[e] Hitachi Perkin-Elmer R-246.

[f] VG Micromass 16F.

[g] Not determined.

Michael Reaction of Fluorenes with α,β-Unsaturated Esters and Ketones Catalyzed by Tetra-*n*-butylammonium Fluoride

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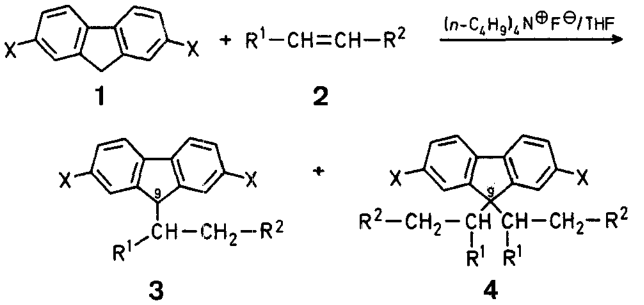
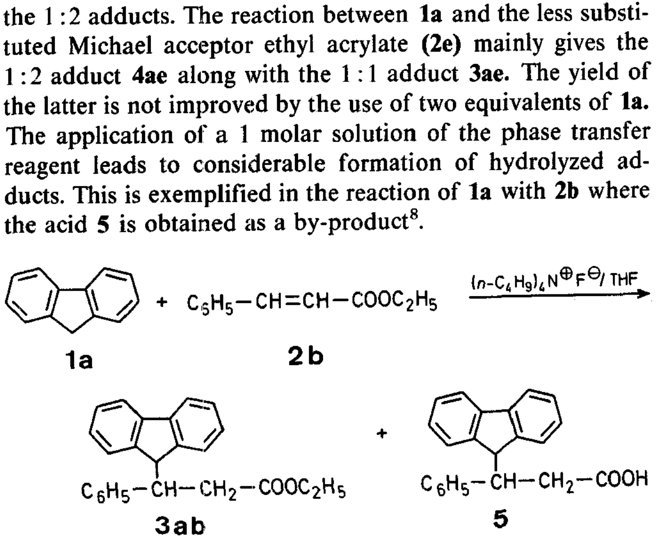
The Michael reaction is perhaps one of the most general methods for C—C bond formation[1]. This reaction is, however, plagued by some shortcomings. Thus, accumulation of substituents near the reaction center may cause lowering of the donor acidity and steric hindrance which prevent the reaction[2,3]. For several years we have been interested in extending the scope of this reaction by employing nonconventional techniques and reagents; e.g. high pressure and phase transfer catalysts having a fluoride ion[4]. Recently, we have found that some of the limitations of the Michael addition can be circumvented by applying high pressure, fluoride ion catalysis, as well as the combined use of these techniques[5].

In this communication, we describe the fluoride ion-catalyzed Michael addition of fluorenes **1** to α,β-unsaturated esters and ketones **2**. These additions have been reported either not to take place or at most to occur sluggishly under classical conditions[6].



The experimentally very simple reaction is performed in a 0.5 molar solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran[7] at room temperature. The yields are moderate to good and have not been optimized (Table). In the reaction of ethyl crotonate (**2a**) as Michael acceptor, the concomitant formation of the 1:2 adducts **4aa** and **4ba** is observed. The use of two equivalents of **2a** results in the increased formation of the 1:2 adducts. The reaction between **1a** and the less substituted Michael acceptor ethyl acrylate (**2e**) mainly gives the 1:2 adduct **4ae** along with the 1:1 adduct **3ae**. The yield of the latter is not improved by the use of two equivalents of **1a**. The application of a 1 molar solution of the phase transfer reagent leads to considerable formation of hydrolyzed adducts. This is exemplified in the reaction of **1a** with **2b** where the acid **5** is obtained as a by-product[8].



The structures of products **3**, **4**, and **5** have been elucidated on the basis of their microanalyses, ^{13}C-N.M.R., and mass spectra.

Table. Michael Adducts 3 and 4 from Fluorenes 1 and α,β-Unsaturated Esters and Ketones 2

Fluorene No.	X	Michael Acceptor No.	R^1	R^2	Product	Yield [%][a]	m.p. [°C]	Molecular formula[b]	I.R. (neat or KBr) $\nu_{C=O}$ [cm^{-1}]	M.S. *m/e* (M^+)	^{13}C-N.M.R. ($CDCl_3$/TMS)[c] δ [ppm]
1a	H	**2a**	CH_3	$—COOC_2H_5$	**3aa**	82[d]	oil	$C_{19}H_{20}O_2$ (280.4)	1720	280	14.2 (q, CH_3); 16.4 (q, CH_3); 34.1 (d, CH); 38.4 (t, CH_2); 52.0 (d, C-9); 60.2 (t, OCH_2); 172.9 (s, C=O)
					4aa	2[d]	oil	$C_{25}H_{30}O_4$ (394.6)	1725	394	14.1 (q, CH_3); 14.8, 15.1 (q, CH_3); 35.1 (d, CH); 36.9, 37.1 (t, CH_2); 59.7, 59.8 (s, C-9); 60.1, 60.3 (t, OCH_2); 173.3 (s, C=O)[e]
1a	H	**2b**	C_6H_5	$—COOC_2H_5$	**3ab**	60[f]	58–59°	$C_{24}H_{22}O_2$ (342.5)	1725	342	13.8 (q, CH_3); 34.1 (t, CH_2); 44.2 (d, CH); 52.8 (d, C-9); 60.1 (t, OCH_2); 172.1 (s, C=O)
1a	H	**2c**	C_6H_5	$—CO—CH_3$	**3ae**	47	93–94°	$C_{23}H_{20}O$ (312.4)	1695	312	38.2 (q, $CO—CH_3$); 42.2 (t, CH_2); 43.0 (d, CH); 53.0 (d, C-9); 207.1 (C=O)
1a	H	**2d**	C_6H_5	—CN	**3ad**	88	152–153°	$C_{22}H_{17}N$ (295.4)	2250 (C≡N)	295	17.8 (t, CH_2); 45.1 (d, CH); 52.3 (d, C-9); 118.7 (s, CN)
1a	H	**2e**	H	$—COOC_2H_5$	**3ae**	4	oil	$C_{18}H_{18}O_2$ (266.4)	1725	266	14.1 (q, CH_3); 27.5 (t, CH_2); 29.6 (t, CH_2); 46.3 (d, C-9); 60.2 (t, OCH_2); 173.5 (s, C=O)
					4ae	26	107°	$C_{23}H_{26}O_4$ (366.5)	1720	366	14.0 (q, CH_3); 29.0 (t, CH_2); 34.7 (t, CH_2); 53.6 (s, C-9); 60.1 (t, OCH_2); 173.3 (s, C=O)
1b	Br	**2a**	CH_3	$—COOC_2H_5$	**3ba**	76	oil	$C_{19}H_{18}Br_2O_2$ (438.2)	1725	438	14.2 (q, CH_3); 16.3 (q, CH_3); 34.0 (d, CH); 38.4 (t, CH_2); 51.9 (d, C-9); 60.5 (t, OCH_2); 172.4 (s, C=O)
					4ba	11	145–145.5°	$C_{25}H_{28}Br_2O_4$ (552.3)	1705	552	14.1 (q, CH_3); 15.0 (q, CH_3); 35.3 (d, CH); 36.8 (t, CH_2); 61.0 (t, OCH_2); 95.0 (s, C-9); 173.2 (s, C=O)
1b	Br	**2b**	C_6H_5	$—COOC_2H_5$	**3bb**	83	112°	$C_{24}H_{20}Br_2O_2$ (500.2)	1725	500	14.0 (q, CH_3); 34.2 (t, CH_2); 44.1 (d, CH); 52.7 (d, C-9); 60.5 (t, OCH_2); 171.8 (s, C=O)
1b	Br	**2c**	C_6H_5	$—CO—CH_3$	**3bc**	69	161.5–162.5°	Ref.[6], m.p. 159–160°	1705	470	30.4 (q, CH_3); 42.5 (t, CH_2); 43.0 (d, CH); 52.9 (d, C-9); 206.6 (s, C=O)

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[a] Yield of pure, isolated product.

[b] Satisfactory microanalyses obtained: C ±0.33, H ±0.28, N −0.25.

[c] *Only the principle, well-defined signals are listed.*

[d] Reaction of **1a** with **2a** in the ratio 1:2 gives **3aa** in 47% yield and **4aa** in 45% yield.

[e] The pairs of signals are possibly due to the presence of conformational isomers.

[f] The use of 1 molar tetra-*n*-butylammonium fluoride in tetrahydrofuran gives **3ab** in 39% yield together with the acid **5** in 20% yield; m.p. 184–185°C.
I.R. (KBr): ν = 1703 cm^{-1} (C=O).
M.S.: *m/e* = 314 (M^+).
^{13}C-N.M.R. ($CDCl_3$): δ = 33.2 (t, CH_2); 43.9 (d, CH); 52.9 (d, C-9); 178.6 ppm (s, C=O).

No Michael addition reaction could be observed between **1a** and diethyl benzylidenemalonate under fluoride ion-catalyzed phase transfer conditions. At 10 kbar in the presence of tetra-*n*-butylammonium fluoride, only a trace amount of **3ab** is obtained, the formation of which has not yet been mechanistically understood.

Reaction of Fluorenes 1 with α,β-Unsaturated Esters and Ketones 2; General Procedure:

A mixture of **1** (5 mmol) and **2** (5 mmol) in a 0.5 molar solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (10 ml) is stirred at room temperature for 100–168 h. Benzene (100 ml) is then added and the solution is washed with water (6 × 30 ml) to remove the catalyst. After drying the organic layer with magnesium sulfate, the solvents are evaporated under reduced pressure and the residual oil is chromatographed on silica gel with benzene/ethyl acetate giving the crude products **3** and **4**, which are purified either by preparative T.L.C. with benzene/hexane or by recrystallization from ethanol/benzene. Flash chromatography can also be used in preparative runs, except for the purification of **3aa**, **4aa**, and **3ab** which require preparative T.L.C.

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[1] J. Mathieu, J. Weil-Raynal, *Formation of C—C Bonds*, Vol. 2, Georg Thieme Verlag, Stuttgart, 1975, p. 152ff.

[2] E. D. Bergman, D. Ginsberg, R. Pappo, *Org. React.* **10**, 179 (1959).

[3] A recent example of an improved procedure for the Michael reaction: A. Gracía-Raso et al., *Synthesis* **1982**, 1037; other examples are cited therein.

[4] E. V. Dehmlow, S. Dehmlow, *Phase Transfer Catalysis*, Verlag Chemie, Weinheim, 1980.
W. E. Keller, Ed., *Compendium of Phase Transfer Reactions and Related Synthetic Methods*, Fluka AG, CH-9470 Buchs, 1979.
J. H. Clark, *Chem. Rev.* **80**, 429 (1980).

[5] K. Matsumoto, *Angew. Chem.* **92**, 1046 (1980); **93**, 803 (1981); *Angew. Chem. Int. Ed. Engl.* **19**, 1013 (1980); **20**, 770 (1981).

[6] R. S. Taylor, R. Connor, *J. Org. Chem.* **6**, 696 (1941).

[7] 1 Molar tetra-*n*-butylammonium fluoride in tetrahydrofuran is commercially available from Aldrich Chemical Co. and is used after dilution to 0.5 molar with tetrahydrofuran.

[8] This is in marked contrast with the previous examples in which the Michael adducts bearing ester grouping did not undergo hydrolysis in the presence of 1 molar tetra-*n*-butylammonium fluoride in tetrahydrofuran, see Ref.[5].