications of the synthon have been demonstrated.1,2) In This communication we wish to report the utilization of the new reagent 1, 4-phenylthio-2-N,N -dimethylaminobutyronitrile,3) as an acyl anion equivalent4) 2.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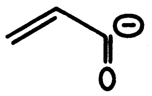
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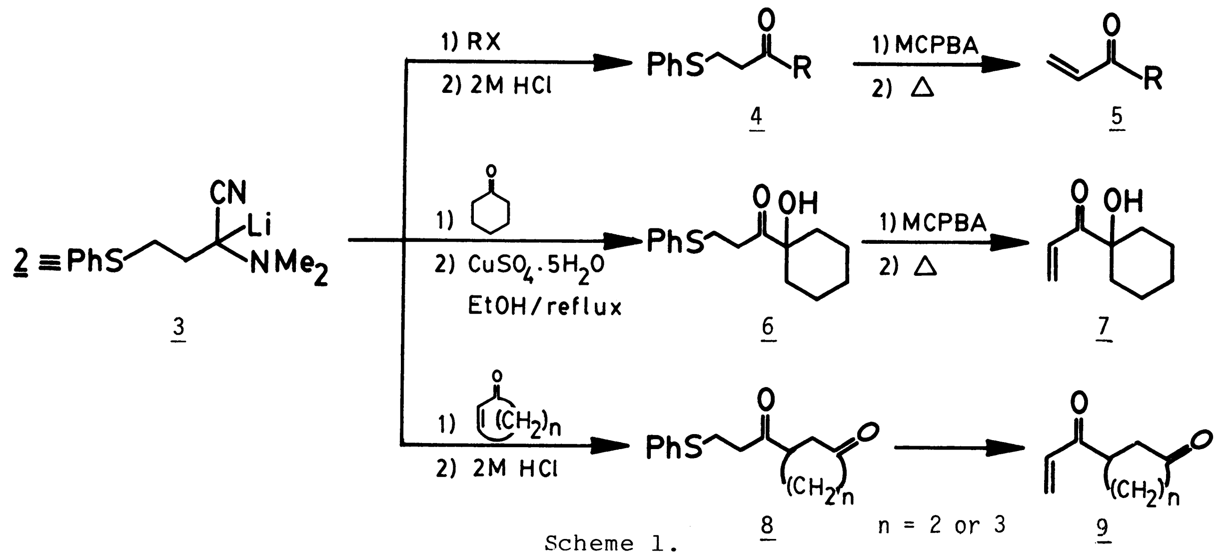
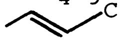
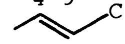
The lithio compound 3 was generated by the reaction of 1 with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78 °C. The anion 3 could undergo alkylation with halides, 1,2- and 1,4-additions to carbonyl and α,β-unsaturated carbonyl compounds, respectively, to give adducts which upon hydrolysis gave the corresponding γ-keto sulfides5) in good yield (Scheme 1).



Scheme 1.

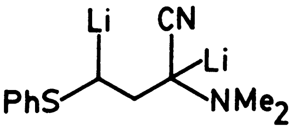
It was found that the yields of γ-keto sulfides could be optimized by using 2.0 to 2.5 equivalents of LDA. The γ-keto sulfides were oxidized by either sodium metaperiodate or m-chloroperbenzoic acid (MCPBA) to give the corresponding labile γ-keto sulfoxides which upon pyrolysis gave vinyl ketones in high yields.[6)] It was found that with low boiling vinyl ketones, the best method to obtain the pure vinyl ketones was to pyrolyze the γ-keto sulfoxides under reduced pressure and the products were trapped in a Dry Ice-acetone bath (Method 1). For higher boiling vinyl ketones, the addition of calcium carbonate[5)] to the pyrolytic mixtures gave products which could be easily purified by preparative layer chromatography (PLC) (Method 2). The results are summarized in Table 1.

Table 1. Reaction of 3 with electrophiles and the synthesis of vinyl ketones

Entry	Electrophiles	γ-Keto sulfides[a)]/%	Vinyl ketones[a)]/%
1	n-C_4H_9Br	4, R = n-C_4H_9-, 95[f)]	5, R = C_4H_9-, 94[b)]
2	CH_2Br	4, R = CH_2-, 87[f)]	5, R = CH_2-, 83[b)]
3	$PhCH_2Br$	4, R = $PhCH_2$-, 61[f)]	5, R = $PhCH_2$-, 81[b)]
4	Cyclohexanone	6, 73[g)]	7, 93[b)]
5	Cyclohexenone	8, 63[f)]	9, 56[c)]
6	Cyclopentenone	8, 64[f)]	9, 53[c)]
7	n-$C_8H_{17}Br$	8, C_8H_{17}-, 81[f)]	5, R = C_8H_{17}-, 89[b,d)]
8	n-$C_9H_{19}Br$	8, C_9H_{19}-, 74[f)]	5, R = C_9H_{19}-, 93[b,e)]
9	n-$C_{11}H_{23}Br$	8, $C_{11}H_{23}$-, 73[f)]	5, R = $C_{11}H_{23}$-, 82[c,e)]
10	n-$C_{13}H_{27}Br$	8, $C_{13}H_{27}$-, 71[f)]	5, R = $C_{13}H_{27}$-, 89[c,e)]
11	$CH_2=CH(CH_2)_8CH_2Br$	8, $CH_2=CH(CH_2)_8CH_2$-, 70[f)]	5, R = $CH_2=CH(CH_2)_8CH_2$-, 82[c,e)]

a) Electrophiles were added to a solution of 3 (1 equiv.) in THF and hexamethylphosphoramide (40:1 V/V) at -78 °C (for carbonyl compounds, 1 equiv. of $ZnCl_2$ was added). The mixture was slowly warmed to room temp. and then stirred overnight. The reaction was quenched with saturated aq. ammonium chloride and the product was isolated with $CHCl_3$. The crude adduct was hydrolyzed with 2M HCl (Method 3) or $CuSO_4 \cdot 5H_2O$ in ethanol (Method 4).[7)] The products, γ-keto sulfides, were purified by PLC with $CHCl_3$ as the mobile phase. The oxidation of γ-keto sulfides was conveniently effected with MCPBA in dichloromethane at -78 °C for 10 min. The resulting γ-keto sulfoxides were immediately pyrolyzed by either Method 1 or 2. b) Pyrolysis by Method 1. c) Pyrolysis of Method 2. d) The vinyl ketone was isolated from *Dictyopteris plagiogramma*.[8)] e) Substances secreted by soldiers of the termite *Cortaritermes silvestri*.[9)] f) Hydrolysis by Method 3. g) Hydrolysis by Method 4.

Attempts to generate the dianion 10 by using excess LDA or n-BuLi in the presence of either diazabicyclo[2.2.2]octane (DABCO) or N,N,N',N'-tetramethylethylendiamine (TMEDA)[10)] were unsuccessful. Only mono-anion 3 was formed as indicated by deuteration and alkylation (with methyl iodide) experiments.



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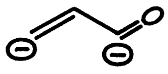

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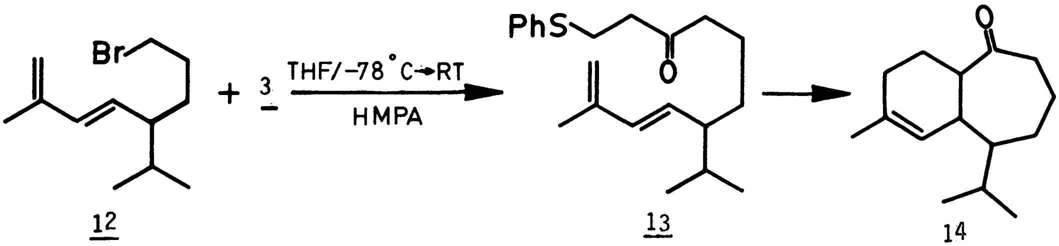
The synthetic potential of the new three-carbon unit was further demonstrated by the synthesis of himachalene11) ring skeleton. Alkylation of 3 with 12 12) (Scheme 2) according to the procedure described previously gave the expected 13 in 84% yield. Oxidation of 13 with MCPBA at $-78\ ^{\circ}$C in dichloromethane followed by pyrolysis in carbon tetrachloride in the presence of calcium carbonate gave 14 directly in 71% yield (from 13).

Our results demonstrated that 1 can be utilized effectively as the anion equivalent 2. Further exploratory work is in progress.



Scheme 2.

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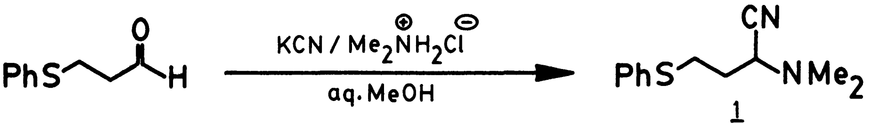
3) Compound 1 was prepared as shown below. The product was purified by column chromatography on silica gel using chloroform:hexane(1:1), (Cf., Ref. 7).



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