

Different *Z/E*-Selectivity Depending upon the Length of the Acyl Side Chain in the Formation of 2,2'-Diacyl-9,9'-bifluorenylidene

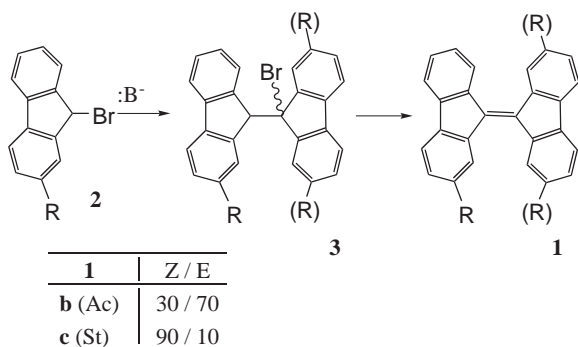
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We studied the formation of 2,2'-diacyl-9,9'-bifluorenylidene from 2-acyl-9-bromofluorene via the corresponding intermediate 9-bromo-9,9'-bifluorenyl. It was found that dehydrobromination of the 9-bromo-9,9'-bifluorenyl derivatives occurred through the E2 elimination sequence, suggesting that the configuration of 9-bromo-9,9'-bifluorenyl isomers determined the stereochemistry of the product. Facile isomerization of the formed 9,9'-bifluorenylidenes may give the observed stereo-selectivity depending upon the length of the acyl side chain.

9,9'-Bifluorenylidene (**1a**, R = H; Scheme 1) has one of the partial structural motifs of fullerenes,¹ and may be a novel starting material for the bottom-up synthesis of elaborate fullerene derivatives. A conventional procedure to prepare **1** is the reaction of the corresponding 9-bromofluorene (**2**) with methanolic potassium hydroxide in acetone.^{2,3} Bethell et al. have proposed that the reaction of **2a** (R = H) to **1a** in *t*-butyl alcohol proceeds via the intermediate 9-bromo-9,9'-bifluorenyl (**3a**, R = H).⁴ They concluded that the reaction of **3a** to **1a** followed the E2 reaction sequence with base.⁵ When starting with **2**, which possessed an electron-withdrawing moiety (R = Br, Cl, CN, and NO₂) at the C₂-position, the conversion obeyed first-order kinetics.⁶ They did, however, not examine possible



Scheme 1.

isomerism of the corresponding **1**.

We have reported that the reaction of 2-acetyl- (**2b**) and 2-stearoyl-9-bromofluorene (**2c**) gave both (*Z*)- and (*E*)-2,2'-diacyl-9,9'-bifluorenylidenes, **1b** and **1c**, respectively.⁷ **2b** mainly gave *E*-isomer, while **2c** gave *Z*-isomer predominantly. 2-Nonanoyl-9-bromofluorene (**2d**) afforded **1d** in a *Z/E* ratio between the cases of **1b** and **1c** (Scheme 1). (*E*)-**1b** is a little more stable than (*Z*)-**1b**; the side chains situate to decrease each other's steric repulsion. On the other hand, (*Z*)-**1c** is more stable than (*E*)-**1c**; we attribute it to the increment of aggregative intra-molecular interaction between side chains.⁷ The mechanism of the stereo-selectivity has not yet been clarified. Here, we briefly report the kinetics of the formation of **1b** and **1c** from **2b** and **2c**, respectively. The results suggest that facile isomerization of formed **1** (R = Ac or St) follows the conventional conversion of **2** to **1**.

First, we examined the reaction of **2a** to **1a** in the presence of cyclohexene (**4**), to verify the possibility of the carbene mechanism.⁸ The ¹H NMR spectra of the products showed no signal attributable to a cyclopropane adduct that could have been formed via the carbene species: Only the peaks due to **1a**,² oxirane **5a** (R = H), and fluorenone (**6a**, R = H) were recognized (Scheme 2 and Table 1).¹⁰ The finding indicates that **1** forms predominantly through the carbanion sequence via the intermediate **3**.

Second, the reaction of **2** to **3** requires a stoichiometrically 0.5 molar amount of potassium hydroxide on the basis of **2**, and the dehydrobromination of **3** to **1** consumes 1 molar amount (or 0.5 mol amount based on **2**) of the base. Then, the reaction of **2b** and **2c** was carried out with a small amount of potassium hydroxide, in order to confirm the formation of **3** as an intermediate (Table 2). Shortage of potassium hydroxide left a larger amount of **3b**, and the yield of **1b** and the ratio of (*E*)-**1b** increased with an increasing amount of base (Runs 1–3). Formed **3b** was roughly a 1:1 mixture of *threo*- and *erythro*-isomers,¹¹ and the *Z/E* ratios of **1b** and **1c** were also 1:1 when the amount of base was insufficient (Runs 1 and 4). The yield of **1c** and the ratio of (*Z*)-**1c** increased with an increasing amount of base (Runs 4–6), in accordance with our previous paper.⁷ These results suggest, at least, no stereo-selectivity at the initial stage of the reaction.

Third, we examined the apparent rate constants for the for-

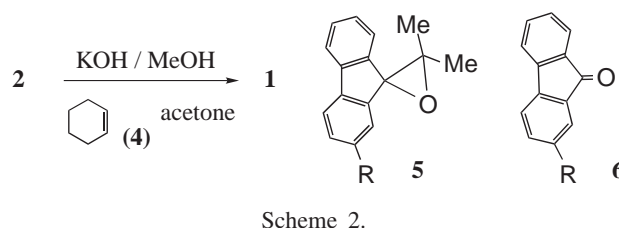


Table 1. Reaction of **2a** in the Presence of **4**

Run	Molar ratio of 4/2a	Products/%		
		1a	5a	6a
1	2	60	28	8
2 ^{a)}	20	5	43	29
3	0	71	24	5

a) **2a** (16%) was recovered.

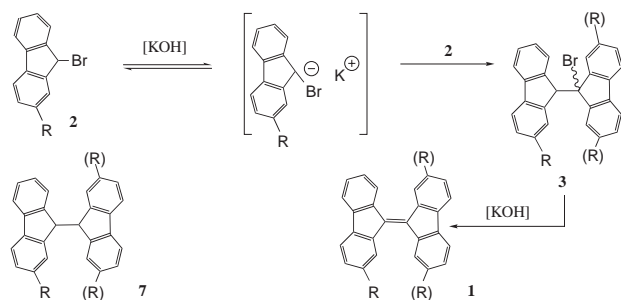
Table 2. Reaction of **2** (R = Ac, St)

Run	Reactant (R =)	Molar ratio of KOH/ 2	Ratio of solvent (mL)/ 2 (mmol)	1		3		5 /%	6 /%	Recvd. 2 /%
				%	Z/E	%	<i>threo</i> / <i>erythro</i>			
1 ^{a)}	2b (Ac)	0.4	100	6	48/52	52	46/54	—	17	26
2 ^{a)}	2b (Ac)	0.8	100	46	29/71	11	40/60	—	25	—
3 ^{a)}	2b (Ac)	1.8	100	67	15/85	—	—	—	19	—
4	2c (St)	0.4	100	20	57/43	—	—	2	22	50
5	2c (St)	0.8	100	28	58/42	—	—	10	27	26
6	2c (St)	1.8	100	32	86/14	—	—	42	16	9
7	2c (St)	1.8	200	38	82/18	—	—	33	15	14

a) Small amounts (<2%) of 2,2-diacetyl-9,9'-bifluorenyl-9-ol and 2-acetyl-9-fluorenyl-9-ol were confirmed.

Table 3. Apparent Rate Constants of the Formation of **1b**, **c** from **2b**, **c** and from **3b**, **c** (L mol⁻¹ s⁻¹)

1	From 2	From 3
b (Ac)	7.1	9.1 × 10
c (St)	9.5	2.8 × 10 ²



Scheme 3.

mation of **1b** and **1c** (as a *Z*- and *E*-mixture) from **2b** and **2c**, and from **3b** and **3c** (*threo*- and *erythro*-mixture), respectively, using absorbance changes of **1** at 466 nm.¹² Here, **3b** and **3c** were synthesized by the reaction of 2,2'-diacetyl-9,9'-bifluorenyl (**7a**; R = Ac, **7b**; R = St) with *N*-bromosuccinimide. The rate of formation of **1** was proportional to the concentrations of the reactant (**2** or **3**) and the base (Table 3). The reaction of **3c** was faster than that of **3b** under the conditions where all the species were soluble.¹³ Table 3 shows that the reaction of **2** to **1** was slower than that of **3** to **1**, indicating that the rate-determining step of **2** to **1** is involved in the step of **2** to **3**. The kinetics suggest that dehydrobromination (**3** to **1**) can proceed via the E2 or E1cB mechanism, and the latter has been excluded by Bethell.⁵ Based on the above results, we suggest the reaction pathway of **2b** and **2c** to **1b** and **1c**, respectively, as in Scheme 3.⁴

Finally, we examined the isomerization of **1** in the presence of base as a preliminary experiment. Conversion of (*Z*)-**1b** to (*E*)-**1b** and that of (*E*)-**1c** to (*Z*)-**1c** were observed under similar conditions of those of the reaction of **2** to **1**.

As a conclusion, it is confirmed that the reaction of **2b** and **2c** gives diastereomeric **3b** and **3c**, respectively, and that the configuration of **3** influences the diastereomeric ratio of **1** formed by the E2 sequence. This mechanism is inconsistent with the observed stereo-selectivity of **1** from **2**.⁷ We thus tentatively assume that the stereo-selectivity is given by facile isomerization of the formed **1** in the presence of base during

the reaction. Further studies on the dependence of the length of the acyl side chain upon the rate of possible isomerization of **1** are now underway.

Experimental

Melting points are uncorrected. NMR (CDCl₃), IR (KBr pellets), and mass spectra were recorded with a Varian VXR-300, JASCO FT/IR-430, and JMX-AX 500 (JEOL, 70 eV), respectively. UV-vis spectra were obtained with a JASCO V-550DS at 19 °C.

Reaction of 2a in the Presence of 4. To a mixture of **2a** (590 mg, 2.4 mmol) and **4** (0.49 mL, 4.8 mmol) in acetone (3 mL) was added KOH (purity 83%; 297 mg, 4.4 mmol) in MeOH (1 mL) at 9–10 °C for 5 min. After stirring for 1 h, the mixture was added to water. The composition of the precipitate was estimated by comparison of the characteristic peaks on the ¹H NMR spectra; δ 8.39 for **1a** (H_{1,1'}), 6.00 for **2a** (H₉), 7.73 for **5a** (H_{4,5}), and 7.64 for **6a** (H_{4,5}).

The residual portion was chromatographed on silica gel with toluene giving **5a**: mp 92–93 °C (from aqueous EtOH); IR 1192 cm⁻¹; ¹H NMR δ 1.70 (6H, s), 7.25 (2H, t, *J* = 7.5 Hz), 7.35–7.42 (4H, m), 7.73 (2H, d, *J* = 7.5 Hz); ¹³C NMR δ 22.1, 64.3, 72.3, 120.2, 124.7, 126.5, 128.6, 141.1, 142.0; ms *m/z* 222 (M⁺), 207, 180, 164.

Reaction of 2c with KOH. A solution of KOH (83%, 28 mg, 0.41 mmol) in MeOH (1 mL) was added at 9–10 °C for 5 min to a mixture of **2c** (257 mg, 0.5 mmol) in acetone (50 mL), and the resulting mixture was stirred for an additional 1 h. The deposit was filtered off and the filtrate was added to water. Both precipitates were subjected to ¹H NMR in order to determine the composition. The characteristic signals are as follows: δ 8.99 for (*E*)-**1b**, **c** (H_{1,1'}), 8.95 for (*Z*)-**1b**, **c** (H_{1,1'}), 6.04 for **2b**, **c** (H₉), 5.23 for *threo*-**3b** (H_{9'}), 5.22 for *erythro*-**3b** (H_{9'}), 7.96 for **5c** (H₁), 8.20 for **6b**, **c** (H₁), 5.64 for 2-acetyl-9-fluorenyl (H₉), 4.90 and 4.92 for 2,2'-diacetyl-9,9'-bifluorenyl-9-ol¹¹ (*threo*- and *erythro*-mixture) (H₉).

The residual parts of the precipitates were chromatographed on silica gel with toluene and **5c** was isolated: mp 78–81 °C (from EtOH); IR 1681 cm⁻¹; ¹H NMR δ 0.88 (3H, t, *J* = 6.7 Hz), 1.25 (28H, s), 1.68–1.77 (2H, m), 1.71 (3H, s), 1.73 (3H, s), 2.98 (2H, t, *J* = 7.4 Hz), 7.30–7.47 (3H, m), 7.79 (2H, d, *J* = 7.7 Hz, H_{4,5}), 7.96 (1H, d, *J* = 1.4 Hz, H₁), 8.04 (1H, d, *J* = 7.7 Hz, H₃); ms *m/z* 488 (M⁺), 446, 249, 222, 207, 193, 179.

Reaction of 2b with K₂CO₃. A mixture of **2b** (87 mg, 0.30 mmol) in acetone (30 mL) was stirred with K₂CO₃ (41 mg, 0.30 mmol) in MeOH (1 mL) at 9–10 °C for 1 h. 2-Acetyl-9-fluorenyl-9-ol (18%) and **2b** (64%) were confirmed by ¹H NMR.

Formation of Diastereomeric 3b. A solution of **2b** (5.74 g, 20 mmol) in acetone (200 mL) was refluxed with a solution of sodium iodide (6.00 g, 40 mmol) in acetone (25 mL) for 5.5 h. Upon usual treatment, 4.1 g of a mixture of *meso*- and *dl*-**7b** (R = Ac) was obtained. The isomeric ratio of the mixture was accounted to be 51:49 by signal strengths at δ 4.93 and 4.92 ppm of ^1H NMR, respectively. By fractional recrystallization from ethanol, *dl*-**7b** was isolated: mp 295–298 °C; ^1H NMR δ 2.31 (6H, s), 4.92 (2H, s), 7.08 (2H, brs, $\text{H}_{8,8'}$), 7.35–7.47 (6H, m), 7.62 (2H, d, J = 7.8 Hz, $\text{H}_{4,4'}$), 7.76 (2H, d, J = 7.5 Hz, $\text{H}_{5,5'}$), 7.84 (2H, dd, J = 8.1, 1.2 Hz, $\text{H}_{3,3'}$). Anal. Found: C, 87.00; H, 5.39%. Calcd for $\text{C}_{30}\text{H}_{22}\text{O}_2$: C, 86.93; H, 5.35%.

The mother solution afforded *meso*-**7b**: mp 244–246 °C; ^1H NMR δ 2.44 (6H, s), 4.93 (2H, s), 6.98 (2H, brs, $\text{H}_{8,8'}$), 7.17 (2H, t, J = 7.2 Hz, $\text{H}_{7,7'}$), 7.32 (2H, t, J = 7.5 Hz, $\text{H}_{6,6'}$), 7.53 (2H, brs, $\text{H}_{1,1'}$), 7.68–7.72 (4H, m), 7.94 (2H, d, J = 7.5 Hz, $\text{H}_{3,3'}$). Anal. Found: C, 86.63; H, 5.28%.

The HPLC chromatograms of *meso*- and *dl*-**7b** showed one and two peaks, respectively, using a chiral column, Chiralpak-IA.

A mixture of *meso*- and *dl*-**7b** (828 mg, 2.1 mmol) and NBS (545 mg, 3.1 mmol) in CCl_4 (60 mL) was refluxed for 18 h. The precipitate consisted of *threo*- and *erythro*-**3b** (45:55) by ^1H NMR (δ 5.23 and 5.22 ppm, respectively).

A mixture of *meso*- and *dl*-**7c** (R = St) was obtained quantitatively in a ratio of 49:51 by the similar reaction of **2c**. The mixture of **7c** was converted into a mixture of *threo*- and *erythro*-**3c** (47:53).

Rate Measurement on Formation of 1b from 2b. **Typical Procedure:** The absorption maxima of **1** were observed at 466 nm with the molar absorptivity of $2.5 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$ for **1b** and $2.2 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$ for **1c**, respectively.

To a stirred (800 rpm) acetone solution of **2b** ($8.82 \times 10^{-5} \text{ M}$, 2 mL) in an optical cell was added KOH–MeOH ($2.67 \times 10^{-3} \text{ M}$, 0.1 mL) at once. The solution corresponded to a mixture of **2b** ($8.40 \times 10^{-5} \text{ M}$) and KOH ($1.27 \times 10^{-4} \text{ M}$). The rate of formation of **1b** was estimated to be an increasing absorption at the initial stage of the reaction. The measurement was repeated at different KOH concentrations (1.27, 1.69, 2.11, and $2.53 \times 10^{-4} \text{ M}$, respectively), and the observed rate was plotted against the concentration of KOH giving a straight line (correlation coefficient = 0.94) of which the slope was the apparent rate constant, as is indicated in Table 3. Also, similar experiments were carried out at different concentrations of **2b** (5.04, 6.72, 8.40, and $10.1 \times 10^{-5} \text{ M}$) and KOH ($1.69 \times 10^{-4} \text{ M}$).

The reaction of **2c** with KOH was done using different concentrations of **2c** (4.71, 9.43, and $18.9 \times 10^{-5} \text{ M}$) with KOH (1.42, 1.64, 2.14, and $2.86 \times 10^{-4} \text{ M}$). Also, the following combinations were measured: **3b** (4.36, 7.63, 10.9, 11.5, and $14.2 \times 10^{-5} \text{ M}$) with KOH (1.52, 2.02, 2.53, and $3.04 \times 10^{-4} \text{ M}$); **3c** (4.46, 5.57, 6.69, 8.36, and $11.3 \times 10^{-5} \text{ M}$) with KOH (1.18, 1.47, 1.67,

1.97, and $2.06 \times 10^{-4} \text{ M}$).

Isomerization of 1 in the Presence of Base. A mixture of **1b** (Z/E = 73/27, 23.1 mg, 56 μmol) and KOH (25 μmol in MeOH) in acetone (5 mL) was stirred at room temperature for 1 h, giving **1b** (Z/E = 6/94, 75%) and **6b** (12%).

A mixture of **1c** (Z/E = 54/46, 43.1 mg, 50 μmol) and KOH (25 μmol in MeOH) in acetone (5 mL) was also treated as described above, affording **1c** (Z/E = 82/18, 82%) and **6c** (5%).

A mixture of **1c** (Z/E = 62/38, 43.1 mg, 50 μmol) in acetone/methanol (5 mL/25 μL) was stirred for 1 h: **1c** (Z/E = 64/36, 89%) was determined by NMR.

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- 9 J. Schmidt, H. Wagner, *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 1797.
- 10 Ketone **6a** should be formed via air-oxidation of **2**, **3**, and **1** in the presence of base. A large excess of solvent resulted in an increase of the oxidized compound **6** (see Run 2 in Table 1). A part of **6** should be formed via 9-fluorenol that was generated from **2** in the presence of potassium carbonate as a contaminant of potassium hydroxide.
- 11 Separation and characterization of the pure *threo*- and *erythro*-**3**, and the related compounds are now in progress.
- 12 Colorless or light yellowish **2**, **3**, **5**, and **6** did not give absorption bands at this wavelength region.
- 13 Although recovered **2** in Table 2 suggests the slower reaction of **2c** than that of **2b**, it is attributable to the poor solubility of **2** (and **1**) under the conditions: solubility of **2b** and **2c** are in the orders of magnitudes 10^{-5} and 10^{-6} M , respectively.