

Synthesis of Type I and IV Cyanolipids¹

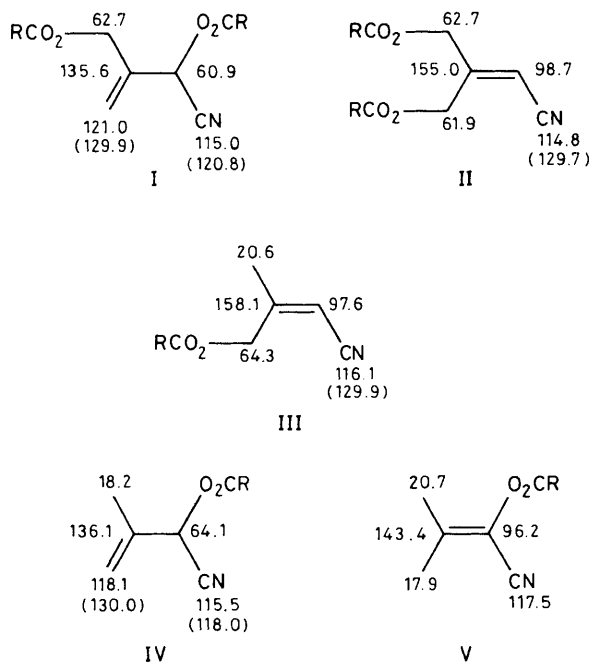
Mugio Nishizawa,* Kenji Adachi, and Yuji Hayashi

Department of Chemistry, Faculty of Science, Osaka City University, Sumiyoshiku, Osaka 558, Japan

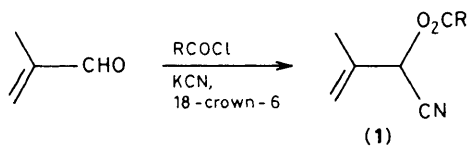
Type I and IV cyanolipids, members of a unique class of plant lipid, have been synthesized efficiently by means of a novel cyanoesterification of aldehydes, and fully characterized by spectral analysis; an artificial 'type V' cyanolipid has also been synthesized.

Cyanolipids are a relatively new class of natural lipids which have been found only in the seed oil of Sapindaceae plants;² they have been classified into four types I–IV (Scheme 1). Recently, we have reported the complete purification of individual type II cyanolipids by h.p.l.c.,³ and the efficient synthesis of type II and III cyanolipids,¹ which allowed us to study the insecticidal activity of these compounds in detail.⁴ We now report the efficient synthesis and full characterization of type I and IV cyanolipids and an artificial 'type V' cyanolipid. The biological activity of these compounds is also interesting.

When methacrolein was treated with oleoyl chloride (2 equiv.) and potassium cyanide (3 equiv.) in the presence of 18-crown-6 (0.1 equiv.) in toluene at room temperature for 2 h



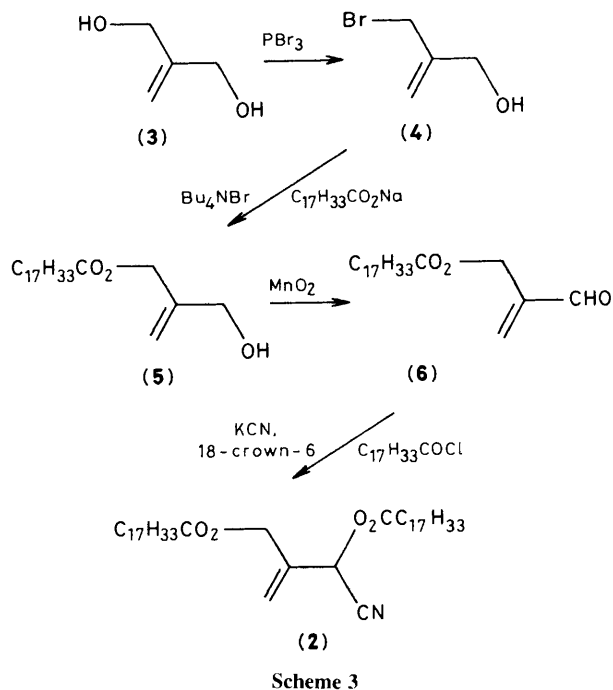
Scheme 1. ¹³C N.m.r. data. Assignments reported by K. L. Mikolajczak and D. Weisleder, *Lipids*, 1978, **13**, 514, are in parentheses.



- (1)
- a; R = Z-Me[CH₂]₇CH=CH[CH₂]₇
 - b; R = C₁₇H₃₅
 - c; R = C₁₉H₃₉
 - d; R = Z-Me[CH₂]₇CH=CH[CH₂]₁₁
 - e; R = C₅H₁₁

Scheme 2

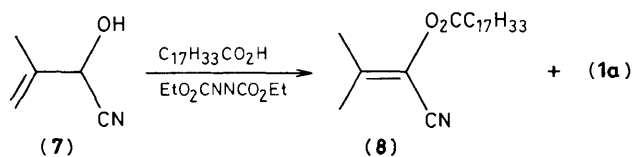
with stirring, the type IV cyanolipid (**1a**)[†] was obtained in 90% yield after silica gel column chromatography,[‡] and characterized by spectral analysis. The type IV cyanolipids (**1b–e**) were also easily prepared in high yield by this procedure (Scheme 2).



Scheme 3

[†] *Spectral data:* (**1a**), i.r. (neat) 3000, 1750, and 1660 cm⁻¹; ¹H n.m.r. δ(CDCl₃) 0.91 (3H, t, *J* 7 Hz), 1.35 (8H, br.), 1.70 (2H, m), 1.92 (3H, s), 2.04 (2H, m), 2.44 (2H, t, *J* 7 Hz), 5.11 (1H, s), 5.39 (3H), and 5.84 (1H, s); ¹³C n.m.r. δ (CDCl₃) 14.1q, 18.2q, 22.8t, 24.7t, 27.2t, 29.1t, 29.4t, 29.6t, 29.7t, 32.0t, 32.6t, 33.8t, 64.1d, 115.5s, 118.1t, 129.7t, 130.1d, 136.0s, and 171.7s. (**2**), i.r. (neat) 3000, 1750, and 1660 cm⁻¹; ¹H n.m.r. δ(CDCl₃) 0.89 (3H, t, *J* 7 Hz), 1.34 (16H, br.), 1.66 (4H, m), 2.04 (4H, m), 2.35 (2H, t, *J* 7 Hz), 2.42 (2H, t, *J* 7 Hz), 4.66 (2H, s), 5.35 (4H, t, *J* 4 Hz), 5.57 (1H, s), 5.71 (1H, s), and 5.98 (1H, s); ¹³C n.m.r. δ (CDCl₃) 14.2q, 22.8t, 24.7t, 24.9t, 27.2t, 29.0t, 29.2t, 29.4t, 29.6t, 29.8t, 32.0t, 33.4t, 34.1t, 61.0d, 62.8t, 115.0s, 121.0t, 129.8d, 130.0d, 143.5s, 171.6s, and 173.1s. (**8**), i.r. (neat) 3050, 2240, 1770, and 1660 cm⁻¹; ¹H n.m.r. δ (CDCl₃) 0.88 (3H, t, *J* 7 Hz), 1.26 (8H, br.), 1.64 (2H, m), 1.76 (3H, s), 2.00 (2H, m), 2.04 (3H, s), 2.45 (2H, t, *J* 7 Hz), and 5.31 (2H, t, *J* 4 Hz); ¹³C n.m.r. δ (CDCl₃) 14.2q, 17.9q, 20.7q, 22.8t, 24.8t, 27.2t, 27.3t, 29.1t, 29.4t, 29.6t, 29.7t, 29.8t, 32.0t, 33.5t, 96.2s, 117.5s, 129.7d, 130.1d, 143.4s, and 170.1s.

[‡] A single by-product was obtained in this step, which was assigned the structure C₁₇H₃₃COCN based on the following data: i.r. (neat) 3000, 2240, 1770, and 1650 cm⁻¹; ¹H n.m.r. δ (CDCl₃) 0.90 (3H, t, *J* 7 Hz), 1.33 (22H, br.), 1.70 (2H, m), 2.02 (2H, m), 2.46 (2H, t, *J* 7 Hz), and 5.39 (2H, t, *J* 4 Hz); ¹³C n.m.r. δ (CDCl₃) 14.1q, 22.7t, 23.6t, 24.4t, 27.1t, 28.9t, 29.0t, 29.4t, 29.6t, 29.7t, 32.0t, 32.7t, 33.3t, 38.5t, 112.1s, 129.6d, 130.1d, and 170.4s. See: R. Chênevert, R. Plante, and N. Voyer, *Syn. Commun.*, 1983, **13**, 403.



Scheme 4

The synthesis of the type I cyanolipid (2) started with the diol (3).⁵ Selective monobromination by exposure to phosphorus tribromide (0.5 equiv.) in tetrahydrofuran (THF) at $-50^\circ C$ for 30 min gave (4) in 53% yield based on starting material. The monobromide (4) was treated with sodium oleate (2 equiv.) in the presence of tetrabutylammonium bromide (0.1 equiv.)¹ in dichloromethane under ultrasonic vibration for 5 h, and the ester (5) was obtained in 78% yield. Manganese dioxide oxidation of (5) in hexane provided the aldehyde (6) (60% yield), which converted into the type I cyanolipid (2)[†] by cyanoesterification ($C_{17}H_{33}COCl$, KCN, 18-crown-6, toluene)[‡] in 80% yield (Scheme 3).

When the cyanohydrin (7), derived from methacrolein, was subjected to Mitsunobu's esterification⁶ ($C_{17}H_{33}CO_2H$, EtO_2CNNCO_2Et , Ph_3P , THF) at $0^\circ C$ for 90 min, an unexpected product (8) (16%) was obtained along with (1a) (11%) (Scheme 4). The structure of (8) was established by spectral analysis.[†] Although the natural occurrence of (8) has not been reported, a cyanogenic glycoside with an analogous skeleton is known,⁷ and we suggest the name type V cyanolipid for this class of compound.

The ^{13}C n.m.r. data of the types I—V cyanolipids with an oleic acid residue (assignments are based on off-resonance decoupling and INEPT experiments)[§] are summarized in Scheme 1.⁸

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[§] We have previously prepared a type III cyanolipid containing a stereoisomeric mixture of the isobutenyl cyanide unit, in which the minor component (*Z*-isomer) shows 1H and ^{13}C n.m.r. resonances overlapped with those reported by Mikolajczak (see refs. 1 and 2). Thus, the natural type III cyanolipid must have a *Z* orientation of the isobutenyl group.