Silicon-Assisted Ethoxycarbonylmethylation of *N*-Methylquinolinium and Isoquinolinium Iodides

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A new regioselective route to 2-ethoxycarbonylmethyl-1,2-dihydro-*N*-methylquinolines and 1-ethoxycarbonylmethyl-1,2-dihydro-*N*-methylisoquinolines is described starting from methylquinolinium or -isoquinolinium iodides and commercially available ethyltrimethylsilyl acetate (ETSA). The methylene carbanion was generated by fluorodesilylation using caesium fluoride. On exposure to air, the ethoxycarbonylmethyl adducts were oxidised, leading to the corresponding alkylidene derivatives **4** and **5,** whereas **2a** in solution led slowly to its regioisomer **6a.**

Introduction

1,2-Disubstituted-1,2-dihydroquinolines have aroused increasing interest with regard to their pharmacological activity.[1] As part of a program directed toward the synthesis of new drugs from functionalized heterocyclic derivatives, we needed to introduce the ethoxycarbonylmethyl group at the C-2 -position of the quinoline ring. Ethoxycarbonylmethylation of quinolinium derivatives has previously been achieved by treating ethyl(tributylstannyl)acetate with quinoline and methyl chloroformate.[2] However, organostannyl reagents are not suitable for drug synthesis. Indeed, they are toxic, polluting, and often difficult to get rid of. Furthermore, this process seems to be limited to quinolines activated by alkyl chloroformate, whereas we needed an alkyl group on the nitrogen atom. In contrast to organostannyl reagents, organosilicon derivatives are well-known for their ability to functionalise without side-effects of pollution or toxicity. In the case of 1-methylquinoliniums, Fukuzumi et al.[3] obtained the C-2- and/or C-4-alkoxycarbonylmethylene adducts when using a large excess of ketene silyl acetal, but this reagent is moisture-sensitive and has to be generated. Looking for a more manageable source of the alkyl acetate anion equivalent, we turned to ethyl trimethylsilyl acetate (ETSA), which is a stable, commercially available, useful reagent.[4] In particular, it has been shown to add to the carbonyl double bond in the presence of fluoride, leading to silyl-Reformatsky products.[5] In contrast, to the best of our knowledge, it has never been used to introduce the ethoxycarbonylmethyl moiety in the heteroaromatic series. We report here a new regioselective route to ethoxycarbonylmethyl-1,2-dihydro-*N*-methyl-quinolines and -isoquinolines starting from methylquinolinium or -isoquinolinium iodides (**1**, **7**) and commercially available ETSA in the presence of fluoride.[6]

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Results and Discussion

As expected, ethyltrimethylsilyl acetate (ETSA) alone did not react with compound **1a**.[7] The same reaction conducted with 1 equivalent of sodium hydroxide led to **2a,** but in only 8% yield, along with the 1-methyl-2-quinolone (34%). In contrast, when **1a** was reacted with ETSA in the presence of dried alkali metal fluoride in acetonitrile solution at reflux, the nucleophilic addition of the methylene anion was systematically observed, leading to **2a** (Scheme 1).[8] The reaction also works at room temperature, but needs 5 h to go to completion instead of 2 h. As expected on the basis of their respective nucleophilic power, caesium fluoride led to a better yield than potassium fluoride (87 and 40%, respectively). Attempts to replace acetonitrile by dichloromethane or THF and alkali metal fluoride by tetrabutylammonium fluoride were unsuccessful. These observations show the importance of using a dissociating solvent[9] and are consistent with a charge-controlled process. The reactions were also conducted with the methylquinoliniums **1b−1e**. We previously observed a dramatic effect of ultrasound upon the regiochemistry of nucleophilic addition to 2-Me- and 3-Me-quinoliniums,[10] leading us to systematically study the influence of the activation mode (reflux or sonication at 10 °C). Examination of Table 1 shows that the experimental conditions here have very weak effects on the regiochemistry of the addition, except with **1e**. The C-2 adducts **2c** and **2d** were isolated as the only product, while **2b** and **2e** were obtained in mixtures with the C-4 regioisomer **3b** and **3e**, respectively. Formation of **3b** is probably due to competition during the addition step rather than to a C-2 → C-4 isomerization. Indeed, the isomer ratio was practically the same when working at reflux

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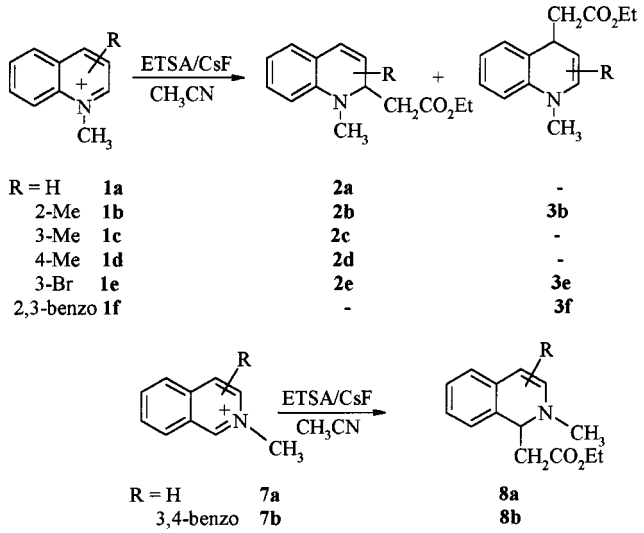
or under sonochemical activation (84:16 and 82:18, respectively). Analogously, the 2,3-benzoquinolinium **1f** and isoquinolinium derivatives **7a/7b** led respectively to **3f** and **8a/8b**. With these substrates, yields vary from 65 to 77% and are systematically higher at reflux (Table 1). The regiochemical assignments were based on NMR chemical shifts and coupling constant values and on ^{1}H, ^{1}H and HMBC experiments.



Scheme 1

Table 1. Ethoxycarbonylmethylation of quinolinium iodides with ETSA/MF/CH_3CN

Substrate	MF	Method[a]	Time [h]	% of the crude **2**:**3** [%]	Yield [%] 2	3
1a	KF	B	3	100:0	**2a**, 40	–
	CsF	A	2	100:0	**2a**, 87	–
	CsF	B	1	100:0	**2a**, 84	–
1b	CsF	A	2	84:16	**2b**, 51	**3b**, 10
	CsF	B	2	82:18	**2b**, 58	**3b**, 14
1c	CsF	A	2	100:0	**2c**, 81	–
	CsF	B	3	100:0	**2c**, 73	–
1d	CsF	A	1.5	100:0	**2d**, 71	–
	CsF	B	3	100:0	**2d**, 67	–
1e	CsF	A	3	82:18	**2e**, 9	**3e**, 2
	KF	A	3	71:29	**2e**, 19	**3e**, 8
	KF	B	3	79:21	**2e**, 44	**3e**,12
1f	CsF	A	3	0:100		**3f**, 65
	CsF	B	3	0:100		**3f**, 72
7a	CsF	A	3		**8a**, 67	
	CsF	B	1		**8a**, 70	
7b	CsF	A	3		**8b**, 60	
	CsF	B	3		**8b**, 77	

[a] A: sonication at 10 °C; B: stirring at reflux.

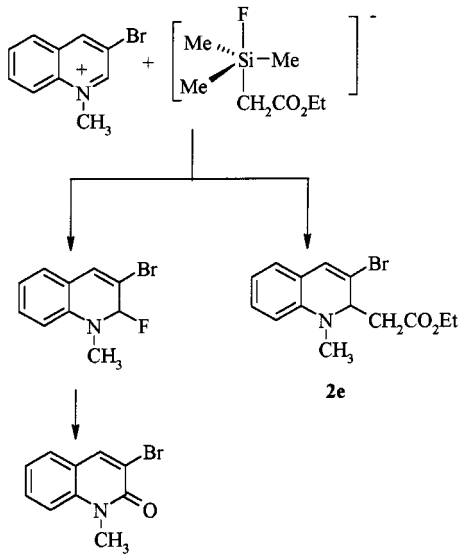
The dramatic effect of both the fluoride and the activation mode observed with the 3-bromoquinolinium **1e** (Table 1) is worthy of note. Indeed, under sonochemical activation, CsF led to the 3-bromo-*N*-methylquinol-2-one as the major product (29%)[11] along with the two ethoxycarbonylmethyl regioisomers (11% yield; **2e/3e** 82:18). Replacing CsF by KF allowed us to obtain the expected adducts in 27% yield under ultrasound (**2e/3e** 71:29) and 56% yield under reflux conditions (**2e/3e** 79:21), whereas only traces of quinolone were detected. This particular behaviour of the 3-bromoquinolinium could be related to the fact that **1e** exhibits the larger positive charge on C-2 in the whole series (Table 2).[12a] Reacting **1e** with caesium fluoride in acetonitrile at reflux led to small amount of bromoquinolone (7% after 3 hours), which could result in the decomposition of a fluoro C-2 adduct.[12b] Another possible fluoride source could be the CsF/ETSA complex itself (Scheme 2). Indeed, it has recently been shown that trimethylsilylacetonitrile reacts with tetramethylammonium fluoride in acetonitrile to form a pentacoordinate silicon complex, which can act as a source of either fluoride or cyanomethylcarbanion, depending on the substrate.[13] Moreover, the authors also reported that CsF, but not KF, led to pentacoordinate complex when reacting with trimethylsilyltrifluoromethane in acetonitrile.[13] Our results are in good agreement with these findings.

During the purification step, an additional more polar product was detected by TLC. It was isolated in low yields ranging from 2−7% by alumina column chromatography and identified as the *N*-methyl-2-ethoxycarbonylmethylidene-dihydroquinolines **4**, **5** (Figure 1). Their structure assignment was based on NMR, SM and elemental analysis. Inspection of the chemical shift data allows a clear understanding of the regiochemistry of these products. It is worth noting that in each case, the H-9 vinylic proton gives rise to a shielded singlet, sensitive to the regiochemistry (δ = 4.73−5.02 in **4**; 5.60 in **5b**). The same is true for the C-9 methine carbon (δ = 81.9−83.8 in **4**; 87.6 in **5b**). Compounds **4** and **5**, are composed of a single isomer, showing that the elimination process is stereospecific. The *E*/*Z* stereochemistry of the exocyclic double bond was assigned with the aid of 2D-NOESY experiments, showing the spatial connectivity depicted in Figure 1. The *E* configuration was confirmed by the presence of a strong H-9/NMe cross-peak in compounds **4a**, **4c**, **4d** and a H-5/H-9 cross-peak in **5b.** In this last case, this assignment was confirmed by the comparison of the ^{1}H and ^{13}C chemical shifts, in particular for H-5 and H-9 (δ = 7.94 and 5.60) with those described for the (*E*)-4-ethoxycarbonylmethylidene-1,4-dihydro-1-methylquinoline (δ = 7.97 and 5.69).[14] From these results, it seems that the elimination process is governed by steric factors, the ethoxycarbonyl group lying away from the bulkier substituent, namely the *N*-methyl group in **4** and the aromatic ring in **5b**.

Spontaneous oxidation in air has been previously reported by Leonard et al. in the case of dihydroquinoline products arising from the reaction of quinolinium with methylene-activated reagents such as nitromethane, malononitrile or ethylcyanoacetate.[15] This led us to examine the stability of compounds **2** and **3** in air. On exposure to air, all adducts led to oxidation products, except the acridine (**3f**) and phenanthridine (**8b**) derivatives. However, the process was very slow, except in the case of **2a** for which the conversion rate reached 100% after ten days. In contrast, **2a** is stable towards caesium fluoride in acetonitrile solution,

Table 2. C-2/C-4 Atomic charges in quinolinium ions and heat of formation of the C-2/C-4 adducts

R	Atomic charges in quinolinium		Heat of formation of the adducts [kcal·mol^{-1}]	
	C−2	C−4	C−2	C−4
H	0.189	0.141	−63.5	−73
2-Me	0.174	0.135	−69.7	−79.7
3-Me	0.195	0.145	−72.5	−81.6
4-Me	0.186	0.117	−72.5	−79.2
3-Br	0.215	0.169	−55.8	−63.4



Scheme 2

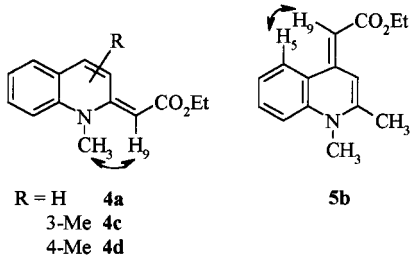
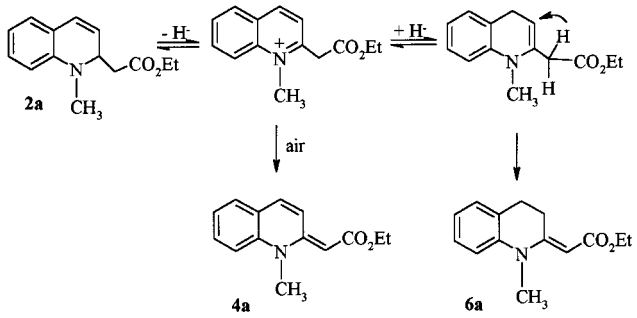


Figure 1. Stereochemistry for compounds **4a, c**, **d** and **5b**

and is recovered unchanged even after two days. An attempt to dehydrogenate **2a** with DDQ (1 equiv. in acetonitrile solution) was unsuccessful. After 2 h at reflux, **2a** remained unchanged, whereas 2 equiv. of DDQ led to its complete degradation. In contrast, $KMnO_4$ in acetone allowed oxidation of **2a** at room temperature, but led to a 73:27 mixture of **4a** and *N*-methylquinol-2-one (76% global yield). In addition, the evolution of **2a** was monitored by GPC and NMR in $CDCl_3$ solution. After 10 days, we only observed traces of **4a**, but surprisingly, its concentration did not increase and a new product identified as **6a** was formed. Seventy days were necessary for the total conversion **2a** → **6a**. No incorporation of deuterium was detected in **6a**, clearly obviating the possibility of the solvent participating as a reducing agent. A 2D-NOESY experiment showed an *E* configuration of the exocyclic double bond as in **4a**. In addition to the strong cross peak H-9/*N*Me, the correlation map also reveals an H-3/Oet cross-peak. This slow but quantitative **2a** → **6a** rearrangement was quite unexpected. It could be the result of two successive hydride shifts by [1,3] sigmatropic migrations of hydrogen or via the formation of a quinolinium-anion ion pair (Scheme 3). We first used a frontier orbital approach to choose between these two hypotheses. A [1,3] sigmatropic rearrangement can be seen as occurring via an imaginary transition state, which consists of a hydrogen atom and an allyl radical. AM1 calculations of the quinolinyl radical led to predict for the first step an antarafacial migration, which should be a thermal process. However, **2a** was recovered unchanged after 7 days in dichloromethane or acetonitrile at reflux. Toluene was then used as the solvent, and the reaction was monitored by GPC. After 7 days at reflux, only 11% of **6a** was present along with 14% of **4a**. After 21 days the composition of the reaction mixture was: **2a** (27%), **4a** (38%) and **6a** (33%). These results show that increasing the temperature does not dramatically accelerate the conversion, but instead leads to the loss of selectivity. Moreover, CCM analysis reveals the presence of tars.



Scheme 3

From a mechanistic point of view, these results are consistent with the formation of the ethoxycarbonylmethylene anion by nucleophilic attack on the silicon, and its addition to the C-2 position, which is the most electrophilic site (Table 2).[12] The regioselectivity of the reaction is remarkable. Indeed, the nucleophilic addition to quinolinium salts is reported to be dependent on substituent effects as well as on the nature of the nucleophilic reagent, leading to competition between C-2 and C-4 additions.[16,17] It is worth noting that we never observed isomerisation of the C-2 adducts during the reaction. Furthermore, comparison of the results obtained at reflux and under sonochemical activation shows that the activation process has no influence

upon the reaction outcome, as shown in Table 1. We previously described the trichloromethylation and acetonylation of quinolinium moieties.[10] The C-2 adduct was obtained as the only product under sonochemical activation, while the C-4 adduct was generally isolated at reflux. This behaviour was interpreted as a thermodynamic process occurring through the heterolytic dissociation of the C_2-C_9 bond in the C-2 adducts, leading to an anion−quinolinium cation pair (Q^+, R^-). Calculation of the heats of formation of the ethoxycarbonylmethylene derivatives showed that the C-4 regioisomer is the most stable (Table 2).[18] The magnitude of this difference in energy is in the same range as for the acetonyl derivatives (9.0 kcal.mol^{-1}), and greater than for the trichloromethyl derivatives (3.2 kcal.mol^{-1}), which both led to the C-2 → C-4 isomerisation. MNDO as well as AM1 calculations of the atomic charges for the C-2 adducts led to a very similar electron distribution, regardless of the nature of the C-2 substituent, showing that the thermal stability of compounds **2a**−**2d** is not governed by electronic effects. These results show the poor migrating ability of the ethoxycarbonylmethyl group relative to the trichloromethyl or the acetonyl group, and could explain the formation of **4a** or **6a** through a common quinolinium−anion ion pair resulting from the heterolytic dissociation of the C_2-H bond (Scheme 3).

Conclusion

ETSA has been shown to allow ethoxycarbonylmethylation of quinolines and isoquinolines. All the products described here are new, except for **2a** and **2d,** which have been previously isolated when treating **1a** and **1d** with the ketene triethylsilyl acetal of ethyl acetate, which is moisture-sensitive and has to be generated.[3] Only the NMR yield was reported, and the experimental protocol was not described. Furthermore, 10 equivalents of the silyl reagent were necessary for the reaction to occur, and it did not work with 2-methylquinolinium. Our process, which is easy to handle and only needs 1 equivalent of a stable and commercially available silyl reagent, constitutes a major improvement for synthesising these derivatives.

Experimental Section

General Remarks: Flash column chromatography techniques (30 cm × 2 cm column) were employed to purify crude products using 70−230 mesh alumina (activity II-III, CH_2Cl_2) under positive air pressure. Ultrasound-promoted reactions were carried out in a common ultrasonic laboratory cleaner filled with water and maintained at a temperature of 0−5 C°. The reaction flask was partially submerged in the sonicator water bath in a place that produced maximum agitation. ^{1}H and ^{13}C NMR spectra were recorded at 250 and 63 MHz, respectively, with TMS as internal standard. Elemental analyses were performed by Service Central d'Analyses du CNRS (F-69390 Vernaison). Synthesis grade acetonitrile (Aldrich) was dried over molecular sieves. Commercial caesium- and potassium fluoride (Aldrich, reagent ACS) were dried prior to use, in a domestic microwave oven. Methiodides **1** and **6** were prepared according to literature procedures.[19] by alkylation of the quinoline with methyl iodide in acetone solution. The mixture was maintained at room temperature until the substrate had reacted completely, as monitored by TLC (SiO_2; Et_2O/CH_2Cl_2, 30:70 v/v). The precipitated salts were filtered off and crystallized. Data for these compounds are identical to those in the literature.[19]

General Procedure: To a stirred solution of quinolinium iodide (7.4 mmol) in acetonitrile (20 mL) was added fluoride (KF or CsF: 8.1 mmol) and ETSA (1.3 g, 8.1 mmol). The mixture was then stirred at reflux or sonicated at 10 °C until the starting material was completely consumed as monitored by TLC (SiO_2, MeOH-Me_2CO, 10:90). The reaction mixture was filtered through Celite and the filtrate was evaporated to dryness. The residue was taken up in cyclohexane (100 mL) and insoluble materials, if present, were removed by filtration and analyzed separately. The solution was evaporated to dryness, leading to an oil which was purified by chromatography, eluting typically with CH_2Cl_2 (Al_2O_3, activity II−III, 70−230 mesh). Yields are reported in Table 1.

2-Ethoxycarbonylmethyl-1,2-dihydro-1-methylquinoline (2a): Oil. − R_f (SiO_2, CH_2Cl_2) = 0.82. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22 (3 H, t, J = 7.1, CH_2CH_3), 2.44 and 2.56 (2 H, AB part of ABX, J = 14.4, 7.6 and 5.3, $COCH_2$), 2.91 (3 H, s, NCH_3), 4.05 and 4.12 (2 H, AB, J = 10.7 and 7.1, CH_3CH_2), 4.47 (1 H, ddd, J = 7.6, 5.5 and 5.3, H-2), 5.78 (1 H, dd, J = 9.5 and 5.5, H-3), 6.44 (1 H, d, J = 9.5, H-4), 6.48 (1 H, d, J = 8.1, H-8), 6.66 (1 H, dd, J = 7.3 and 7.2, H-6), 6.93 (1 H, dd, J = 7.2, and 1.5, H-5), 7.12 (1 H, ddd, J = 8.1, 7.3 and 1.5, H-7). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.2 (CH_2CH_3), 36.5 (NCH_3), 38.0 ($CO\,CH_2$), 57.6 (C-2), 60.6 (CH_3CH_2), 111.0, 117.1, 123.8, 126.3, 126.9, 129.2 ($CHsp^2$), 121.8, 144.2 (Cq), 171.4 (CO). − MS; *m/z*: 231 (M^+, 6.4), 144 (M − CH_2COOEt, 100). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1630 (C=C), 1725 (C=O). − $C_{14}H_{17}NO_2$.(231.3): calcd. C 72.70, H 7.41, N 6.06, O 13.83; found C 72.55, H 7.62, N 6.09, O 13.36.

2-Ethoxycarbonylmethyl-1,2-dihydro-1,2-dimethylquinoline (2b): Oil. − R_f (SiO_2, CH_2Cl_2) = 0.69. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.09 (3 H, t, J = 7.1, CH_2CH_3), 1.56 (s, 3 H, CH_3–2), 2.32 and 2.78 (2 H, AB syst., d, J = 13.2, $COCH_2$), 2.86 (3 H, s, NCH_3), 3.92 and 3.96 (2 H, AB part of ABX_3, J = 10.7 and 7.1, CH_3CH_2), 5.52 (1 H, d, J = 9.8, H-3), 6.36 (1 H, d, J = 9.8, H-4), 6.50 (1 H, d, J = 8.2, H-8), 6.60 (1 H, dd, J = 7.3 and 7.2, H-6), 6.86 (1 H, dd, J = 7.2, and 1.4, H-5), 7.08 (1 H, ddd, J = 8.2, 7.3 and 1.4, H-7). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.0 (CH_2CH_3), 30.9 (NCH_3), 28.3 (CH3−2), 44.5 ($CO\,CH_2$), 59.0 (C-2), 60.4 (CH_3CH_2), 110.3, 116.7, 125.0, 126.7, 128.8, 129.2 ($CHsp^2$), 121.1, 144.8 (Cq), 170.8 (CO). − MS; *m/z*: 245 (M^+, 4.4), 158 (M − CH_2COOEt, 100). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1650 (C=C), 1723 (C=O). − $C_{15}H_{19}NO_2$ (245.3): calcd. C 73.44, H 7.81, N 5.71, O 13.04; found C 73.36, H 8.01, N 5.43, O 13.11.

2-Ethoxycarbonylmethyl-1,2-dihydro-1,3-dimethylquinoline (2c): Oil. − R_f (SiO_2, CH_2Cl_2) = 0.65. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.18 (3 H, t, J = 7.1, CH_2CH_3), 1.88 (d, 3 H, J = 1.2, CH_3–2), 2.34 and 2.50 (2 H, AB part of ABX, J = 14.3, 4.9 and 6.3, $COCH_2$), 2.92 (3 H, s, NCH_3), 4.00 and 4.03 (2 H, AB part of ABX_3, J = 10.7 and 7.1, CH_3CH_2), 4.29 (1 H, dd, J = 6.3, 4.9, H-2), 6.20 (1 H, q, J = 1.2, H-4), 6.49 (1 H, dd, J = 8.1, 0.6, H-8), 6.66 (1 H, ddd, J = 7.4, 7.3 and 0.6, H-6), 6.89 (1 H, dd, J = 7.3 and 1.3, H-5), 7.08 (1 H, ddd, J = 8.1, 7.4 and 1.3, H-7). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.0 (CH_2CH_3), 20.8 (CH_3−3),

36.1 (CO *C*H$_2$), 36.7 (NCH$_3$), 60.7 (CH$_3$*C*H$_2$), 62.3 (C-2), 111.0, 117.3, 122.2, 125.9, 128.2 (CHsp^2), 122.8, 132.5, 142.5 (Cq), 172.1 (CO). − MS; *m/z*: 245 (M$^+$, 1.9), 158 (M − CH$_2$COOEt, 100). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1630 (C=C), 1725 (C=O). − $C_{15}H_{19}NO_2$ (245.3): calcd. C 73.44, H 7.81, N 5.71, O 13.04; found C 73.30, H 7.76, N 5.59, O 13.23.

2-Ethoxycarbonylmethyl-1,2-dihydro-1,4-dimethylquinoline (2d): Oil. − R_f (SiO$_2$, CH$_2$Cl$_2$) = 0.78. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.22 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 2.04 (d, 3 H, *J* = 1.4, CH$_3$–4), 2.39 and 2.53 (2 H, AB part of ABX, *J* = 14.4, 7.5 and 5.3, COCH$_2$), 2.91 (3 H, s, NCH$_3$), 4.04 and 4.12 (2 H, AB part of ABX$_3$, *J* = 10.9 and 7.1, CH$_3$C*H*$_2$), 4.40 (1 H, dddd, *J* = 7.5, 5.8, 5.3 and 1.9, H-2), 5.65 (1 H, d, *J* = 5.8, H-3), 6.50 (1 H, dd, *J* = 7.8, 1.0, H-8), 6.71 (1 H, ddd, *J* = 7.6, 7.5 and 1.0, H-6), 7.12 (1 H, dd, *J* = 7.5 and 1.5, H-5), 7.14 (1 H, ddd, *J* = 7.8, 7.6 and 1.5, H-7). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.2 (CH$_2$*C*H$_3$), 18.8 (CH$_3$–4), 37.7 (CO *C*H$_2$), 36.6 (N*C*H$_3$), 60.5 (CH$_3$*C*H$_2$), 57.4 (C-2), 111.0, 116.8, 121.4, 123.7, 128.9 (CHsp^2), 123.3, 131.1, 144.1 (Cq), 171.6 (CO). − MS; *m/z*: 245 (M$^+$, 2.7), 158 (M − CH$_2$COOEt, 100). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1650 (C=C), 1727 (C=O). − $C_{15}H_{19}NO_2$ (245.3): calcd. C 73.44, H 7.81, N 5.71, O 13.04; found C 73.55, H 7.69, N 5.56, O 13.08.

3-Bromo-2-ethoxycarbonylmethyl-1,2-dihydro-1-methylquinoline (2e): Oil. − R_f (SiO$_2$, CH$_2$Cl$_2$) = 0.65. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.20 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 2.50 (m, 2 H, COCH$_2$), 2.93 (3 H, s, NCH$_3$), 4.01 and 4.08 (2 H, AB part of ABX$_3$, *J* = 10.8 and 7.1, CH$_3$C*H*$_2$), 4.67 (1 H, dd, *J* = 6.1, 5.2, H-2), 6.76 (1 H, s, H-4), 6.52 (1 H, d, *J* = 8.1, H-8), 6.67 (1 H, dd, *J* = 7.4, and 7.3, H-6), 6.88 (1 H, dd, *J* = 7.4 and 1.4, H-5), 7.15 (1 H, ddd, *J* = 8.1, 7.3 and 1.4, H-7). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.0 (CH$_2$*C*H$_3$), 36.2 (CO *C*H$_2$), 37.2 (NCH$_3$), 60.9 (CH$_3$*C*H$_2$), 64.8 (C-2), 111.9, 117.8, 126.4, 128.5, 129.5 (CHsp^2), 115.5, 121.7, 142.0 (Cq), 171.0 (CO). − MS; *m/z*: 311 ({^{81}Br}M$^+$, 6.2), 309 ({^{79}Br}M$^+$, 6.2), 222 (M − CH$_2$COOEt, 100). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1620 (C=C), 1725 (C=O). − $C_{14}H_{16}NBrO_2$ (310.2): calcd. C 54.20, H 5.20, N 4.52, O 10.32; found C 53.95, H 5.31, N 4.43, O 10.46.

4-Ethoxycarbonylmethyl-1,4-dihydro-1,2-dimethylquinoline (3b): Oil. − R_f (SiO$_2$, CH$_2$Cl$_2$) = 0.30. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.22 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 1.97 (br. s, 3 H, CH$_3$–2), 2.44 (2 H, m, COCH$_2$), 3.16 (3 H, s, NCH$_3$), 4.12 (2 H, q, *J* = 7.1, CH$_3$C*H*$_2$), 4.19 (1 H, m, H-4), 4.61 (1 H, d, *J* = 4.9, H-3), 7.1−7.6 (4 H, m). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.4 (CH$_2$*C*H$_3$), 20.1 (CH$_3$–2), 32.7, 34.9, 44.5 (CO *C*H$_2$), 60.3 (CH$_3$*C*H$_2$), 98.2, 111.6, 120.6, 126.9, 128.2 (CHsp^2), 118.3, 138.0, 142.4 (Cq), 172.1 (CO). − MS; *m/z*: 245 (M$^+$), 158 (M − CH$_2$COOEt, 100). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1650 (C=C), 1723 (C=O). − $C_{15}H_{19}NO_2$ (245.3): calcd. C 73.44, H 7.81, N 5.71, O 13.04; found C 73.56, H 7.65, N 5.56, O 12.89.

3-Bromo-4-ethoxycarbonylmethyl-1,4-dihydro-1-methylquinoline (3e): Oil. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.30 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 2.50 (m, 2 H, COCH$_2$), 3.09 (3 H, s, NCH$_3$), 4.15 (2 H, m, CH$_3$C*H*$_2$), 4.30 (1 H, dd, *J* = 4.8, 7.7, H-4), 6.36 (1 H, s, H-2), 6.60−7.12 (4 H, m). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.2 (CH$_2$*C*H$_3$), 38.0 (NCH$_3$), 42.5 (CO *C*H$_2$), 43.2 (C-4), 60.5 (CH$_3$*C*H$_2$), 111.5, 121.6, 127.5, 128.8, 133.8 (CHsp^2), 93.6, 122.2, 133.7, (Cq), 171.4 (CO). − $C_{14}H_{16}NBrO_2$ (310.2): calcd. C 54.20, H 5.20, N 4.52, O 10.32; found C 54.45, H 5.27, N 4.33, O 10.53.

9-Ethoxycarbonylmethyl-9,10-dihydro-10-methylacridine (3f): Oil. − R_f (SiO$_2$, CH$_2$Cl$_2$) = 0.77. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.25 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 2.64 (2 H, d, *J* = 7.6, COC*H*$_2$), 3.42 (3 H, s, NCH$_3$), 4.15 (2 H, q, *J* = 7.1, CH$_3$C*H*$_2$), 4.61 (1 H, t, *J* = 7.6, H-9), 6.98−7.08 (4 H, m), 7.29−7.38(4 H, m). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.3 (CH$_2$*C*H$_3$), 33.06 (NCH$_3$), 40.86 (C-9), 42.1 (CO *C*H$_2$), 60.4 (CH$_3$*C*H$_2$), 112.4, 120.9, 127.5, 128.1 (CHsp^2), 126.3, 142.6 (Cq), 171.7 (CO). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1594 (C=C), 1729 (C=O). − $C_{18}H_{19}NO_2$ (281.4): calcd. C 76.84, H 6.81, N 4.98, O 11.37; found C 76.45, H 7.01, N 4.83, O 11.58.

(*E*)-2-Ethoxycarbonylmethylidene-1,2-dihydro-1-methylquinoline (4a). − By Aerobic Oxidation of 2a: A solution of **2a** (500 mg, 2.2 mmol) in dichloromethane (10 mL) was deposited in a Petri dish (6 cm diameter), which was kept at room temperature open to air. Slow evaporation of the solvent led to a thin film of **2a.** Crystallization occurred slowly owing to the formation of **4a.** The oxidation was completed within 10 days, affording pale yellow crystals. NMR analysis of the crude product showed the formation of **4a** as the only product. It was purified by chromatography on silica gel (CH$_2$Cl$_2$/EtOH 95:5) leading to **4a** as a pale yellow solid (435 mg, 87%).

By Oxidation with KMnO$_4$: KMnO$_4$ (300 mg, 1.8 mmol) was added to a stirred solution of **2a** (500 mg, 2.2 mmol) in acetone (10 mL). Stirring was continued at room temperature for 18 h. Filtration of the reaction mixture through Celite followed by workup identical to the procedure described above gave **4a** (280 mg, 56%) and *N*-methylquinol-2-one (72 mg, 20%).[11]

4a: R_f (SiO$_2$, CH$_2$Cl$_2$) = 0.25; m.p. 146 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$). − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.30 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 3.42 (3 H, s, NCH$_3$), 4.15 (2 H, q, *J* = 7.1, CH$_3$C*H*$_2$), 4.81 (1 H, d, *J* = 0.6, H-9), 7.19 (1 H, dd, *J* = 9.8, 0.6, H-4), 8.52 (1 H, d, *J* = 9.8, H-3), 7.19 (1 H, dd, *J* = 7.9, 0.9, H-8), 7.08 (1 H, ddd, *J* = 7.4, 7.4 and 0.9, H-6), 7.35 (1 H, dd, *J* = 7.4 and 1.6, H-5), 7.41 (1 H, ddd, *J* = 7.9, 7.4 and 1.6, H-7). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.8 (CH$_2$*C*H$_3$), 34.5 (NCH$_3$), 58.7 (CH$_3$*C*H$_2$), 83.3 (CH-9), 113.6, 121.4, 121.7, 128.2, 130.2, 131.6 (CHsp^2), 122.7, 140.5, 153.0 (Cq), 168.5 (CO). − MS; *m/z*: 229 (M$^+$, 69.2), 184 (M − OEt, 67.1). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1621 (C=C), 1728 (C=O). − $C_{14}H_{15}NO_2$ (229.3): calcd. C 73.34, H 6.59, N 6.11, O 13.96; found C 72.95, H 6.71, N 6.06, O 14.06.

(*E*)-2-Ethoxycarbonylmethylidene-1,2-dihydro-1,3-dimethylquinoline (4c): Yellow solid, m.p. 64 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$). − R_f (Al$_2$O$_3$, CH$_2$Cl$_2$) = 0.75. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.30 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 2.15 (s, 3 H, CH$_3$–3), 3.59 (3 H, s, NCH$_3$), 4.15 (2 H, q, *J* = 7.1, CH$_3$C*H*$_2$), 5.02 (1 H, br. s, H-9), 7.06 (1 H, s, H-4), 6.24 (1 H, d, *J* = 8.3, H-8), 7.10 (1 H, dd, *J* = 7.9 and 7.1, H-6), 7.30 (1 H, dd, *J* = 7.9 and 1.5, H-5), 7.39 (1 H, ddd, *J* = 8.3, 7.1 and 1.5, H-7). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.6 (CH$_2$*C*H$_3$), 20.1 (CH$_3$–3), 44.1 (NCH$_3$), 58.9 (CH$_3$*C*H$_2$), 83.8 (CH-9), 115.5, 122.2, 126.6, 129.1, 129.9 (CHsp^2), 123.1, 131.5, 141.2, 153.8 (Cq), 166.9 (CO). − MS; *m/z*: 243 (M$^+$, 64.3), 198 (M − OEt, 66). − IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 1664 (C=C), 1734 (C=O). − $C_{15}H_{17}NO_2$ (243.3): calcd. C 74.05, H 7.04, N 5.76, O 13.15; found C 73.80, H 7.19, N 5.51, O 12.92.

(*E*)-2-Ethoxycarbonylmethylidene-1,2-dihydro-1,4-dimethylquinoline (4d): Yellow solid, m.p. 102 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$). − R_f (SiO$_2$, CH$_2$Cl$_2$) = 0.32. − ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.29 (3 H, t, *J* = 7.1, CH$_2$C*H*$_3$), 2.35 (s, 3 H, CH$_3$–4), 3.39 (3 H, s, NCH$_3$), 4.15 (2 H, q, *J* = 7.1, CH$_3$C*H*$_2$), 4.73 (1 H, br. s, H-9), 8.43 (1 H, s, H-3), 7.10 (1 H, dd, *J* = 7.9, 7.3, H-6), 7.16 (1 H, d, *J* = 8.2, H-8), 7.49 (1 H, dd, *J* = 7.9 and 1.5, H-5), 7.39 (1 H, ddd, *J* = 8.2, 7.3 and 1.5, H-7). − ^{13}C NMR (62.89 MHz, CDCl$_3$): δ = 14.8 (CH$_2$*C*H$_3$), 19.2 (CH$_3$–4), 34.5 (NCH$_3$), 58.6 (CH$_3$*C*H$_2$), 81.9 (CH-9), 113.9, 120.4, 121.5, 124.6, 129.9 (CHsp^2), 123.7, 138.6, 152.9

(Cq), 168.6 (CO). − MS; *m/z*: 243 (M^+, 50.3), 198 (M − OEt, 66), 171 (M − $COOCH_2CH_2$, 100). − IR (neat) $\tilde{\nu}_{max}/cm^{-1}$ = 1667 (C=C), 1729 (C=O). − $C_{15}H_{17}NO_2$ (243.3): calcd. C 74.05, H 7.04, N 5.76, O 13.15; found C 73.85, H 7.16, N 5.61, O 12.97.

(*E*)-4-Ethoxycarbonylmethylidene-1,4-dihydro-1,2-dimethylquinoline (5b): Pale yellow solid, m.p. 110 °C (C_6H_{12}/CH_2Cl_2). − R_f (SiO_2, CH_2Cl_2) = 0.30. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (3 H, t, *J* = 7.1, CH_2CH_3), 2.34 (s, 3 H, CH_3–2), 3.55 (3 H, s, NCH_3), 4.17 (2 H, q, *J* = 7.1, CH_3CH_2), 5.60 (1 H, br. s, H-9), 7.75 (1 H, s, H-3), 7.18 (1 H, dd, *J* = 7.5, 7.4, H-6), 7.27 (1 H, d, *J* = 8.4, H-8), 7.47 (1 H, dd, *J* = 8.4 and 7.4, H-7), 7.94 (1 H, d, *J* = 7.5, H-5). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.4 (CH_2CH_3), 21.6 (CH_3–2), 33.6 (NCH_3), 58.0 (CH_3CH_2), 87.6 (CH-9), 106.1, 114.5, 122.5, 123.8, 130.0 ($CHsp^2$), 122.2, 139.6, 143.3, 145.4 (Cq), 169.6 (CO). − MS; *m/z*: 243 (M^+, 42.2), 198 (M − OEt, 61). − IR (neat) $\tilde{\nu}_{max}/cm^{-1}$ = 1667 (C=C), 1730 (C=O). − $C_{15}H_{17}NO_2$ (243.3): C 74.05, H 7.04, N 5.76, O 13.15; found C 73.98, H 7.11, N 5.69, O 12.95.

(*E*)-2-Ethoxycarbonylmethylidene-1,2,3,4-tetrahydro-1-methylquinoline (6a): A solution of **2a** (100 mg, 0.43 mmol) in $CDCl_3$ (1 mL) in an NMR tube was kept at room temperature. The 2a→6a isomerization was monitored by ^{1}H NMR spectroscopy, until **2a** had disappeared (70 d). The following ^{1}H signals were used to confirm that conversion took place: for **2a**, the NCH_3 singlet at 2.91 and the H-3 dd at 5.78; for **6a**, the NCH_3 singlet at 3.30 and the H-9 singlet at 4.95. The reaction was also followed by GC (capillary column JWDB-5MS 30 m × 0.25 mm × 0.25 μm). The GC oven temperature programming was 5 °C.min^{-1} starting from 220 °C until 280 °C. Retention time (min) were respectively **2a** 3.3, **6a** 4.9, **4a** 6.8. Within 10 days, the signals of **2a** began to decrease, whereas **6a** appeared. After 70 days on standing, the NMR spectra showed the presence of only **6a**. Evaporation of the solvent led to **6a** (98 mg, 98% yield).). − R_f (SiO_2, CH_2Cl_2) = 0.62. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (3 H, t, *J* = 7.1, CH_2CH_3), 2.65 (2 H, m), 3.30 (3 H, s, NCH_3), 3.43 (2 H, m), 4.14 (2 H, q, *J* = 7.1, CH_3CH_2), 4.95 (1 H, br. s, H-9), 5.35 (1 H, d, *J* = 7.3, H-3), 6.95 (2 H, m), 7.11 (1 H, m),7.20 (1 H, m). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.6 (CH_2CH_3), 24.8 (CH_2), 25.5 (CH_2), 35.0 (NCH_3), 58.8 (CH_3CH_2), 87.1, 115.1, 121.9, 127.2, 127.3 ($CHsp^2$), 128.8, 141.6, 159.3, 168.6 (Cq). − MS; *m/z*: 231 (M^+, 100), 202 (M − Et, 11.6), 186 (M − OEt, 69.2). − $C_{14}H_{17}NO_2$ (231.3): calcd. C 72.70, H 7.41, N 6.06, O 13.83; found C 72.37, H 7.20, N 6.13, O 14.01.

1-Ethoxycarbonylmethyl-1,2-dihydro-2-methylisoquinoline (8a): Oil. − R_f (SiO_2, CH_2Cl_2) = 0.68. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (3 H, t, *J* = 7.1, CH_2CH_3), 2.50 and 2.71 (2 H, AB part of ABX, *J* = 14.1, 7.1 and 6.2, $COCH_2$), 2.94 (3 H, s, NCH_3), 4.04 (2 H, q, *J* = 7.1, CH_3CH_2), 4.80 (1 H, ddd, *J* = 7.1, 6.2 and 1.1, H-1), 5.35 (1 H, d, *J* = 7.3, H-3), 6.03 (1 H, dd, *J* = 7.3 and 1.3, H-4), 6.80−6.96 (2 H, m), 6.98 (1 H, ddd, *J* = 7.5, 7.2 and 1.3), 7.10 (1 H, ddd, *J* = 7.3, 7.2, and 1.8). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.1 (CH_2CH_3), 36.3 (CO CH_2), 40.5 (NCH_3), 59.3 (C-1), 60.5 (CH_3CH_2), 97.6, 122.7, 124.7, 125.6, 127.6, 136.1 ($CHsp^2$), 128.1, 132.4 (Cq), 171.7 (CO). − MS; *m/z*: 231 (M^+, 7.6), 144 (M − CH_2COOEt, 100). − IR (neat) $\tilde{\nu}_{max}/cm^{-1}$ = 1725 (C=O). − $C_{14}H_{17}NO_2$ (231.3): calcd. C 72.70, H 7.41, N 6.06, O 13.83; found C 72.39, H 7.25, N 6.16, O 14.06.

6-Ethoxycarbonylmethyl-5,6-dihydro-5-methylphenanthridine (8b): Oil. − R_f (SiO_2, CH_2Cl_2) = 0.56. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (3 H, t, *J* = 7.1, CH_2CH_3), 2.40 and 2.63 (2 H, AB part of ABX, *J* = 14.2, 7.9 and 5.6, $COCH_2$), 3.04 (3 H, s, NCH_3), 4.04 (2 H, q, *J* = 7.1, CH_3CH_2), 4.82 (1 H, dd, *J* = 7.9, 5.6, H-6), 6.50−7.80 (8 H, m). − ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 14.1 (CH_2CH_3), 36.7 (CO CH_2), 37.4 (NCH_3), 61.1 (C-6), 60.6 (CH_3CH_2), 113.3, 118.4, 122.9, 123.4, 126.0, 127.1, 128.0, 129.4 ($CHsp^2$), 122.5, 130.7, 134.9, 144.1 (Cq), 171.7 (CO). − MS; *m/z*: 281 (M^+, 3.4), 194 (M − CH_2COOEt, 100). − IR (neat) $\tilde{\nu}_{max}/cm^{-1}$ = 1725 (C=O). − $C_{18}H_{19}NO_2$ (281.4): calcd. C 76.84, H 6.81, N 4.98, O 11.37; found C 76.68, H 6.83, N 4.79, O 11.48.

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[1] See as example: J. Babiak, H. M. Elokdah, C. P. Miller, T. S. Sulkowski, *U.S. US 5,939,435,* **1999**, American Home Product Corporation, USA.
[2] T. G. Murali Dhar, C. Gluchowski, *Tetrahedron Lett.* **1994**, *35*, 989−992.
[3] [3a] J. Otera, Y. Wakahara, H. Kamei, T. Sato, H. Nazaki, S. Fukuzumi, *Tetrahedron Lett.* **1991**, *32*, 2405−2408. − [3b] S. Fukuzumi, M. Fujita, S. Noura, J. Otera, *Chem. Lett.* **1993**, 1025−1028.
[4] See as examples: D. J. Ager. In *Encyclopaedia of Reagents for Organic Synthesis*, Ed. Paquette, John Wiley & Sons, Inc.: New York, **1995**, Vol. 4, pp 2523−2525 and references therein.
[5] [5a] R. Latouche, F. Texier-Boullet, J. Hamelin, *Bull. Soc. Chim. Fr.* **1993**, *130*, 535−546. − [5b] M. Bellassoued, N. Ozanne, *J. Org. Chem.* **1995**, *60*, 6582−6584. − [5c] S. Jolivet, S. Abdallah-El-Ayoubi, D. Mathe, F. Texier-Boullet, J. Hamelin, *J. Chem. Research* **1996**, 300−301. − [5d] E. Nakamura, M. Shimizu, I. Kuwajima, *Tetrahedron Lett.* **1976**, *20,* 1699−1702.
[6] For preliminary results, see M. Grignon-Dubois, F. Diaba, *J. Chem. Research* **1998**, 660−661.
[7] Silicon reagents are known to be weaker nucleophiles than tin reagents: see for example A. Hosomi, H. Iguchi, M. Endo, H. Sakurai, *Chem. Lett*. **1979**, 977−980.
[8] The formation of a Si−F bond (142 kcal.mol^{-1}) is usually a highly exothermic process, which provides the driving force for a number of useful synthetic reactions. For reviews, see as examples: [8a] W. P. Weber in *Silicon Reagents for Organic Synthesis*, Springer Verlag, Berlin, 1983. − [8b] E. W. Colvin, *Silicon Organic Synthesis*, Butterworths, London, 1981. − [8c] G. G. Yakobson, N. E. Akhmetova, *Synthesis* **1983**, 169−184. − [8d] J. H. Clark, *Chem. Rev.* **1980**, *80*, 429−452.
[9] The larger dielectric constant of acetonitrile (ε = 35.94) allows for the formation of a solvent-separated ion pair, while THF (ε = 7.58) or dichloromethane (ε = 8.93) should hinder the dissociation. A. Loupy, B. Tchoubar, D. Astruc, *Chem. Rev.* **1992**, 1141−1165 and references therein.
[10] [10a] F. Diaba, I. Lewis, M. Grignon-Dubois, S. Navarre, *J. Org. Chem.* **1996**, *61*, 4830−4832. − [10b] M. Grignon-Dubois, F. Diaba, M.-C. Grelier-Marly, *Synthesis* **1994**, 800−804.
[11] Melting point as well as spectroscopic data are identical to literature: La Coste, W. *Ber.* **1882**, *15,* 186. M. Grignon-Dubois, A. Meola, *Synth. Commun.* **1995**, *25 (19)*, 2999−3006.
[12] [12a] Atomic charges in quinoliniums were calculated with Hyperchem, version 5 (Hypercube, Inc. Gainsville, 32601 Fl). The results come from an MNDO single-point calculation of the optimized geometry (final gradient ≤ 0.005 kcal. Å^{-1}mol^{-1}), using an RHF Hamiltonian. In the case of the C-2 adducts, the AM1 method was also used. − [12b] These kinds of derivatives appear to be unknown in the literature.
[13] D. J. Adams, J. H. Clark, L. B. Hansen, V. C. Sanders, S. Tavener, *J. Fluor. Chem*. **1998**, *92*, 123−125.
[14] J. Levillain, M. Vazeux, *Synthesis* **1995**, 56−62 .
[15] [15a] N. J. Leonard, R. L. Foster, *J. Am. Chem. Soc.* **1951**, *73*, 3325−3329. − [15b] N. J. Leonard, R. L. Foster, *J. Am. Chem. Soc.***1952**, *74*, 2110−2111. − [15c] O. N. Chupakhin, V. N. Charushin, *Tetrahedron* **1988**, *44*, 1−34.
[16] For reviews, see: [16a] N. Y. Sidgewick, F. R. S. Sidgewick, *The Organic Chemistry of Nitrogen;* Clarendon Press, Oxford, **1966**, p 718. − [16b] J. Gurnos, *Quinolines,* Wiley, New York, **1982**.
[17] See, for example: [17a] J. Metzger, H. Larivé, E.-J. Vincent, R. Dennilauler, R. Baralle, C. Gaurat, *Bull. Soc. Chim. Fr.* **1967**,

30−40. − [17b] G. T. Pilyugin, B. M. Gutsulyak, *Usp. Khim.* **1963**, *32 (4)*, 389−432 (*Chem. Abstr.* **1963**, *59*, 3889b). − [17c] J. W. Bunting, W. G. Meathrel, *Tetrahedron Lett.* **1971**, 133−136. − [17d] S. Fukuzumi, S. Noura, *J. Chem. Soc., Chem. Commun.* **1994**, 287−288. − [17e] M. Maeda, *Chem. Pharm. Bull.* **1990**, *38*, 2577−2580.

[18] Heats of formation for the pair of regioisomers were calculated on a 486 PC-compatible running the programs PCMODEL, version 4.1 and GMMX, version 1.0 (from Serena Software, P.O. Box 3076, Bloomington, IN 47402−3076). Both use the features of Allinger's MMX force-field, including pi-valence electron self-consistent field calculations.

[19] [19a] O. Doebner, W. Miller, *Ber.* **1883**, *16*, 2464−2472. − [19b] C. F. Duffin, *Adv. Heterocycl. Chem.* **1964**, *3*, 1−56.

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