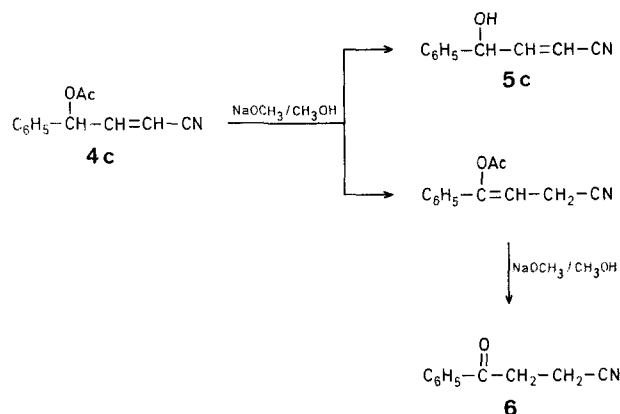


The methanolysis of **4c** is in part accompanied by a base-catalyzed hydrogen shift so that in this case a 2.5:1 mixture of 4-hydroxy-4-phenyl-2-butenitrile (**5c**) and 4-oxo-4-phenylbutanenitrile (**6**) is obtained.



Compounds **5c** and **6** were not separated because their R_F values are too similar. Instead, the mixture **5c**+**6** was oxidized to give a readily separable mixture of the desired unsaturated ketone **1c** and the saturated ketone **6**.

Ene-Dicarbonyl Synthons: An Efficient Synthesis of 3-Cyanopropenal and 2-Cyanovinyl Ketones (4-Oxo-2-alkenenitriles)

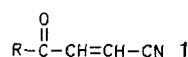
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In the course of our studies on the synthesis of natural products we required several synthons having the general structure **1**.



These unsaturated cyanocarbonyl compounds may provide an attractive entry into other function-differentiated fumaric acid derivatives via simple manipulations. The currently available syntheses of these compounds involve Wittig-type olefination of glyoxal derivatives¹, dehydrohalogenation of suitably substituted saturated precursors², two step displacement of 2-halo-1-alkenyl ketones³, or chemical modification of β -acylacrylic acid derivatives⁴. These approaches are frequently long and cumbersome.

We describe here a convenient and high-yield synthesis of carbonyl compounds **1** from the readily available 2-alkenals **2**. Compounds **2** are easily converted into the cyanohydrin acetates **3** which undergo an essentially quantitative palladium-catalyzed isomerization⁶ to the 4-acetoxy-2-alkenenitriles⁷ **4**. Recently, a palladium(0)-catalyzed isomerization of **3c** into **4c** in 70% yield using 10 mol% of catalyst was reported⁸. In our hands, this conversion proceeded with nearly quantitative yield when freshly distilled **3c** and solvent and only 0.3 mol% of catalyst were used. Solvolysis of acetates **4** gave the 4-hydroxy-2-alkenenitriles **5** which were oxidized with oxalyl chloride/dimethyl sulfoxide under mild conditions to afford the desired products **1** in good overall yields.

2-Acetoxy-3-alkenenitriles (3):

The 2-alkenals **2** are converted into the cyanohydrin acetates **3** following the procedures of Ref.⁵. However, in the case of crystalline cyanohydrins, better yields of **3** may be obtained by preparing the cyanohydrin acetates **3** by a two-step reaction via acetylation of the isolated cyanohydrins.

4-Acetoxy-2-alkenenitriles (4); General Procedure:

To a stirred solution of the freshly distilled 2-acetoxy-3-alkenenitrile (**3**; 0.1 mol) in dry tetrahydrofuran (25 ml) under nitrogen, tetrakis(triphenylphosphine)-palladium⁶ (0.116–0.578 g, 0.1–0.5 mol%) is added at room temperature. The reaction which may be exothermic (temperature rise up to 60°C within the first 10 min) is monitored by T.L.C. (silica gel, ethyl acetate/hexane 1/4) or by ¹H-N.M.R. spectroscopy. After the starting material has been completely consumed (10 min–24 h) the mixture is filtered through a short silica gel column and product **4** is eluted with dichloromethane. The filtrate is flash-evaporated and the residual product purified by kugelrohr distillation.

4-Hydroxy-2-alkenenitriles (5); General Procedure:

Sodium methoxide (54 mg, 1 mmol) is added to a stirred solution of the 4-acetoxy-2-alkenenitrile (**4**; 0.1 mol) in anhydrous methanol (50 ml) and stirring is continued for 5–9 min [pH should be checked periodically and maintained at 8.5, if necessary, by the addition of further sodium methoxide] until compound **4** can no more be detected by T.L.C. (silica gel; ether/hexane 1/1 as eluent; development with 1%

Table. 4-Acetoxy- (4), 4-Hydroxy- (5), and 4-Oxo-2-alkenenitriles (1) prepared

Product	Yield ^a [%]	m.p. [°C] or b.p. [°C]/torr	Molecular formula or Lit. m.p. or b.p.	(E:Z)-Ratio	¹ H-N.M.R. (CDCl ₃ /TMS _{int}) δ [ppm]
4a	97	60–80°/0.2 ^b	98–99°/12 ⁹	81:19	(E): 2.13 (s, 3H); 4.73 (dd, 2H, J=4.4, 2.1 Hz); 5.61 (dt, 1H, J=16.4, 2.1 Hz); 6.75 (dt, 1H, J=16.4, 4.4 Hz) (Z): 2.13 (s, 3H); 4.87 (dd, 2H, J=5.8, 1.7 Hz); 5.54 (dt, 1H, J=11.4, 1.7 Hz); 6.55 (dt, 1H, J=11.4, 5.8 Hz)
4b	95	60–80°/0.2 ^b	C ₇ H ₉ NO ₂ (139.2) ^c	80:20	(E): 1.36 (d, 3H, J=6.7 Hz); 2.09 (s, 3H); 5.36–5.63 (m, 2H); 6.65 (d, 1H, J=21.3 Hz) (Z): 1.42 (d, 3H, J=6.6 Hz); 2.13 (s, 3H); 5.36–5.63 (m, 2H); 6.66 (d, 3H, J=6.7 Hz)
4c ⁸	93	115–125°/0.2 ^b		83:17	(E): 2.13 (s, 3H); 5.59 (dd, 1H, J=16.2, 1.7 Hz); 6.35 (dd, 1H, J=4.8, 1.7 Hz); 6.79 (dd, 1H, J=16.2, 4.8 Hz); 7.3–7.4 (m, 5H) (Z): 2.14 (s, 3H); 5.42 (dd, 1H, J=10.0, 4.7 Hz); 6.55 (m, 2H); 7.38 (s, 5H)
5a	86	100–102°/1	122–122.5°/12 ¹⁰	pure (E)	(E): 4.33 (dd, 2H, J=3.4, 2.3 Hz); 5.71 (dt, 1H, J=16.3, 2.3 Hz); 6.87 (dt, 1H, J=16.3, 3.4 Hz)
5b	90	76–78°/0.5	68–70°/0.3 ¹¹	pure (E)	(E): 1.32 (d, 3H, J=2.3 Hz); 4.46 (ddq, 1H, J=16.3, 3.9, 2.3, 1.9 Hz); 5.65 (dd, 1H, J=16.3, 1.9 Hz); 6.78 (dd, 1H, J=16.3, 3.9 Hz)
5c+6 (mixture)	83	not separated		pure (E) 5c:6=2.5:1	(E)-5c: 5.29 (dd, 1H, J=3.9, 2.0 Hz); 5.76 (dd, 1H, J=16.2, 2.0 Hz); 6.79 (dd, 1H, J=16.2, 3.9 Hz); 7.33 (s, 5H) 6: 2.73 (dt, 2H, J=6.7, 1.1 Hz); 3.36 (dt, 2H, J=6.7, 1.1 Hz); 7.22–8.0 (m, 5H)
1a	66 ^d	40–50°/0.2 ^b	(E): 68°/15 ¹⁰	at –30°C pure (E) at –60°C 2:1	(E): 6.38 (d, 1H, J=16.5 Hz); 6.90 (dd, 1H, J=16.5, 6.5 Hz); 9.70 (d, 1H, J=6.5 Hz) (Z): 10.11 (d, 1H, J=7.1 Hz) ^e
1b	89	50–60°/0.2 ^b	71°/11 ³	pure (E)	(E): 2.37 (s, 3H); 6.31 (d, 1H, J=16.4 Hz); 6.97 (d, 1H, J=16.4 Hz)
1c	98	80–82° ^c	82° ⁴	pure (E)	(E): 6.56 (d, 1H, J=16.1 Hz); 7.81 (d, 1H, J=16.1 Hz); 7.4–8.04 (m, 5H)

^a Yield of isolated product, based on starting material.

^b Kugelrohr distillation.

^c calc. C 60.42 H 6.52 N 10.07
found 60.37 6.46 10.21

^d Although T.L.C. analysis indicated that compound 5a was converted in entirety into 1a, the high reactivity of the latter compound accounted for the lower yield of isolated 1a.

^e The position of the vinylic protons of (Z)-1a could not be measured accurately from the spectrum on the E:Z mixture of aldehydes; only the chemical shift of the aldehydic proton was obtained.

vanillin—1% conc. sulfuric acid in 95% ethanol). The solvent is flash-evaporated and the residual product 5 quickly chromatographed through a short column of silica gel (50 g) using dichloromethane as eluent. The solution is concentrated and the residual product further purified by distillation, kugelrohr distillation, or chromatography.

From 4c as starting material, a 2.5:1 mixture of 5c and 4-oxo-4-phenylbutanenitrile (6) is obtained. This mixture is subjected to the subsequent oxidation without previous separation of the components.

4-Oxo-2-alkenenitriles (1); General Procedure:

The oxidation is carried out using a ratio 5 : oxalyl chloride : dimethyl sulfoxide : triethylamine of 1 : 1 : 2 : 2; an excess of triethylamine should be avoided.

A mixture of dimethyl sulfoxide (6.8 ml, 88 mmol) and dry dichloromethane (5 ml) is added to a stirred solution of oxalyl chloride (4 ml, 44 mmol) in dry dichloromethane (50 ml) at –63°C (cooled with a slurry of chloroform and liquid nitrogen). The mixture is stirred for 5 min; then, a solution of the 4-hydroxy-2-alkenenitrile (5; 44 mmol) in dichloromethane (5–10 ml) is added and stirring is continued for 2–3 min. Then, triethylamine (6.8 ml, 88 mmol) is added and stirring is continued while the progress of the reaction is followed by T.L.C. (silica gel plates developed with 1% vanillin/1% sulfuric acid in 95% ethanol; heating of the plates leads to coloration which is characteristic of the components of the reaction mixture). Upon completion of the

reaction, the mixture is quickly filtered through a silica gel column. The filtrate is evaporated and the residue is further purified by distillation, kugelrohr distillation, chromatography, or crystallization.

In the preparation of 1c, a mixture of nitriles 5c and 6 (obtained from 4c) is used as starting material so that a 2.5:1 mixture of products 1c and 6 is obtained which is separated by column chromatography on silica gel using ethyl acetate/hexane 1:4 as eluent; yield of 1c: 60%; m.p. 80–82°C (Ref.⁴, m.p. 82°C); yield of 4-oxo-4-phenylbutanenitrile (6): 23%; m.p. 76°C (Ref.¹³, m.p. 76°C).

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¹ C. Raulet, *Bull. Soc. Chim. Fr.* **1974**, 531.

² S. Motoki, S. Satsumabayashi, T. Masuda, *Bull. Chem. Soc. Jpn.* **39**, 1519 (1966). The dehydrobromination of 2-bromo-3-cyanopropanal dimethyl acetal can be carried out quantitatively at room temperature using 1,4-diazabicyclo[2.2.2]octane (DABCO) as catalyst instead of the reported 10% sodium hydroxide at low temperature, which gave only 78% yield.

³ W. R. Benson, A. E. Pohland, *J. Org. Chem.* **29**, 385 (1964).

- ⁴ A. N. Nesmeyanov, M. I. Rybinskaya, *Dokl. Akad. Nauk SSSR* **115**, 315 (1957).
F. Farina, P. Victory, *Tetrahedron Lett.* **1969**, 3219.
F. Farina, M. J. Gomez, M. V. Martin, *An. Quim.* **70**, 900 (1974).
F. Farina, P. Victory, *An. Quim.* **68**, 843 (1972).
S. Ohuchida, N. Hamanaka, M. Hayashi, *Tetrahedron Lett.* **22**, 1349 (1981).
- ⁵ R. Palm, H. Ohse, H. Cherdron, *Angew. Chem.* **78**, 1096 (1966); *Angew. Chem. Int. Ed. Engl.* **5**, 994 (1966).
F. Nerdel, H. Rachel, *Chem. Ber.* **89**, 671 (1956).
- ⁶ D. R. Culson, *Inorg. Synth.* **13**, 121 (1972).
- ⁷ For other allylic acetate rearrangements via addition elimination see: P. M. Henry, *J. Am. Chem. Soc.* **94**, 5200 (1972).
L. E. Overman, F. M. Knoll, *Tetrahedron Lett.* **1979**, 34.
- ⁸ T. Mandai, S. Hashio, J. Goto, M. Kawada, *Tetrahedron Lett.* **22**, 2187 (1981).
- ⁹ R. Rambaud, M. Vessiere, *Bull. Soc. Chim. Fr.* **1961**, 1567.
- ¹⁰ A. van Dormael, *Trav. Lab. chim. gen. Univ. Louvain* **34** (1942–1947); *C. A.* **44**, 8325 (1950).
- ¹¹ F. Johnson, J. P. Panella, A. A. Carlson, D. H. Hunneman, *J. Org. Chem.* **27**, 2437 (1962).
- ¹² A. J. Mancuso, S.-L. Huang, D. Swern, *J. Org. Chem.* **43**, 2480 (1978).
- ¹³ C. F. H. Allen, M. R. Gilbert, D. M. Joung, *J. Org. Chem.* **2**, 227 (1937).