A Convenient Method for the Preparation of Conjugated Olefins from Allylic Acetates and Aldehydes. Synthesis of Pellitorine

Yuhko TSUKAHARA, Hideki KINOSHITA,* Katsuhiko INOMATA, and Hiroshi KOTAKE
Department of Chemistry, Faculty of Science, Kanazawa University, Kanazawa 920
(Received March 28, 1984)

Synopsis. A variety of allylic acetates were treated with sodium bromide and triphenylphosphine in the presence of 5 mol% of [Pd(PPh$_3$)$_4$] to give the phosphonium salts, which were converted to the ylids *in situ* and allowed to react with various aldehydes to afford the corresponding conjugated olefins in good yields. Furthermore, this procedure was applied to the synthesis of an insecticidal substance, Pellitorine.

In the previous paper,[1] it was reported that the reaction of allylic acetates with sodium *p*-toluenesulfinate in THF–MeOH catalyzed by [Pd(PPh$_3$)$_4$] gave regiocontrolled allylic sulfones in good yields. On the basis of this finding, we thought that the reaction of allylic acetates with alkali halides such as NaBr and LiI instead of sodium *p*-toluenesulfinate would give the corresponding allylic halides under the same reaction conditions. When geranyl acetate was treated with NaBr in the presence of a catalytic amount of [Pd(PPh$_3$)$_4$] and one equiv of triphenylphosphine, the corresponding phosphonium salt (**1**) was actually isolated.[2]

In this paper, we wish to report an efficient procedure for the preparation of conjugated olefins in one-pot from allylic acetates *via* the formation of the triphenylphosphonium salts (**1**). Thus, to a solution of one equiv of PPh$_3$ and 5 mol% of [Pd(PPh$_3$)$_4$] in dry THF were added a solution of one equiv of cinnamyl acetate in dry THF and a solution of two equiv of NaBr in dry MeOH under N_2. After the reaction mixture was stirred for 1.5 h at room temperature, it was successively treated with 1.2 equiv of BuLi and 1.1 equiv of benzaldehyde at −17 °C and stirred for 4 h at room temperature. The usual work-up gave the desired 1,4-diphenyl-1,3-butadiene (**2a**) in 83% yield.

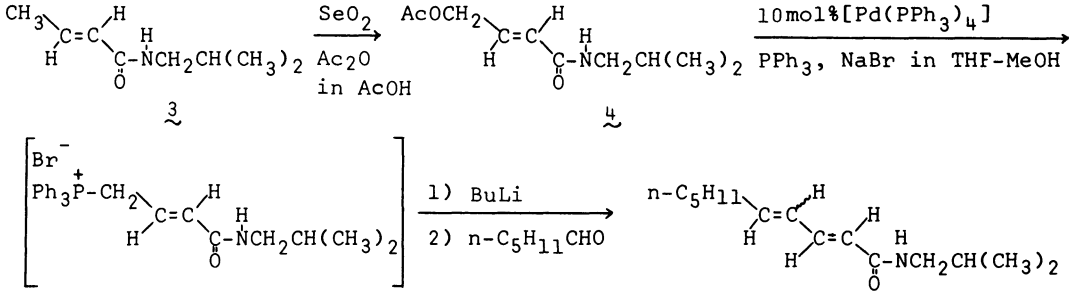
In a similar manner, various conjugated olefins (**2b—g**) were prepared in good yields as shown in Table.

Next, the present method was applied to the synthesis of Pellitorine (**5**),[3] a crystalline insecticidal substance isolated from *Anacyclus pyrethrum DC.* roots, from the allylic acetate(**4**) prepared by oxidation of (*E*)-*N*-isobutyl-2-butenamide (**3**) and hexanal according to the following scheme. Pellitorine (**5**, 2*E*, 4*E*-) and its 2*E*,4*Z*-isomer were obtained in 31% and 24% yields, respectively. The latter isomer could be converted into Pellitorine (**5**) in a quantitative yield by treatment with a catalytic amount of I_2.

As mentioned above, the present method proved to be a very useful procedure for the preparation of conjugated olefins[4] from easily available acetates.

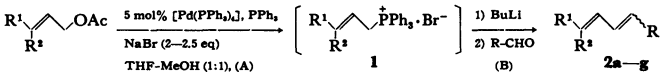
Experimental

HPLC analyses were performed with a Waters M6000 A instrument using a 30 cm×3.9 mm column (μ-Polasil, particle size-10 μm, detection 254 nm). Thin-layer chromatography (TLC) was performed on Merck's silica gel 60 PF_{254}



Scheme 1. Synthesis of Pellitorine

TABLE 1. CONVERSION OF ALLYLIC ACETATES TO CONJUGATED OLEFINS



Allylic acetate	R–CHO	Reaction conditions (A)	Reaction conditions (B)	Yield of 2/%	Stereochemistry
Ph–⟋–OAc	Ph–CHO	r.t., 1.5 h	−17°—r.t., then r.t., 4 h	83 (2a)	1*E*, 3*Z*: 1*E*, 3*E* (79:21)
Ph–⟋–OAc	O_2N–C$_6$H$_4$–CHO	r.t., 1.5 h	−17°—r.t., then r.t., 3 h	84 (2b)	1*E*, 3*E* only
Ph–⟋–OAc	Ph–⟋–CHO	r.t., 1.5 h	−17°—r.t., then r.t., 3 h	82 (2c)	1*E*, 3*Z*, 5*E*: 1*E*, 3*E*, 5*E* (77:23)
Ph–⟋–OAc	CH_3CH_2CHO	r.t., 1.5 h	−17°—r.t., then r.t., 4 h	81 (2d)	1*E*, 3*Z*: 1*E*, 3*E* (47:53)
⟋⟋⟋–OAc	Ph–CHO	reflux, 2 h	−17°—r.t., then r.t., overnight	85 (2e)	1*Z*, 3*E*: 1*E*, 3*E* (70:30)
⟋⟋⟋–OAc	⟋⟋⟋–CHO	reflux, 2 h	−17°—r.t., then r.t., overnight	76 (2f)	6*E*, 8*Z*, 10*E*: 6*E*, 8*E*, 10*E* (50:50)
⟋⟋–OAc	Ph–CHO	reflux, 2 h	−17°—r.t., then r.t., overnight	73 (2g)	1*Z*: 1*E* (45:55)

(Art. 7749).

*Preparation of Conjugated Olefins (**2a—g**).* **2a**: To a solution of PPh_3 (131 mg, 0.5 mmol) and $[Pd(PPh_3)_4]$ (29 mg, 0.025 mmol) in dry THF (1.5 ml) were added a solution of cinnamyl acetate (88 mg, 0.5 mmol) in dry THF (0.5 ml) and a solution of NaBr (103 mg, 1 mmol) in dry MeOH (2 ml) under N_2. After stirring for 1.5 h at room temperature, the reaction mixture was cooled to −17 °C and a hexane solution (*ca.* 15%) of 1.2 equiv of BuLi was added at the temperature. The mixture was stirred for 30 min at room temperature and cooled to −17 °C again. Then, a solution of benzaldehyde (59 mg, 0.55 mmol) in dry THF (0.5 ml) was added. The reaction mixture was gradually warmed and kept at room temperature for 4 h. After quenching the reaction with aq KCN (7 mg, 0.1 mmol), the product was extracted with AcOEt and subjected to preparative TLC (solvent; hexane) to give **2a** consisting of two isomers in 83% yield (86 mg). They were separable with a pre-coated TLC plate (Merck's silica gel $60F_{254}$, Art.5715, solvent; hexane) and their stereochemistry was assigned by comparison of UV spectra and melting point with those reported in literatures. Ratio of the isomers was determined by HPLC analysis of the crude product (solvent; hexane, flow rate 1 ml/min). 1*E*,3*E*-isomer: Mp 144—149 °C (lit, 147—149 °C).[5] UV (hexane) 329 nm (lit, 328 nm).[6] 1*E*,3*Z*-isomer: An oil; IR (neat) 980, 745, 720, 692, and 680 cm^{-1}. The 1*E*,3*Z*-isomer was readily converted to the 1*E*,3*E*-isomer with the aid of a catalytic amount of I_2 in benzene–ether.

2b: Mp 177.0—178.5 °C (lit, 172 °C).[7]

2c: Ratio of the isomers was determined by HPLC analysis using "iso-octane" as eluent. The stereochemistry of the isomers was assigned by UV spectra comparing with the reported ones.[8]

2d: An oil. The stereochemistry and ratio of the isomers were determined by 100 MHz ^1H-NMR spectrum. 1*E*,3*E*-isomer: NMR ($CDCl_3$) δ=1.05 (t, *J*=7.4 Hz, 3H), 2.17 (m, 2H), 5.85 (dt, *J*=6.3, 14.8 Hz, 1H), 6.18 (dd, *J*=9.4, 14.8 Hz, 1H), 6.42 (d, *J*=15.4 Hz, 1H), 6.76 (dd, *J*=9.4, 15.4 Hz, 1H), and 7.10—7.45 (m, 5H). 1*E*,3*Z*-isomer: NMR ($CDCl_3$) δ=1.05 (t, *J*=7.4 Hz, 3H), 2.17 (m, 2H), 5.54 (dt, *J*=7.4, 10.5 Hz, 1H), 5.98—6.25 (m, 1H), 6.42 (d, *J*=15.4 Hz, 1H), 6.76 (dd, *J*=9.4, 15.4 Hz, 1H), and 7.10—7.45 (m, 5H). MS (of the mixture) *m/z* 158 (M^+) and 129 ($M^+-C_2H_5$). IR (of the mixture, neat) 980 736, and 680 cm^{-1}.

2e: An oil. Ratio of the isomers was determined by HPLC analysis (solvent; "iso-octane." flow rate 0.5 ml/min). 1*E*,3*E*-isomer: IR (neat) 951, 740, and 680 cm^{-1}.[2] 1*Z*,3*E*-isomer: IR (neat) 790 and 690 cm^{-1}; NMR ($CDCl_3$) δ=1.60 (s, 3H), 1.68 (s, 3H), 1.81 (s, 3H), 2.00—2.30 (m, 4H), 5.04 (br, 1H), and 5.83—7.57 (m, 8H). MS (of the mixture) *m/z* 226 (M^+) and 157 ($M^+-CH_2CH{=}C(CH_3)_2$).

2f: An oil. Ratio of the isomers was determined by GLC analysis (Shimazu GC 6A, 10% Silicone SE-30 on 60-80 mesh Shimalite W, 210 °C). The mixture was separated by preparative TLC (30% silver nitrate-impregnated silica gel). 6*E*,8*E*,10*E*-isomer: IR (neat) 986 and 951 cm^{-1}.[2] 6*E*,8*Z*,10*E*-isomer: IR (neat) 760 cm^{-1}. NMR (of the mixture, $CDCl_3$) δ=1.58 (s, 6H), 1.65 (s, 6H), 1.73 (s, 6H), 1.93—2.30 (m, 8H), 5.05 (br, 2H), and 5.07—6.50 (m, 4H).

2g: An oil. Determination of the stereochemistry and ratio of the isomers were performed as described for **2e**. 1*E*-isomer: IR (neat) 980 and 950 cm^{-1}.[3] 1*Z*-isomer: IR (neat) 783, 740, and 686 cm^{-1}. MS (of the mixture) *m/z* 158 (M^+) and 143 (M^+-CH_3). NMR (of the mixture, $CDCl_3$) δ=1.80 (s, 6H), and 5.72—7.63 (m, 8H).

*(E)-N-Isobutyl-2-butenamide (**3**).* To a solution of triethylamine (1.518 g, 15 mmol) and isobutylamine (1.646 g, 22.5 mmol) in dry CH_2Cl_2 (20 ml) was added dropwise a solution of crotonoyl chloride (1.568 g, 15 mmol) in dry CH_2Cl_2 (10 ml) at 0 °C under N_2. Usual work-up gave the desired product which was recrystallized from hexane. Yield, 2.063 g (97%). Mp 70.5—72.0 °C. IR (KBr) 3240, 2960, 1660, 1615, 1550, 1230, and 978 cm^{-1}. NMR ($CDCl_3$) δ=0.92 (d, *J*=6.5 Hz, 6H), 1.47—2.26 (m, 1H), 1.83 (dd, *J*=2.0, 7.0 Hz, 3H), 3.13 (dd, *J*=6.0, 6.0 Hz, 2H), 5.87 (dd, *J*=2.0, 15.0 Hz, 1H), 6.14 (br, 1H), and 6.81 (dq, *J*=7.0, 15.0 Hz, 1H). Found: C, 67.78; H, 10.89; N, 9.74%. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92%.

*(E)-Isobutyl-4-acetoxy-2-butenamide (**4**).* A mixture of **3** (565 mg, 4 mmol), acetic anhydride (449 mg, 4.4 mmol), water (73 mg, 4 mmol), and acetic acid (5 g, 83 mmol) was refluxed for 75 min under N_2. Selenium(IV) oxide (533 mg, 4.8 mmol) was added to it by portions. The mixture was refluxed for about 10 h and worked up in the usual way. The product was isolated by preparative TLC (solvent; hexane:AcOEt=1:1 v/v). Yield, 120 mg (15%). IR (neat) 3293, 2960, 1740, 1670, 1630, 1550, 1270, 1235, and 980 cm^{-1}; NMR ($CDCl_3$) δ=0.92 (d, *J*=6.5 Hz, 6H), 1.47—2.14 (m, 1H), 2.07 (s, 3H), 3.11 (dd, *J*=6.0, 6.0 Hz, 2H), 4.65 (dd, *J*=1.5, 5.0 Hz, 2H), 6.06 (dd, *J*=2.0, 15.4 Hz, 1H), 6.12 (br, 1H), and 6.73 (dt, *J*=5.0, 15.4 Hz, 1H); CI-MS *m/z* 200 (M^++1).

*Preparation of Pellitorine (**5**).* To a solution of PPh_3 (110 mg, 0.42 mmol) and $[Pd(PPh_3)_4]$ (42 mg, 0.036 mmol) in dry THF (1.5 ml) were added a solution of **4** (71 mg, 0.36 mmol) in dry MeOH (3 ml) and a solution of NaBr (86 mg, 0.84 mmol) in dry MeOH (1.5 ml) under N_2. The mixture was refluxed for 4 h and cooled to −17 °C. Then, a hexane solution of BuLi (0.396 mmol) was added with vigorous stirring followed by the addition of a solution of hexanal (40 mg, 0.396 mmol) in dry THF (1 ml). The reaction mixture was gradually warmed up to room temperature and worked up in the usual way. Two fractions were obtained by preparative TLC (Merck's Aluminum oxide 60 PF_{254}, Type E, solvent; benzene:AcOEt=8:1 v/v). From the first fraction of lower R_f value, Pellitorine (**5**) was obtained in 31% yield (25 mg). Its Mp, IR, and NMR data were identical with those of the reported ones.[9] Mp 89—90 °C (lit, 89—90 °C). 4*Z*-isomer was obtained from the second fraction of higher R_f value as an oil. It could be converted to Pellitorine in a quantitative yield by treatment with a catalytic amount of I_2 in benzene for 1 h at room temperature. Yield, 19 mg (24%, an oil); IR (neat) 3250, 1635, 1598, 1528, 1262, 982, and 858 cm^{-1}; NMR ($CDCl_3$) δ=0.66—1.10 (t, 3H), 0.92 (d, *J*=6.0 Hz, 6H), 1.10—2.53 (m, 9H), 3.12 (dd, *J*=6.0, 6.0 Hz, 2H), 5.37—6.27 (m, 4H), and 7.27—7.70 (m, 1H); MS *m/z* 223 (M^+).

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