249. Activated C,H-Acids: *N*-Alkyl-9-fluorenimines

Preliminary Communication

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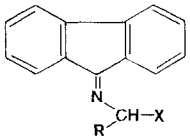
Summary

N-Substituted 9-fluorenimines **1** are easily prepared from primary amines or aminoesters and 9-fluorenimine: their conjugate carbanions **2** are formed by the action of alkoxides and are reprotonated to **1** or to the tautomeric 9-alkylidenamino-fluorenes **3** depending upon substituents.

2-Aza-allylic carbanions are frequently used in organic synthesis [1]; when asymmetrically substituted they have focused considerable interest as ambident anions in prototropic equilibria [2]. Deprotonation of alkylidenamino-substituted C,H-acids is usually accomplished by rather sophisticated bases [1], unaccessible on large scale preparations. To circumvent this difficulty we are presently investigating [3] the potentiality of alkylidenamino-substituted C,H-acids further activated by incorporating one of the ends of the aza-allylic moiety into a frame endowed on its own by high acidity. We report now an easy and expeditious synthesis of 9-fluorenimines **1**, a class of C,H-acids in which the fluorenylidene residue plays the role of such an activating group, and for which deprotonation is expected to occur with conventional bases such as alkoxides. In fact, carbanions **2** can be generated under mild conditions: their reaction with the simplest electrophile, the proton, has been investigated, and preliminary results on the tautomerization of **1** into the tautomeric 9-alkylidenamino derivatives **3** upon protonation of **2** are also reported.



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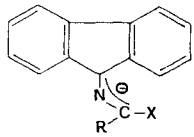

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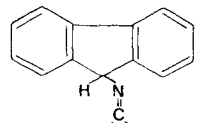

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Table. *Physical properties and selected ^{1}H-NMR. data of compounds* **1** *and* **3**

Product	R	X	M.p. [°C] (Solvent) (B.p./Torr)[a]	^{1}H-NMR. data ($CDCl_3$) [δ, ppm]		
				CH	X	R
1a	Me_2CH	H	(166/1)	3.99 (*d*, CH_2)		2.26 (*m*, CH); 1.15 (*d*, Me)
1b	Ph	H	79–80 (MeOH)	5.40 (*s*, CH_2)		7.1–7.8 (arom. H)
1c	Ph	Me	63–65 (EtOH)	5.73 (*qa*)	1.71 (*d*)	7.1–7.9 (arom. H)
1d	Me	CO_2Me	71–73 (2-PrOH)	5.27 (*qa*)	3.81 (*s*)	1.68 (*d*)
1e	Ph	CO_2Me	126–127 (MeOH)	6.28 (*s*)	3.71 (*s*)	7.1–8.1 (arom. H)
1f	$PhCH_2$	CO_2Me	110–112 (MeOH)	5.45 (*t*)	3.71 (*s*)	3.47 (*m*, CH_2); 7.1–7.4 (arom. H)
3a	Me_2CH	H	(175/0.5)	5.22 (*s*)	8.21 (*d*)	2.65 (*m*, CH); 1.03 (*d*, Me)
3b	Ph	H	139–141 (EtOH) [8]	5.43 (*s*)	8.74 (*s*)	7.4–8.0 (arom. H);
3c	Ph	Me	164–166 (EtOH) [2a]	5.80 (*s*)	2.60 (*s*)	7.2–7.8 (arom. H)

[a]) Evaporative distillation, bath temperature.

Although fluorenone is known to react with aromatic amines to give the corresponding anils [4], its reaction with benzylamine under acid catalysis (boron trifluoride etherate, *p*-toluenesulfonic acid in benzene) is of limited synthetic value since a complex mixture is obtained: ^{1}H-NMR. analysis indicates that both tautomers **1b** and **3b** are formed (s. *Table*), together with *N*-benzylidenebenzylamine[2]). Recent data on transamination reactions between 9-oxofluorene-1-carboxylic acid and amines [5] are in accord with our results.

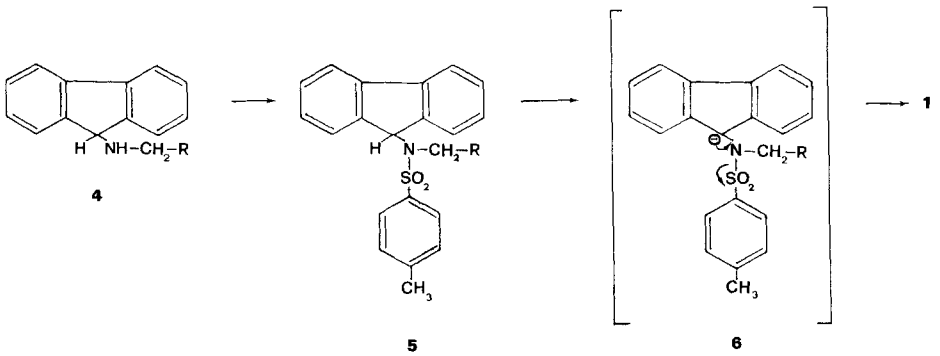
Successful preparation of 9-fluorenimines **1** was performed by transimination between aliphatic primary amines or aminoesters and 9-fluorenimine [6]: pure products could be usually collected by filtration upon running the transimination in the solvent from which the final products crystallize. Instead of the free aminoesters, their more readily available and more stable hydrochloride salts could be used in the transimination provided equimolar amounts of triethylamine were present[3]). Conditions are extremely mild (room temp., CH_2Cl_2 or alcoholic solvents): slow bubbling of dry nitrogen in the stirred reaction mixture frequently increased the rate of conversion by withdrawing ammonia from the solution. The *Table* reports physical properties of the isolated compounds together with ^{1}H-NMR. peaks characteristic for structural assignment. Tautomeric purity was also checked by ^{1}H-NMR. sometimes by comparison with samples of the fluorenyl tautomers **3**, which were obtained from 9-aminofluorene and the corresponding aldehyde in ethyl ether, and in the presence of a dehydrating agent (Na_2SO_4, K_2CO_3).

The acidity of the *Schiff* bases **1** is distinctly dependent upon substitution. Deep purple aza-allylic anions are cleanly and quantitatively formed under nitrogen upon treatment of substrates **1d–f** with dry sodium methoxide in THF; potassium *t*-butoxide (in DMSO) is instead necessary to deprotonate the *Schiff* bases **1a–c**.

[2]) This product would originate from benzylamine and benzaldehyde, in turn formed by hydrolysis of **3b**.

[3]) The reaction of fluorenimine with glycine methyl (or ethyl) ester in methanol does not produce the expected *Schiff* base but follows a different, more complicated pathway on which we shall report shortly.

Scheme



Preliminary results were obtained for the reaction of anions **2** with the simplest electrophile, the proton. Also in this case substituents appear to play an important role in determining the regioselectivity of the protonation. Thus, upon cautious quenching with water in the cold, anions **2d–f** revert to the starting material **1d–f** with no detectable evidence of tautomerization, while anions **2a–c** afford only the tautomerized products **3a–c**. The delicate effect that substituents R and X have on the acidity of 9-fluorenimines **1** and on the transformation of one tautomer into the other is best exemplified by an alternative *N*-alkylfluorenimine synthesis, centered on the base promoted *p*-toluenesulfinate 1,2-elimination from the *p*-toluenesulfonamides **5a** and **5b**[4]) along the *Scheme*[5]).

The amides **5** (**5a**: m.p. 121–123° (EtOH), 80%; **5b**: m.p. 139–141° (EtOH), 70%) were obtained by conventional procedures (tosyl chloride, triethylamine, $CHCl_3$ reflux, 24 h) from amines **4a** and **4b**[4]) (**4a**: isolated as water-insoluble hydrochloride, m.p. 248–252° (EtOH); **4b**: isolated as water-insoluble hydrochloride, m.p. 174–176° (EtOH)). The latter were prepared in sulfolane and DMSO, respectively (room temp., 72 h, 86% and 60%, respectively), starting from 9-chlorofluorene (10 mmol) and isobutylamine or benzylamine (20 mmol).

Treatment of **5a** (3 mmol) with dry sodium methoxide (8 mmol) in DMSO (4 ml, 24 h, room temp.) under nitrogen, and subsequent quenching with water led to the isolation of **1a** (71%). Treatment of **5b** (1.3 mmol) with dry sodium methoxide (1.4 mmol) in DMSO (10 ml, 24 h, room temp.), and subsequent quenching with water resulted in the formation of both tautomers **1b** and **3b** (ratio *ca.* 4:6). The results indicate therefore that, if the methylene group contiguous to the imine *N*-atom is benzylic as in **1b**, it is acidic enough to ionize with sodium methoxide in DMSO with consequent partial tautomerization of the initial substrate upon quenching.

Exploitation of the synthetic usefulness of 2-azaallylic carbanions **2** towards various electrophiles is presently under active investigation.

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[4]) **a**: R = $CH(CH_3)_2$, **b**: R = Ph.

[5]) This imine synthesis is analogous to that reported starting from trifluoromethane sulfonamides [7]: in the present case however, the elimination occurs under much milder conditions thanks to the presence of the acidic H-atom of the fluorenyl residue.

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