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

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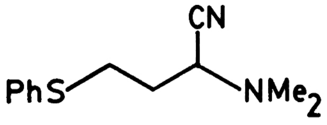
Syntheses of vinyl ketones and the himachalene skeleton from 4-phenylthio-N,N -dimethylaminobutyronitrile were demonstrated.

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 equivalent[4] 2.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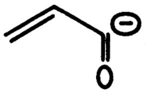
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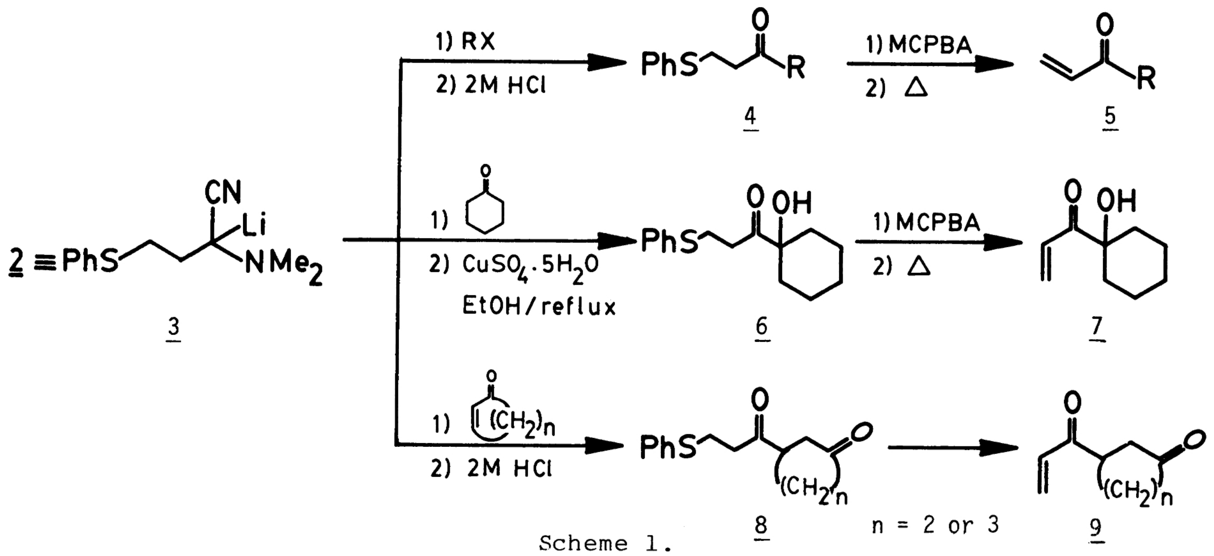
The lithio compound 3 was generated by the reaction of 1 with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78 °C. The anion 3 could undergo alkylation with halides, 1,2- and 1,4-additions to carbonyl and α,β-unsaturated carbonyl compounds, respectively, to give adducts which upon hydrolysis gave the corresponding γ-keto sulfides[5] in good yield (Scheme 1).



Scheme 1.

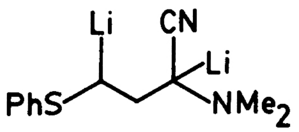
It was found that the yields of γ-keto sulfides could be optimized by using 2.0 to 2.5 equivalents of LDA. The γ-keto sulfides were oxidized by either sodium metaperiodate or m-chloroperbenzoic acid (MCPBA) to give the corresponding labile γ-keto sulfoxides which upon pyrolysis gave vinyl ketones in 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 $\underline{3}$ with electrophiles and the synthesis of vinyl ketones

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

a) Electrophiles were added to a solution of $\underline{3}$ (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 $CuSO_4.5H_2O$ 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 $\underline{10}$ 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 $\underline{3}$ was formed as indicated by deuteration and alkylation (with methyl iodide) experiments.



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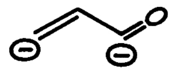

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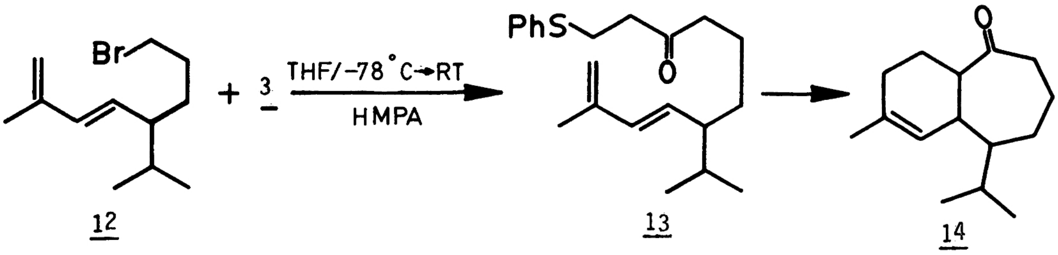
The synthetic potential of the new three-carbon unit was further demonstrated by the synthesis of himachalene[11] ring skeleton. Alkylation of 3 with 12[12] (Scheme 2) according to the procedure described previously gave the expected 13 in 84% yield. Oxidation of 13 with MCPBA at -78 °C in dichloromethane 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.



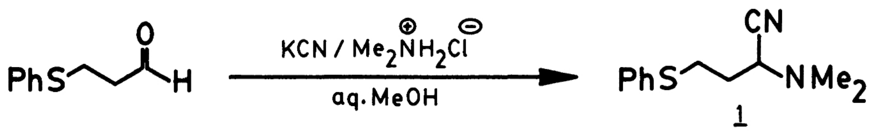
Scheme 2.

References

1) For leading references see: P. Bakuzis, M.L.F. Bakuzis, and T.F. Weingartner, Tetrahedron Lett., 1978, 2371; Y. Nagao, K. Seno, and E. Fujita, ibid., 1979, 3167; C. Shih and J.S. Swenton, ibid., 22, 4217 (1981); S.D. Lombaert, B. Lesur, and L. Ghosez, ibid., 23, 4251 (1982); R. Goswami and D.E. Corcoran, ibid., 23, 1463 (1982); H.J. Cristau, B. Chaband, and C. Niangoran, J.Org.Chem., 48, 1527 (1983); N.H. Werstiuk, Tetrahedron, 39, 205 (1983).

2) R.M. Jacobson and J.W. Clader, Tetrahedron Lett., 21, 1205 (1980); P. Prempree, T. Siwapinyoyos, C. Thebtaranonth, and Y. Thebtaranonth, ibid., 21, 1169 (1980); R.M. Jacobson, G.P. Lahm, and J.W. Clader, J.Org.Chem., 45, 395 (1980).

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).



4) J.C. Clinet and G. Linstrumelle, Tetrahedron Lett., 1978, 1137; S.J. Gould and B.D. Remillard, ibid., 1978, 4353.

5) C.L. Bumgardner, J.R. Lever, and S.T. Purrington, Tetrahedron Lett., 23, 2379 (1982) and references cited therein.

6) For selected references on preparation of vinyl ketones see: P.A. Grieco, D. Boxler, and C.S. Pogonowski, J.Chem.Soc., Chem.Commun., 1974, 497; R.C. Cookson and P.J. Parsons, ibid., 1978, 821; J.C. Floyd, Tetrahedron Lett., 1974, 2877; R. Block, Tetrahedron, 39, 639 (1983); C.E. Russell and L.S. Hegedus, J.Am.Chem.Soc., 105, 943 (1983).

7) V. Reutrakul, S. Nimgirawath, S. Panichanun, and P. Ratananukul, Chem.Lett., 1979, 399.

8) P. Roller, K. Au, and R.E. Moore, Chem.Commun., 1971, 503.

9) R. Baker and S. Walmsley, Tetrahedron, 38, 1899 (1982).

10) T.M. Dolak and T.A. Bryson, Tetrahedron Lett., 1977, 1961; E. Watanabe, N. Imai, K. Inomata, H. Kinoshita, and H. Kotake, Bull.Chem.Soc. Jpn., 55, 3225 (1982).

11) Cf. E. Wenkert and K. Naemura, Syn.Commun., 3, 45 (1973).

12) D.F. Taber and B.P. Gunn, J.Am.Chem.Soc., 101, 3992 (1979).

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