CHEMISTRY LETTERS, pp. 313-314, 1980. © The Chemical Society of Japan 1980

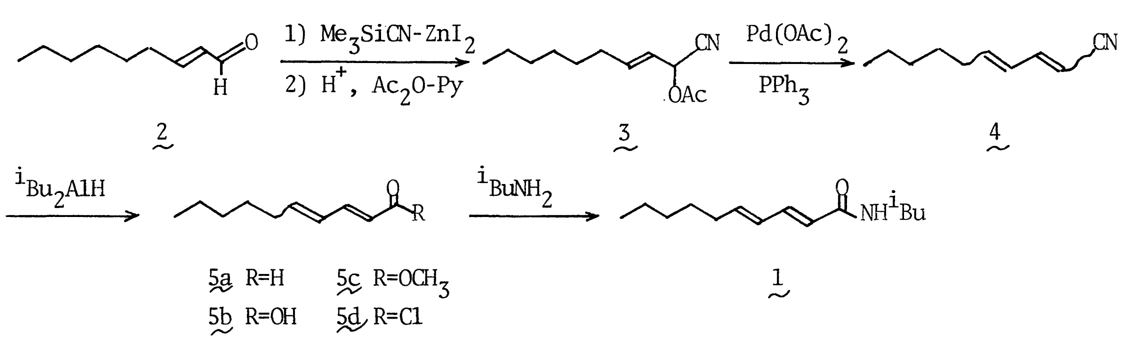
A NEW SYNTHETIC METHOD FOR PELLITORINE

Tadakatsu MANDAI, Jiso GOTOH, Junzo OTERA, and Mikio KAWADA
Okayama University of Science, Ridai-cho, Okayama 700

A stereoselective synthesis of N-isobutyl-E,E-2,4-decadienamide, so called pellitorine is described in which the elimination reaction of acetic acid from 2-acetoxy-E-3-decenenitrile providing 2,4-decadienenitrile in a high yield was used as a key reaction.

We have reported the palladium catalyzed elimination reaction of acetic acid or phenol affording a terminal conjugated diene from a variety of allylic acetates and allylic phenyl ethers,1) and the reactions have been successfully applied to the efficient syntheses of several natural products.2,3) In this communication, we wish to report a new synthetic method for pellitorine by applying the conjugated diene formation reaction to the preparation of 2,4-decadienenitrile, a good precursor for pellitorine. Pellitorine is an insecticidal compound isolated from Anacyckus Pyrethrum roots, and its structure was determined as N-isobutyl-E,E-2,4-decadienamide.4) A number of syntheses of pellitorine have proceeded via E,E-2,4-decadienoic acid or its esters as the key intermediates.5-9) Our synthetic route is depicted in the following scheme.

Scheme



The starting E-2-nonenal (2) was prepared as the following procedures. The dianion of propargyl alcohol10) was alkylated with 1-bromohexane in liquid NH_3 to give 2-nonyn-1-ol in 40% yield, which was reduced to E-2-nonenol in 93% yield with $LiAlH_4$11) in refluxing THF. Oxidation of the allylic alcohol by CrO_3 gave E-2-nonenal (2) in 73% yield. E-2-nonenal (2) (5.60 g, 40 mmol) was treated with Me_3SiCN12) (4.75 g, 48 mmol) and a catalytic amount of ZnI_2 in methylene chloride at 20° for 1 hr and the mixture was then hydrolyzed to a cyanohydrine with 1N HCl. The crude cyanohydrine was converted to 2-acetoxy-E-3-decenenitrile (3) with Ac_2O-Py in 90% yield from 2 after distillation (150°/8 Torr): NMR (CCl_4) δ 0.70-1.10 (t, 3H, CH_3), 1.10-1.70 (m, 8H, CH_2), 1.90-2.40 (m, 2H, $CH_2C=C$), 2.05 (s, 3H, $OCOCH_3$), 5.20-6.40 (m, 3H, CH=CH); IR (film) 1755, 1642, 965, 920 cm^{-1}.

The acetate 3 (2.09 g, 10 mmol) thus obtained was heated at 140° (oil bath) in dry diglyme or xylene under nitrogen atmosphere in the presence of $Pd(OAc)_2$ (22.4 mg, 0.1 mmol) and PPh_3 (262 mg, 1 mmol) for 1 hr to give the dienenitriles 4 in 86% yield after column chromatographic purification (silica gel, hexane-ether 30:1). Unfortunately, the dienenitriles **4** were found to be a mixture of four geometrical isomers by GLC analysis (PEG 20M Celite 545, area ratio 26:5:9:60); NMR (CCl_4) δ 0.70-1.10 (t, 3H, CH_3), 1.10-1.70 (m, 6H, CH_2), 1.90-2.50 (m, 2H, $CH_2C=C$), 4.90-5.40 (m, 1H, olefinic), 5.70-7.30 (m, 3H, olefinic); IR (film) 2200, 1640, 995 cm^{-1}.

The dienenitriles **4** (1.49 g, 10 mmol) were treated with $^{i}Bu_2AlH$ (1.2 eq.) in dry ether at -50° for 30 min, at 20° for 30 min, and at 45° for 30 min. The mixture was hydrolyzed with 1N HCl to give dienals **5a** in 80% yield, which were a mixture of two geometrical isomers by GLC analysis (PEG 20M Celite 545, area ratio 10:90); NMR (CCl_4) δ 0.70-1.10 (t, 3H, CH_3), 1.10-1.70 (m, 6H, CH_2), 2.00-2.50 (m, 2H, $CH_2C=C$), 5.75-6.40 (m, 3H, olefinic), 6.70-7.30 (m, 1H, olefinic), 9.45 (d, 1H, J=8 Hz, CHO); IR (film) 1685, 1640, 990 cm^{-1}. It is known that cis-α,β-unsaturated aldehyde readily changes to its trans isomer under acidic condition. In our results, isomerization of 2-olefin accompanied by that of 4-olefin probably occurred during the hydrolysis of aldimines to give E,E-isomer stereoselectively. The isomeric dienals **5a** were oxidized by $AgNO_3$-NaOH mixture[13)] to the corresponding dienoic acids **5b** in 52% yield. These acids **5b** were converted to their methyl esters **5c** with CH_2N_2 and they were analyzed by GLC (area ratio 10:90); NMR (CCl_4) δ 0.70-1.10 (t, 3H, CH_3), 1.10-1.80 (m, 6H, CH_2), 1.80-2.50 (m, 2H, $CH_2C=C$), 3.65 (s, 3H, OCH_3), 5.50-6.20 (m, 3H, olefinic), 6.90-7.40 (m, 1H, olefinic); IR (film) 1720, 1640, 1620 cm^{-1}; MS (m/e) 182 (M^+). The acid chlorides **5d** were treated with $^{i}BuNH_2$ in ether to give a crude oil of pellitorine (**1**) which was purified by recrystallization from hexane to afford white crystals: NMR ($CDCl_3$) δ 0.70-1.10 (t, 3H, CH_3, d, 6H, CH_3CCH_3), 1.10-1.80 (m, 7H, CH_2, CH), 1.80-2.40 (m, 2H, $CH_2C=C$), 3.10 (t, 2H, NCH_2), 5.60-6.20 (m, 3H, olefinic), 6.90-7.40 (m, 1H, olefinic); IR (nujol) 3300, 1660, 1630 cm^{-1}; MS (m/e) 223 (M^+), 151 (M^+-$^{i}BuNH_2$); mp 91°-92° (lit.[4)] 90°).

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(Received January 5, 1980)