

Deacylations and Syntheses of Some 9-Acylfluorenes

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Deacylations of substituted 9-acetyl-, 9-propionyl-, 9-benzoyl-fluorene, and 9-fluorenyl 9-methyl-9-fluorenyl ketones were studied; the reactivity of deacylation was enhanced by the substitution of the 9-hydrogen atom on 9-acetylfluorene. The reaction of 9-acetylfluorene with ethyl nitrate afforded 9-*aci*-nitrofluorene.

Deacylation promoted by a base has been known already to occur in the active methylene to which an acyl group is attached. In fluorene derivatives, 9-benzoylfluorene (**1**) gave fluorene (**2**) and benzoic acid,¹⁾ and 9-chloro-9-acetylfluorene (**3**) afforded 9,9'-bifluorenyl (**4**).²⁾ The present work deals with the deacylation of 9-acylfluorenes in order to clarify the reactivities on the 9-carbon atom of fluorenes.

Deacetylation of 9-acetylfluorene (**5**)³⁾ yielded **2** and ethyl acetate; the yield of **2** increased (28—96%) with the increase of base concentration (1—20%) and with the extension of the reaction time (1—10 h). The deacetylation may be explained by the nucleophilic attack of ethoxide anion on the carbonyl carbon atom of carbonyl in **5** to form the intermediary carbanion (A) as the reverse-Claisen-type condensation (Scheme 1).

The deacylation of some 9-acylfluorenes was carried out as shown in Table 1. The substituent effect in the deacylation of 9-propionyl- (**6**),⁴⁾ 2-ethyl-9-acetyl- (**7**), and 2-bromo-9-acetylfluorene (**8**) was observed to be less significant in comparison with that of **5**. The reaction of 9,9-dibenzoylfluorene (**9**)⁵⁾ with base afforded **1**, which was further converted to **2** by debenzoylation.

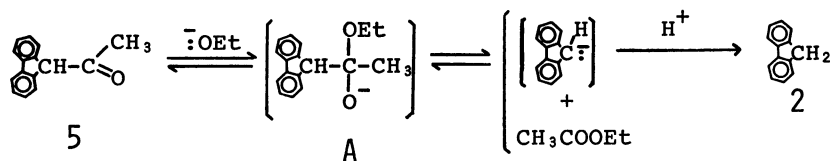
The elimination was accelerated remarkably in the deacetylation of **3**, 9-methyl- (**10**),⁶⁾ and 9-hydroxy-9-acetylfluorene (**11**).⁷⁾ The ethoxide anion may be able to attack on the two positions of **5**, that is, the 9-carbon

and the carbonyl carbon atoms. The 9-acetylfluorene-9-ide anion would be stabilized by resonance as enolate anion and **5** is less reactive under these conditions. The substitution on the 9-position of **5** prevents the attack on this position and results in the significant formation of the elimination product.

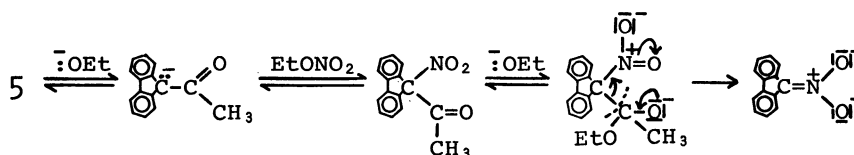
The reaction of **5** with ethyl nitrate in the presence of sodium ethoxide gave pure 9-*aci*-nitrofluorene⁸⁾ in good yield. The ethoxide anion removes a proton from the 9-position on the **5**. The resulting carbanion may afford the intermediary 9-nitro-9-acetylfluorene by an attack of ethyl nitrate, and this was converted to 9-*aci*-nitrofluorene by the action of a second ethoxide anion and by the tautomeric effect of the nitro group (Scheme 2).

The deacetylation of the substrate containing an electron-attracting group proceeds more readily than that having an electron-releasing group. Actually, the progress of the deacylations for **3** and also for **10** was followed by means of gas chromatography; the **10** still remained in a considerable amount (37%) at the reaction step in which all the **3** had been consumed. Chloride **3** gave 9,9'-bifluorenylidene (46%) and **4** (trace), and the ethylene was reduced to **4** under similar conditions.

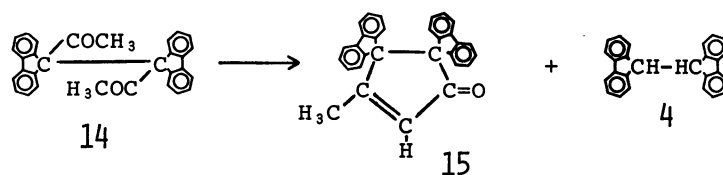
The reactivity of the carbonyl group in 9-*t*-butyl-9-acetylfluorene (**12**) is hindered by the bulky substituent



Scheme 1.



Scheme 2.



Scheme 3.

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TABLE 1. CHARACTERIZATION AND DEACYLATION OF 9-ACYLFLUORENES

Compound	Characterization		Deacylation	
	¹ H-NMR chemical shift ^{a)} δ (ppm); J (Hz)	ν (C=O) on IR spectrum (cm ⁻¹)	Fluorene %	Recovd %
5	1.60 (—CH ₃); 4.78 (>CH—)	1698	42 (2)	45
6	0.78 (—CH ₃ , $J=6.3$); 1.75(—CH ₂ —); 4.64 (>CH—)	1700	42 (2)	38
7	1.26 (—CH ₃ , $J=6.0$); 1.46 (—COCH ₃); 2.67 (—CH ₂ —); 4.59 (>CH—)	1701	45 (2-Ethyl-)	45
8	1.65 (—CH ₃); 4.75 (>CH—)	1698	55 (2-Bromo-) ^{b)}	
9		1680	23(1); 26(2)	
1	5.37 (>CH—)	1681	66 (2)	26
10	1.37 (—CH ₃); 1.57 (—COCH ₃)	1702	94 (9-Methyl-)	trace
11	1.54 (—CH ₃); 4.78 (—OH)	1700	96 (9-Hydroxy-)	trace
12	0.99 (—CH ₃); 1.36 (—COCH ₃)	1699	34 (9- <i>t</i> -Butyl-)	57
13	2.19 (—CH ₃); 2.87 (—CH ₂ —, $J=4.8$); 4.45 (>CH—)	1707		99

a) Measured in CDCl₃ or CCl₄. b) In addition, 2-bromo-9-acetyl-9-hydroxyfluorene (2%, mp 154—155 °C, IR: (OH) 3460; (C=O) 1704 cm⁻¹) and 2,2'-dibromo-9,9'-diacetyl-9 9'-bifluorenyl (0.3%, mp 238—240 °C, IR: (C=O) 1705 cm⁻¹) were isolated.

TABLE 2. CHARACTERIZATION AND DEACYLATION OF 9-ACYLFLUORENES

Compound	Characterization		Deacylation	
	¹ H-NMR chemical shift δ (ppm) (Solvent)	ν (C=O) on IR spectrum (cm ⁻¹)	Time h	Products (%)
16	1.78 (—CH ₃); 4.52 (>CH—) (Pyridine- <i>d</i> ₆)	1700	1	2 (31); 17 (10); 18 (31); 9-Methylfluorene (9); Recovd (42)
16			10	2 (58); 17 (22); 18 (30); 9-Methylfluorene (41)
18	1.69 (—CH ₃); 1.04 (—CH ₃ , $J=7.0$ Hz); 3.97 (—CH ₂ —) (CCl ₄)	1721	10	9-Methylfluorene (18); 17 (14); Recovd (67)
19	3.63 (—CH ₃); 4.71 (>CH—) (CCl ₄)	1729	10	2 (8); 20 (57); Ethyl ester of 20 (10)

from the approach of an attacking ethoxide ion, therefore, the yield of 9-*t*-butylfluorene⁹⁾ decreased. No deacetylation was observed in the cases of 9-acetylfluorene (**13**)¹⁰⁾ and 2-acetylfluorene.¹¹⁾ This finding shows that deacylation occurs when the acyl group is attached directly to the active 9-position of fluorenes. The anomalous lower field (2.19 ppm) of the methyl chemical shift of **13** compared with that (1.60 ppm) of **5** is ascribed to the predominant conformation of **13** and **5**; the mobile methyl group of **13** may be located further away from the shield zone of the aromatic rings than that of **5**.

The reaction of 9,9'-diacetyl-9,9'-bifluorenyl (**14**)²⁾ afforded dehydrate compound **15** accompanied by **4** (Scheme 3); **15** would be formed by the intramolecular aldol-type condensation.

The same reaction of 9-fluorenyl 9-methyl-9-fluorenyl ketone (**16**) yielded **2**, 9-methylfluorene, 9-methylfluorene-9-carboxylic acid (**17**),¹²⁾ and its ethyl ester (**18**),¹³⁾ as summarized in Table 2. The ester **18** gave 9-methylfluorene and **17**. Similarly, methyl fluorenyl-9-carboxylate (**19**) yielded **2**, the corresponding carboxylic acid (**20**), and its ethyl ester. The ratio of the yields of these products indicates that **16** cleaves into 9-fluorenyl anion and **18**, but not into 9-methylfluorenyl anion and an ester of **20**; this may be attributed to

the stability of the 9-fluorenyl anion formed, which is greater than that of the methyl derivative.

Experimental

All the melting points are uncorrected. The instruments used in this experiment have been described elsewhere.¹¹⁾

Deacylation of 9-Acylfluorene. General Procedure: Sodium metal (1.15 g) was treated with 33 ml of dry ethanol, then 5 mmol of substrate was added, and the mixture was refluxed for 10 h under an atmosphere of dry nitrogen. Upon cooling, the reaction mixture was poured into 150 ml of 3% hydrochloric acid and the resulting precipitate was purified by a combination of alumina-column chromatography, vacuum sublimation, and recrystallization.

Reaction of 14 with Sodium Ethoxide. A 2.070 g portion of **14** was refluxed with 3.4 g of sodium ethoxide in 330 ml of dry benzene for 10 h to give 0.450 g of 3-methyl-4,5-bis(2,2'-biphenyl-ylene)-2-cyclopenten-1-one (**15**), 0.012 g of **4**, and 0.010 g of fluorenone. Mp of **15**: 233.5—234.5 °C. IR: (C=O) 1694 cm⁻¹. Mass: m/e 396 (M⁺), 381, and 352. NMR (benzene-*d*₆): δ 1.29 (3H, s), 6.47 (1H, s), and 6.65—7.35 (16H, m) ppm. Found: C, 90.96; H, 5.17%. Calcd for C₃₀H₂₀O: C, 90.88; H, 5.09%.

Reaction of 5 with Ethyl Nitrate. A soln of 2.08 g of **5**, 1.82 g of ethyl nitrate, and 0.68 g of sodium ethoxide in 20 ml of dry ethanol was refluxed for 2 h. Upon cooling, 100 ml of

benzene and 150 ml of water were added to the reaction mixture and the aqueous layer was neutralized with hydrochloric acid to yield 1.53 g of 9-*aci*-nitrofluorene, mp 154 °C (dec). IR: (OH) 2770; (NO₂) 1653, 1441 cm⁻¹.

2-Ethyl-9-acetylfluorene (7). Compd **7** was prepared by means of the same procedure as used for **5** in a 34% yield, bp 142–144 °C/2 Torr (uncorr.). Mass: *m/e* 236 (M⁺).

2,4-Dinitrophenylhydrazone, mp 200–202 °C. IR: (NH) 3320; (NO₂) 1614, 1589 cm⁻¹. Found: C, 66.68; H, 4.95; N, 13.58%. Calcd for C₂₃H₂₀O₄N₄: C, 66.33; H, 4.84; N, 13.46%.

2-Bromo-9-acetylfluorene (8). The title compd was obtained by the same method as described above, yield 30%, mp 66–67 °C. Mass: *m/e* 288, 286 (M⁺), 245, 243, and 207. Found: C, 62.95; H, 3.64%. Calcd for C₁₅H₁₁OBr: C, 62.74; H, 3.86%.

9-*t*-Butyl-9-acetylfluorene (12). Compd **12** was obtained by a procedure similar to that of **10** in a 39% yield, mp 76.5–77 °C. Mass: *m/e* 264 (M⁺), 249, 221, 208, 206, 191, and 165. Found: C, 86.73; H, 7.77%. Calcd for C₁₉H₂₀O: C, 86.32; H, 7.63%.

9-Acetylfluorene (13). This compd was synthesized by the reaction of α-(9-fluorenyl)acetyl chloride with methylmagnesium iodide in the presence of cadmium chloride: yield 58%, mp 62–63 °C (lit.¹⁰ mp 57 °C). Mass: *m/e* 222 (M⁺), 179, and 165.

9-Fluorenyl 9-Methyl-9-fluorenyl Ketone (16). To a soln of 9-methyl-9-lithiofluorene (prepared from 0.96 g of lithium chips, 9.4 g of butyl bromide, and 10.3 g of 9-methylfluorene in 100 ml of xylene) was added dropwise 12.0 g of 9-fluorenyl-carbonyl chloride in 60 ml of xylene at 0 °C with stirring for

30 min, then the mixture was boiled for 1 h to afford 6.45 g of **16**, mp 226–227.5 °C. Mass: *m/e* 372 (M⁺), 179, and 165. Found: C, 90.27; H, 5.57%. Calcd for C₂₈H₂₀O: C, 90.29; H, 5.41%.

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