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PREPARATION OF 4-HYDROXY-2-ALKENENITRILES FROM PHENYLSULFINYLACETONITRILE WITH KETONES OR ALDEHYDES, AND ITS SYNTHETIC APPLICATION TO SUBSTITUTED FURANS(1)

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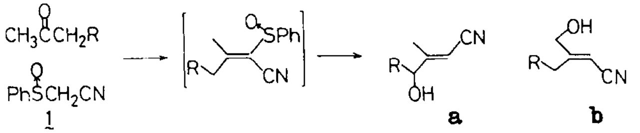
Summary: The reaction of phenylsulfinylacetonitrile **1** with ketones or aldehydes gave 4-hydroxy-2-alkenenitriles which were converted to 2- and/or 3-substituted furans by the treatment with diisobutylaluminumhydride(DIBAL) followed by acid hydrolysis.

As part of our continuing interest in the reaction of organosulfur compound, the reaction of sulfinylactivated methylene compounds was a matter of prime interest because of the various functionalization by the sulfinyl group. In this communication, we describe a reaction of phenylsulfinylacetonitrile **1** with ketones or aldehydes in the presence of base, to give directly 4-hydroxy-2-alkenenitriles(2) which are useful synthons for substituted furans,(1) and point out the regioselectivity of the hydroxy group in the case of the reaction of **1** with 2-alkanone.

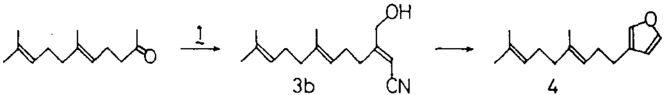


2 R=n-C_5H_{11}

3 R=geranyl

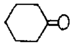
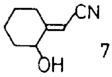
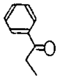
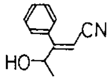
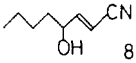
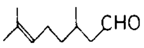
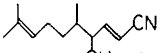
As a typical procedure, **1** was treated with 2-octanone(1.2 equiv.) and piperidine(1 equiv.) in methanol at room temperature for 10 hr. The reaction mixture was concentrated and washed with diluted hydrochloric acid and extracted with ether. The extract was concentrated and the residue was purified by column chromatography on alumina with dichloromethane and followed with methanol. From the methanol eluate, 4-hydroxy-3-methyl-2-nonenenitrile **2a**(3) was obtained in 84% yield as a sole product. The same substrates were treated with piperidine(1 equiv.) in refluxing benzene for 8 hr and with piperidine-acetic acid(each 0.2 equiv.) in refluxing benzene for 34 hr, to give a mixture of **2a** and 3-hydroxymethyl-2-nonenenitrile **2b**(4) in the ratio of 1:1(62% yield) and in the ratio of 1:7(76% yield) respectively. Each of them was isolated by column chromatography on silica gel with n-hexane/ether(1/1). Similarly, the treatment of geranylacetone with **1** and piperidine(1 equiv.) in methanol at r.t. for 17 hr, and piperidine(0.2 equiv.) in refluxing benzene for 10 hr afforded **3a**(85% yield) and a mixture of **3a** and **3b**(5) (1:6, 54% yield) respectively. Other typical reactions are summarized in Table 1.

4-Hydroxy-2-alkenenitrile thus obtained was converted to substituted furan by the reduction using DIBAL followed by acid hydrolysis.(1) For example, **3b**, which was isolated by column chromatography on silica gel, was treated with DIBAL(2.2 equiv.) in dry ether for 1 hr at -5°C. The reaction mixture was hydrolyzed with hydrochloric acid(1N) for 2 hr to give sesquiterpene furan **4**[6](dendrolasin) in 75% yield based on **3b**.



3b 4

Table 1

Ketone or Aldehyde	Base (mol equiv.)	Solvent	Temp (°C)	Time (hr)	Product yield(%)
	piperidine (1)	CH_3OH	r.t.	15	 71
	CH_3ONa (1)	CH_3OH	r.t.	10	 45
	piperidine (1)	benzene	r.t.	1.5	 81
	piperidine (1)	benzene	r.t.	1	 94

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1) The conversion of 4-hydroxy-2-alkenenitrile to furan has been reported by us: T. Mandai, S. Hashio, J. Goto, and M. Kawada, Tetrahedron Lett., **22**, 2187(1981).

2) It has been reported that the reaction of methyl phenylsulfinylacetate with aldehyde, in the presence of catalytic amount of piperidine-acetic acid, gave the corresponding 2-phenylsulfinyl-2-alkenoate; M. Onaka and T. Mukaiyama, 41st Anual Meeting of Chem. Soc. Jpn., Abstract II. 983(1980) Osaka. Moreover, the conversion of α-phenylsulfinyl αβ-unsaturated ester(or ketone) to γ-hydroxy αβ-unsaturated ester(or ketone) has been known; H. Kosugi, H. Uda, and S. Yamagiwa, Chem. Comm., 192(1975); T. Fujisawa, K. Sakai, H. Shirakata, and S. Sasaki, 37th Anual Meeting of Chem. Soc. Jpn., Abstract II. 909(1978) Tokyo.

3) NMR($CDCl_3$) δ 2.00 (3H, d, J 1 Hz, $C=CCH_3$), 4.10 (1H, m, $C\underline{H}(OH)C=C$), 5.48 (1H, t, J 1 Hz, C=CHCN).

4) NMR δ 2.33 (2H, t, J 7 Hz, $CH_2C=C$), 4.15 (2H, d, J 2 Hz, $C=CC\underline{H}_2(OH)$), 5.52 (1H, t, J 2 Hz, C=CHCN).

5) NMR δ 4.12 (2H, d, J 2 Hz, $C=CC\underline{H}_2(OH)$), 5.01 (2H, m, C=CH), 5.46 (1H, t, J 2 Hz, C=CHCN).

6) Synthesis of dendrolasin from geranylacetone has been reported (20% overall yield); M. E. Garst and T. A. Spencer, J. Am. Chem. Soc., **95**, 250(1973).

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