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PREPARATION OF UNSATURATED NITRILES BY THE MODIFICATION  
OF MITSUNOBU-WILK PROCEDURE

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**ABSTRACT:** An efficient one-step procedure for the conversion of unsaturated alcohols into the corresponding nitriles by the modification of Mitsunobu-Wilk reaction is described.

The conversion of unsaturated alcohols into the corresponding nitriles is an important method in elongation of the chain by one carbon<sup>1</sup>. The resulting unsaturated nitriles are useful synthetic intermediates for the synthesis of biologically active compounds (e.g. sex pheromones).<sup>1,2</sup>

The direct transformation of saturated alcohols into the corresponding nitrile have been achieved by Mitsunobu. His one-pot procedure was performed under mild condition using triphenylphosphine and HCN in the presence of diethyl azodicarboxylate<sup>3</sup>. Recently, Wilk made the method more convenient by replacing HCN with acetone cyanohydrin<sup>4</sup>.

However, our attempts for the conversion of (*Z,Z*)-3,6-octadien-1-ol to the corresponding nitrile according to the procedure of Mitsunobu-Wilk, adding subsequently DEAD and acetone cyanohydrin to a solution of PPh<sub>3</sub> and alcohol, were unsuccessful. Here, no reactions were observed and most of the starting material was recovered.









We therefore studied the transformation of unsaturated alcohols carrying conjugated or unconjugated olefinic functions and wish to report the successful preparation of unsaturated nitrile.

A slight modification of the above procedure, namely, subsequent additions of DEAD, alcohol and acetone cyanohydrin to a cold solution of PPh<sub>3</sub>, followed by stirring at r.t., resulted smooth reactions and the unsaturated nitriles were isolated in good yields (Table).

We have also applied this procedure for the conversion of diphenylcarbinol into diphenylacetonitrile. This transformation had been performed by Wilk in 10% yield. With the above modification we obtained the desired product in 30% yield (Table, entry 5).

In summary, under modified condition described above, unsaturated alcohols can now be converted conveniently into the corresponding nitrile by Mitsunobu-Wilk method, in good yield.

Table. Conversion of Alcohols to Nitriles

Entry	Substrate	Time (h)	Product	Yield (%) <sup>a</sup>
1		10		70
2		3		50
3		16		61
4		20		59
5	Ph <sub>2</sub> CH-OH	20	Ph <sub>2</sub> CH-CN	30

<sup>a</sup>Yields refer to isolated, chromatographically homogeneous material

## EXPERIMENTAL

$^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra were recorded with a Varian WXR-400 instrument at 400 and 100 MHz: internal standard TMS. The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Gas chromatographic analyses were conducted on Hewlett-Packard 5890 instrument equipped with a flame-ionization detector and employing a silica capillary column (5m x 0,53 mm ID).

### General Procedure:

To a stirred solution of triphenylphosphin (1.0 g, 3.8 mmol) in dry ether (10 ml) was added dropwise diethyl azodicarboxylate (0.66 g, 3.8 mmol) at  $-20^\circ\text{C}$ , under  $\text{N}_2$ . The resulting mixture was stirred for 20 min under cooling, then alcohol (2.5 mmol) was added dropwise at  $-20^\circ\text{C}$ . After stirring for 20 min at  $-20^\circ\text{C}$ , a solution of acetone cyanohydrin (0.32 g, 3.75 mmol) in dry ether (1 ml) was added and the mixture was stirred at this temperature for 4 h. The reaction mixture was allowed to warm to r.t. and stirred for the time indicated in Table. The white precipitate was filtered off and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (hexane/acetone, 10:0.5) to afford pure nitriles (Table, entries 1-5).

**(Z,Z)-Nona-3,6-dienitrile.** HPLC:  $R_t=4.96$  min.

$^1\text{H}$ -NMR ( $\text{CDCl}_3$ ): 0.99 (t, 3H,  $J=7\text{Hz}$ ,  $\text{CH}_3$ ), 2.07 (m, 2H,  $\text{CH}_2$ ), 2.89 (m, 2H,  $\text{CH}_2$ ), 3.12 (dt, , 2H,  $J=7\text{Hz}$ ,  $\text{CH}_2$ ), 5.25-5.75 (m, 4H, 2 $\text{CH}=\text{CH}$ ).

**$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):** 14.14 (C-9), 15.59 (C-8), 20.63 (C-2), 25.51 (C-5), 118.51 (C-N), 124.936 (C-7 and C-6), 133.34 (C-4), 134 (C-3).

**(E,E)-Hepta-3,5-dienenitrile.** HPLC:  $R_t=2.55$  min.

**$^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):** 1.77 (dm, 3H,  $J=6.5\text{Hz}$ ,  $\text{CH}_3$ ), 3.14 (dm, 2H,  $J=6\text{Hz}$ ,  $\text{CH}_2$ ), 5.40 (dt, 1H,  $J=15$  and  $6\text{Hz}$ , =CH), 5.77 (dq, 1H,  $J=4.5$  and  $7\text{Hz}$ , =CH), 6.04 (ddq, 1H,  $J=15.10$  and  $2\text{Hz}$ , =CH), 6.33 (ddt, 1H,  $J=15$ , 10, and  $1\text{Hz}$ , =CH).

**$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):** 18.14 (C-7), 20.35 (C-2), 119.14 (C-N), 127.95 (C-5), 129.66 (C-4), 131.49 (C-6), 134.98 (C-3).

**(Z)-Tridec-9-enenitrile.** HPLC;  $R_t=5.44$  min.

**$^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):** 0.9 (t, 3H,  $J=6\text{Hz}$ ,  $\text{CH}_3$ ), 1.37 (m, 2H,  $\text{CH}_2$ ), 1.25-1.5 (m, 8H, 4 $\text{CH}_2$ ), 1.65 (m, 2H,  $\text{CH}_2$ ), 2.0 (m, 2H,  $\text{CH}_2$ ), 2.35 (t, 2H,  $J=7\text{Hz}$ ,  $\text{CH}_2$ ), 5.36 (m, 2H,  $\text{CH}=\text{CH}$ ).

**$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):** 13.82 (C-13), 17.13 (C-12), 22.89 (C-11), 25.37 (C-5), 27.11 (C-4), 28.65 (C-6), 28.67 (C-3), 28.92 (C-2), 29.31 (C-7), 29.58 (C-8), 119.84 (C-N), 129.77 (C-10), 129.87 (C-9).

**(E,E)-Trideca-9,11-dienenitrile.** HPLC;  $R_t=6.15$  min.

**$^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):** 1.25-1.5 (m, 8H, 4 $\text{CH}_2$ ), 1.65 (m, 2H,  $\text{CH}_2$ ), 1.73 (d, 3H,  $J=7\text{Hz}$ ,  $\text{CH}_3$ ), 2.05 (m, 2H,  $\text{CH}_2$ ), 2.33 (t, 2H,  $J=7\text{Hz}$ ,  $\text{CH}_2$ ), 5.48-5.65 and 5.95-6.06 (m, 4H,  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ).

**$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):** 13.82 (C-13), 17.12 (C-5), 18.01 (C-4), 25.35 (C-5), 28.61 (C-3), 28.79 (C-2), 29.24 (C-7), 32.44 (C-8), 119.83 (C-6), 28.61 (C-

3), 28.79 (C-2), 29.24 (C-7), 32.44 (C-8), 119.83 (C-N), 126.87 (C-11), 130.42 (C-10), 131.62 (C-9), 131.81 (C-12).

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