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On the Mechanism of the Rearrangement of 7-Vinylnorcaradienes

Shigeo Kohmoto,* Naohiro Nakayama, Jun-ichi Takami, Keiki Kishikawa, Makoto Yamamoto, and Kazutoshi Yamada

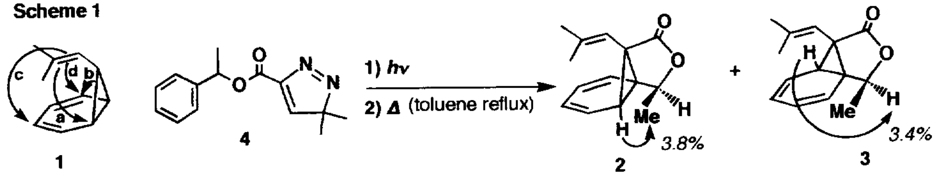
Department of Materials Science, Faculty of Engineering, Chiba University, Yayoi-cho, Inage-ku, Chiba 263, Japan

Abstract: Thermal rearrangement of diastereomeric 7-vinylnorcaradienes **2** and **3** resulted in the formation of three products, two of which were derived from the vinylcyclopropane-cyclopentene rearrangement and the third from the Cope rearrangement. Almost identical product ratios from **2** and **3** suggested the existence of a common biradical as an intermediacy. The kinetic versus thermodynamic control of the rearrangement was achieved by the choice of the substituent (X) in norcaradienes **9**. Copyright © 1996 Elsevier Science Ltd

Since the discovery of the vinylcyclopropane-cyclopentene rearrangement,[1] there has been a continuous argument regarding its mechanism, namely, whether it is a symmetry allowed concerted 1,3-sigmatropic shift or a stepwise process via a biradical pathway,[2] and this issue still remains a current topic.[3] The ring-walk rearrangement known as the Berson-Willcott rearrangement[4] of norcaradienes,[5] structurally a family of divinylcyclopropanes,[6] was also the subject of mechanistic interest. The conflicting results on this 1,5-shift[7] were finally reconciled.[8] In conjunction with these rearrangements of vinylcyclopropanes, our recent synthesis of stable 7-vinyl norcaradienes,[9] a higher vinylogue "trivinylcyclopropanes", has prompted us to study their rearrangement mechanism. A few investigations on its rearrangement were carried out from mechanistic viewpoints.[10, 11] Owing to the arrangement of three vinyl units in 7- vinylnorcaradiene **1**, four types of rearrangements: the 1,3- (path **a**), the 1,5- (path **b**), the 3,3- (path **c**), and the 3,5-shift (path **d**) can possibly occur (Scheme 1). The 1,3- and the 3,5-shift correspond to the vinylcyclopropane-cyclopentene rearrangement. Without a diastereomeric marker, the 1,3- and 3,5-shifts afford the same product and the 1,5-shift reproduces **1**. In order to simplify the complexity of the rearrangement, we designed the 1,7-γ-lactone ring-fused 7-vinylnorcaradienes with a diastereomeric marker; **2** and **3**. Due to the ring-fusion, the concerted 1,3- and 1,5-sigmatropic rearrangements were sterically impossible. An nteresting substituent effect was observed on the kinetic versus thermodynamic control of the rearrangement of **9**.

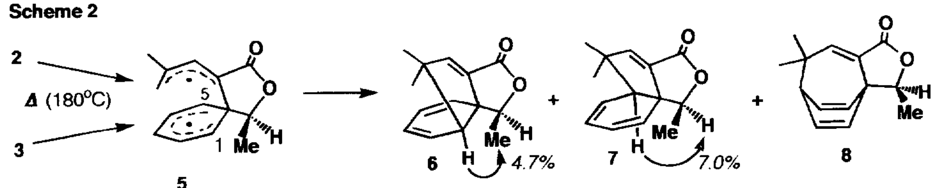
Synthesis of **2** and **3** was carried out by an intramolecular cyclization of vinylcarbene via a cyclopropene route.[12] The addition of 2-diazopropane to the corresponding propiolic acid 1-phenylethyl ester gave *3H*-pyrazole **4**[13] (62%). Subsequent photolysis of **4** in benzene irradiated with a high-pressure mercury lamp (40 min) afforded the corresponding cyclopropene. After the evaporation of benzene, the resulting cyclopropene was thermolyzed in refluxing toluene (15 h) to give two diastereomeric norcaradienes **2**[13] (38%) and **3**[13] (14%) separated by preparative HPLC (column; Merck Si60, 7μm). Interconversion between these two isomers via the 1,5-shift was not detected at this temperature. The NOE relations as shown in the Scheme 1 attested to their stereochemistry. Thermolysis of **2** in benzene at 180 °C in a sealed tube for 6 h resulted in the formation of **6**,[13] **7**,[13] and **8**[13] via the 1,3-, the 3,5-, and the 3,3-shift, respectively, in an almost

Scheme 1



(NOE relations are shown with arrrows)

Scheme 2



	6	7	8
ratio from 2	15%	48%	37%
ratio from 3	17%	51%	32%

quantitative yield and these isomers were separated by preparative HPLC (column; Merck Si60, 7μm). Since the reactivity of the radical sites at C_1 and C_5 of the biradical intermediate should be identical, the observed difference in the ratio of the 1,3- and the 3,5-shift might be caused by the steric effects of the methyl group. Control experiments showed that these three products were stable under the reaction conditions (at 180 °C for 6 h). Almost equivalent results were obtained in the thermolysis of **3**. Stereochemistry of **6** and **7** was deduced from their NOE difference spectra (Scheme 2). Almost identical product ratios, either derived from **2** or **3**, suggested the involvement of the common intermediacy or transition state. Such an intermediacy or transition state can be well defined by the biradical **5** which is similar to those proposed for the ring walk rearrangement,[4] but should be more stable due to the stabilization by 2-methyl-1-propenyl and alkoxycarbonyl groups.

In order to control the course of the rearrangement, vinylcyclopropane - cyclopentene versus Cope rearrangements, the substituent effect on the rearrangement of **9** was examined through kinetics monitoring of ^{1}H-NMR spectroscopy. The thermolysis was carried out in a sealed tube with benzene as a solvent in the temperature range of 130 °C to 160 °C, and resulted in the quantitative formation of the rearrangement products. At the early stage of the reaction, both vinylcyclopropane - cyclopentene and Cope rearrangements followed the pseudo first order rate law. The difference in the E_a between the formation of **2** and that of **3** (ΔE_a) showed that the vinylcyclopropane - cyclopentene rearrangement was kinetically favorable in the rearrangements of **9a**, **9b**, and **9c** with little substituent effect on ΔE_a. Large substituent effects on the heat of formation (ΔH_f) of the rearrangement products were predicted from their $\Delta\Delta H_f$ (ΔH_f of **11** minus ΔH_f of **12**) calculated by AM1. The $\Delta\Delta H_f$ varied from +4.7 kcal/mol (**9a**) to -8.4kcal/mol (**9d**) (Table 1). The calculated results indicated that **11**was thermodynamiucally stable when X=H, while **12** became
unstable when X=Ph. The calculated results were almost comparable to the experimental results. In the case of **9a**, **12a** was thermally stable so that the rearrangement occurred by kinetic control. The rearrangements of **12b** and **12c** to **11a** and **11b**, respectively, were observed at higher thermolysis temperature (over 170 °C). Similar continuos rearrangement in a sequence of the 3,3- to 1,3-shifts was reported by Davies et al.[11] Therefore, the rearrangements of **9b** and **9c** were governed by kinetic control at lower thermolysis temperature and by thermodynamic control at higher thermolysis temperature. Not a trace amount of the corresponding Cope rearrangement product was detected in the rearrangement of **9d** in the temperature range of 130 °C to 180 °C, and only **11d** was isolated (96% yield at 180 °C for 6h). In this case, the rearrangement was controlled thermodynamically. This interesting substituent effect on kinetic control versus thermodynamic control may originate in the magnitude of the steric hindrance between the subsituent (X) and the *gem*-dimethyl group in the biradical **10**. The largest steric hindrance might be raised by the phenyl group. The stabilization of **10** by the substituent X could be the driving force of the carbon - carbon bond cleavage.

Scheme 3

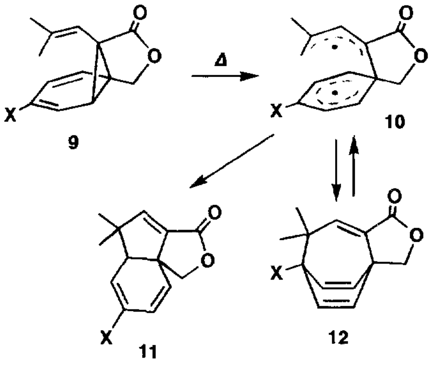


Table 1. ΔE_a (kcal/mol)[a] and $\Delta\Delta H_f$ (kcal/mol)[b] of the rearrangement of vinylnorcaradienes

Compound	X	E_a (kcal/mol)		ΔE_a	$\Delta\Delta H_f$
		11	**12**		
9a	H	26.4	30.9	-4.5	+4.7
9b	Me	21.5	27.2	-5.7	+2.5
9c	Cl	27.4	32.0	-4.6	-1.2
9d	Ph			----	-8.4

[a] The difference in E_a between the formation of **11** and that of **12**.

[b] The difference in ΔH_f (ΔH_f of **11** minus ΔH_f of **12**) calculated by AM1.

The rearrangement of 7-vinylnorcaradiene whose configuration was locked by the ring-fusion with a γ-lactone ring proceeded via a biradical pathway, and the course of the rearrangement, either the vinylcyclopropane or Cope rearrangement, could be controlled by the substituent effect.

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13 All new compounds gave satisfactory spectroscopic and analytical data.

2: colorless oil; IR (NaCl) 2980, 2930, 1775, 1385, 1265, 1120, 1065 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 6.26 (dd, J = 9.0, 6.6 Hz, 1H), 6.18 (ddd, J = 9.0, 6.6, 1.0 Hz, 1H), 6.08 (ddd, J = 9.0, 5.5, 1.0 Hz, 1H), 5.90 (d, J = 9.0 Hz, 1H), 4.93 (q, J = 6.2 Hz, 1H), 4.44 (qq, J = 1.3, 0.9 Hz, 1H), 2.96 (d, J = 5.5 Hz, 1H), 1.64 (d, J = 1.3 Hz, 3H), 1.56 (d, J = 0.9 H, 3H); ^{13}C NMR (CDCl$_3$, 22.4 MHz) δ 178.02 (s), 142.58 (s), 126.41 (d), 124.92 (d), 122.59 (d), 120.38 (d), 112.86 (d), 77.15 (d), 56.86 (s), 44.86 (d), 24.91 (q), 24.07 (s), 18.58 (q), 18.26 (q); HRMS (FAB) calcd for $C_{14}H_{17}O_2$ (MH$^+$) 217.1228, found 217.1229.

3: white crystals; mp. 84.5 - 85.5 °C (hexane - ethyl acetate); IR (KBr) 2950, 2820, 1755, 1455, 1340, 1170, 1120, 1055 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 6.26 (dd, J = 8.8, 7.2 Hz, 1H), 6.21 (dd, J = 8.8, 7.2 Hz, 1H), 6.09 - 6.05 (m, 2H), 4.53 (q, J = 6.4 Hz, 1H), 4.38 (qq, J = 1.3, 1.1 Hz, 1H), 3.04 (d, J = 5.7 Hz, 1H), 1.64 (d, J = 1.3 Hz, 3H), 1.62 (d, J = 1.1 Hz, 3H), 1.60 (d, J = 6.4 Hz, 3H); ^{13}C NMR (CDCl$_3$, 125.6 MHz) δ 177.91 (s), 142.84 (s), 126.30 (d), 124.95 (d), 122.83 (d), 118.87 (d), 113.06 (d), 78.16 (d), 59.16 (s), 51.28 (d), 25.41 (q), 24.59 (s), 19.04 (q), 18.97 (q); HRMS (FAB) calcd for $C_{14}H_{17}O_2$ (MH$^+$) 217.1228, found 217.1223. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.60; H, 7.38.

6: white crystals, mp. 94.5 - 95.5 °C; IR (KBr) 2970, 2920, 1770, 1455, 1380, 1285, 1170, 1100, 1050 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 6.62 (s, 1H), 6.09 (dd, J = 9.6, 5.5 Hz, 1H), 5.94 (dd, J = 9.6, 5.5 Hz, 1H), 5.82 (d, J = 9.6 Hz, 1H), 5.72 (dd, J = 9.6, 6.0 Hz, 1H), 4.45 (q, J = 6.6 Hz, 1H), 2.72 (d, J = 6.0 Hz, 1H), 1.28 (s, 3H), 1.22 (d, J = 6.6 Hz, 3H), 1.07 (s, 3H); ^{13}C NMR (CDCl$_3$, 125.65 MHz) δ 165.45 (s), 148.82 (d),136.37 (s),127.24 (d), 124.71 (d), 124.47 (d), 121.64 (d), 85.92 (d), 59.33 (s), 56.43 (s), 50.34 (d), 27.72 (q), 22.95 (q), 16.80 (q); HRMS (FAB) calcd for $C_{14}H_{17}O_2$ (MH$^+$) 217.1228, found 217.1233. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.63; H, 7.48.

7: white crystals; mp. 122.5 - 123.5 °C; IR (KBr) 2970, 1755, 1375, 1105, 1030 cm^{-1}; ^{1}H NMR (CDCl$_3$, 270 MHz) δ 6.58 (s, 1H), 6.08 (m, 2H), 5.65 (m, 1H), 5.58 (m, 1H), 4.09 (q, J = 6.5 Hz, 1H), 2.55 (d, J = 6.1 Hz, 1H), 1.29 (d, J = 6.5 Hz, 3H), 1.27 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (CDCl$_3$, 22.4 MHz) δ 165.97 (s), 147.59 (d), 138.88 (s), 124.92 (d), 124.23 (d), 123.13 (d), 89.50 (d), 59.73(s), 57.07 (s), 54.68 (d), 27.77 (q), 22.70 (q), 15.30 (q); HRMS (FAB) calcd for $C_{14}H_{17}O_2$ (MH$^+$) 217.1288, found 217.1234. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.70; H, 7.44.

8: white crystals; mp. 151.0 - 152.0 °C (hexane - ethyl acetate); IR (KBr) 2970, 1745, 1670, 1245, 1215, 1040 cm^{-1}; ^{1}H NMR (CDCl$_3$, 270 MHz) δ 6.72 (d, J = 8.5 Hz, 1H), 6.39 (d, J = 7.9 Hz, 1H), 6.26 (dd, J = 8.5, 6.5 Hz, 1H), 6.24 (dd, J = 7.9, 6.5 Hz, 1H), 5.92 (d, J = 2.0 Hz, 1H), 4.77 (q, J = 7.0 Hz, 1H), 3.04 (ddd, J = 6.5, 6.5, 2.0 Hz, 1H), 1.56 (d, J = 7.0 Hz, 3H), 1.15 (s, 3H); ^{13}C NMR (CDCl$_3$, 22.4 MHz) δ 169.25 (s), 144.49 (d), 141.44 (d), 136.40 (d), 132.67 (s), 131.93 (d), 131.27 (d), 81.29 (d), 46.96 (d), 34.52 (s), 26.94 (q), 17.84 (q); HRMS (FAB) calcd for $C_{14}H_{17}O_2$ (MH$^+$) 217.1228, found 217.1225. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.65; H, 7.47.

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