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Notes

Organosilicon Entry to the Regioselective Cyanomethylation of Quinolinium Methiodides

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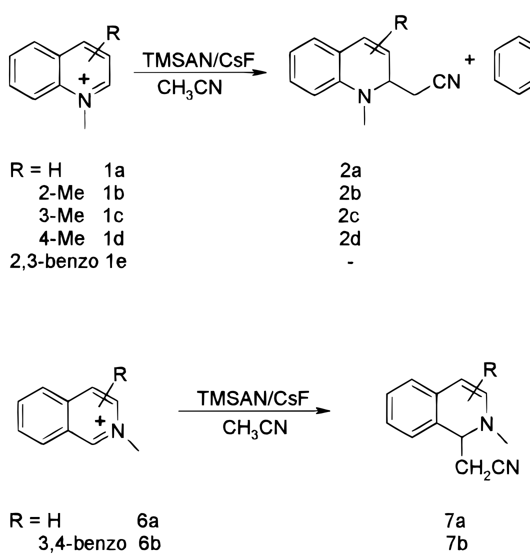
As part of a program directed toward the synthesis of new drugs from functionalized heterocyclic derivatives, we needed to introduce the cyanomethyl group on the C-2 position of the quinoline ring. In the literature, we only found examples related to the C-4 addition of active cyanomethylenes such as malononitrile, ethyl cyanoacetate, or phenylacetonitrile in basic media.[1] From these results, we first tried to generate the cyanomethyl moiety using sodium hydroxide and acetonitrile. All our attempts to functionalize **1a** in this way failed, and the 1-methyl-2-quinolone was systematically obtained as the only product. The pK_a of acetonitrile (24−25) does not allow the proton abstraction leading to the anion to compete with the addition of the hydroxide anion to the methiodide. Replacing sodium hydroxide with *t*-BuOK led to the same results. This led us to turn to trimethylsilylacetonitrile (TMSAN), which is a commercially available useful reagent.[2] In particular, it has been shown to be a synthetic equivalent for the anion of acetonitrile in condensation with carbonyl compounds.[3,4] In contrast, to the best of our knowledge, it has never been used to introduce the cyanomethyl moiety in the heteroaromatic series. We report here a regioselective route to cyanomethyl-1,2-dihydro-*N*-methylquinolines and -isoquinolines starting from methylquinolinium or -isoquinolinium iodides (**1**, **6**) and TMSAN in the presence of fluoride.[5]

Scheme 1



R = H	1a	2a	-
2-Me	1b	2b	3b
3-Me	1c	2c	-
4-Me	1d	2d	-
2,3-benzo	1e	-	3e

R = H	6a	7a
3,4-benzo	6b	7b

Results and Discussion

We first verified than TMSAN alone did not allow the reductive cyanomethylation of the 1-methylquinolinium iodide, **1a**. In contrast, when **1a** was reacted with TMSAN in the presence of dried alkali metal fluoride in acetonitrile solution, the nucleophilic addition of the methylene anion was systematically observed leading to **2a** (Scheme 1). As expected on the basis of their respective nucleophilic power, cesium fluoride led to a better yield than potassium fluoride (43 and 28%, respectively). Attempts to replace acetonitrile by methylene chloride or THF and alkali metal fluoride by tetrabutylammonium fluoride were unsuccessful. These observations are consistent with a charge-controlled process. As we previously observed a dramatic effect of ultrasound upon the regiochemistry of nucleophilic addition to quinoliniums,[6] the influence of the activation mode (reflux or sonochemical at 10 °C) was systematically compared. Examination of Table 1 shows that the experimental conditions have only very weak effects on the regiochemistry of the addition. The reactions were also conducted with the methylquinoliniums **1b**−**d.** The C-2 adducts **2c**,**d** were isolated as the only product, while **2b** was obtained in mixture with its C-4 regioisomer **3b.** Formation of **3b** is probably due to competition during the addition step rather than an isomerization C-2 → C-4. Indeed, the isomer ratio was not very different when working at reflux (74:26) or under sonochemical activation (88:12). The regiochemical assignments were based on NMR chemical shifts and coupling constant values and on ^{1}H, ^{1}H and HMBC experiments. Analogously, the isoquinolinium derivatives **6a**,**b** led to **7a**,**b** (yields 51 and 59%, respectively).

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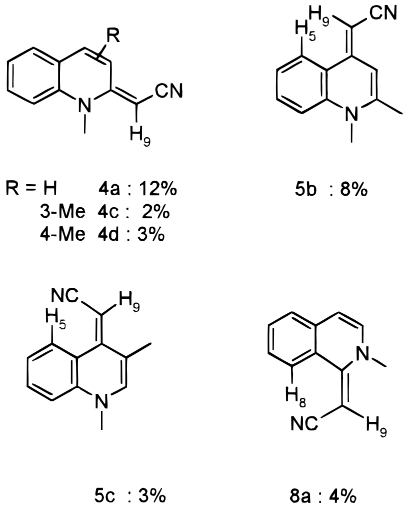
Table 1. Cyanomethylation of Quinolinium Iodides with TMSAN/CsF/CH$_3$CN

substrate	method[a]	time (h)	% of the crude **2**/**3**	yields (%) **2**	yields (%) **3**
1a	A	2	100/0	**2a**: 55	
	B	3.5	100/0	**2a**: 29	
1b	A	2	88/12	**2b**: 21	**3b**: 11
	B	2	74/26	**2b**: 29	**3b**: 14
1c	A	2	100/0	**2c**: 45	
	B	2	100/0	**2c**: 54	
1d	A	2	100/0	**2d**: 57	
	B	2	100/0	**2d**: 46	
1e	A	4			**3e**: 58
	B	4			**3e**: 52

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



R = H 4a : 12%
3-Me 4c : 2%
4-Me 4d : 3%

5b : 8%

5c : 3%

8a : 4%

Figure 1.

In an attempt to improve the yields, we increased the reaction time in the case of **1a**−**d** (3 h instead of 2). This was unsuccessful, but an additional more polar product was detected on TLC plate for the reactions conducted under sonochemical activation. It was isolated in low yields ranging from 2 to 12% by alumina column chromatography and identified to the *N*-methyl cyanoalkylidenedihydroquinolines **4**, **5**, **8** (Figure 1). Only traces of these products were detected at reflux. 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. Notable is the H$_9$ vinylic proton, which exhibits in each case a strongly shielded singlet sensitive to the regiochemistry (3.88−4.16 ppm in **4**; 4.39−4.66 ppm in **5**). The same is true for the C$_9$ methine carbon (58.8−60.1 ppm in **4**; 64.6−67 in **5**). A chemical shift calculation was performed in the case of **4a** using the TurboMole and TurboNMR softwares within the Insight package program.[7] Comparison of the calculated (H$_9$ 3.65; C$_9$ 67.86) and measured values (H$_9$ 3.89; C$_9$ 60.1) is in good agreement with the proposed structure. This oxidation probably starts with the abstraction of one of the methylene protons by the fluoride anion. Compounds **4**, **5**, and **8** are constituted by a single isomer, showing that the elimination process is stereoselective. The *E*/*Z* stereochemistry of the exocyclic double bond was assigned with the aid of 2D-NOESY experiments, showing the spatial relation depicted in Figure 1. The *E* configuration in compounds **4a**, **4c**, and **4d** was confirmed by the presence of a strong cross-peak H$_9$/NMe and H$_5$/H$_9$ in **5b**. In contrast, a cross-peak Me-3/H$_9$ demonstrates the *Z* configuration in **5c**. In the case of **5b**, this assignment was confirmed by the comparison of the ^{1}H and ^{13}C chemical shifts, in particular for H$_5$, H$_9$, and C$_9$ (7.66, 4.66, and 64.6 ppm) with those described for the *(E)*-4-cyanomethylidene-1,4-dihydro-1-methylquinoline (7.73, 4.8, and 67.4).[8] From these results, it seems that the elimination process is governed by steric factors, the cyano group lying away from the bulkier substituant, i.e., the *N*-methyl group in **4**, **5c**, and **8** and the aromatic ring in **5b**.

Table 2. Heat of Formation of the C-2/C-4 Adducts and C-2/C-4 Atomic Charges in Quinoliniums

R	heat of formation (kcal·mol^{-1}) of the adducts C-2	heat of formation (kcal·mol^{-1}) of the adducts C-4	atomic charges in quinolinium C-2	atomic charges in quinolinium C-4
H	58.4	50.0	0.189	0.141
2-Me	52.4	43.5	0.174	0.135
3-Me	49.9	41.6	0.195	0.145
4-Me	49.6	43.9	0.186	0.117

From a mechanistic point of view, these results are consistent with the formation of the cyanomethylene anion by nucleophilic attack at the silicon[9] and its addition to the ortho position versus nitrogen, which is the most electrophilic site (Table 2).[10] The regiospecificity 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 a competition between C-2 and C-4 additions.[11,12] In the particular case of cyanoalkyl groups, the addition always occurred at position 4.[1] It is worth noting that we never observed isomerization of the C-2 adducts during the reaction. Moreover, 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.[6] The C-2 adduct was obtained as the only product under sonochemical activation, while C-4 adducts was generally isolated at reflux. This behavior was interpreted as a thermodynamic process via the heterolytic dissociation of the C$_2$−C$'_1$ bond in the C-2 adducts,

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[7] Insight II. from MSI, San Diego. Calculations were performed during the 30 days grace delay. Optimization was performed at the Hartree−Fock level using double (DZ) or triple-ζ (TZ) basis. The best results were obtained with DZ unpolarized basis for ^{13}C and TZ unpolarized basis for ^{1}H.

(8) Levillain, J.; Vazeux, M. *Synthesis* **1995**, 56.

(9) It has been shown that TMSAN reacts with Bu$_4$NF to form pentacoordinated silycenium species, which can act as the cyanomethyl carbanion source. See: Adams, D. J.; Clark, J. H.; Hansen, L. B.; Sanders, V. C.; Tavener, S. *J. Fluor. Chem.* **1998**, *92*, 123.

(10) 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 cases of the C-2 adducts, the AM1 method was also used.

(11) For reviews, see: (a) Sidgewick, N. Y.; Sidgewick, F. R. S. *The Organic Chemistry of Nitrogen*; Clarendon Press: Oxford, 1966, p 718. (b) Dyke, S. F. *Adv. Heterocycl. Chem.* **1972**, *14*, 279. (c) Gurnos, J. *Quinolines*; Wiley: New York, **1982**.

(12) See, for example: (a) Leonard N. J.; Foster, R. L. *J. Am. Chem. Soc.* **1951**, *73*, 3325. *(b) ibid* **1952**, *74*, 2110. (c) Metzger, J.; Larivé, H.; Vincent, E.-J.; Dennilauler, R.; Baralle, R.; Gaurat, C. *Bull. Soc. Chim. Fr.* **1967**, 30. (d) Pilygun, G. T.; Gutsulyak, B. M. *Russ. Chem. Rev.*, **1963**, *32*, 167. (e) Bunting, J. W.; Meathrel, W. G. *Tetrahedron Lett.* **1971**, 133. (f) Fukuzumi, S.; Noura, S. *J. Chem. Soc., Chem. Commun.* **1994**, 287. (g) Maeda, M. *Chem. Pharm. Bull.* **1990**, *38*, 2577.

leading to an anion−quinolinium cation pair (Q$^+$, R$^-$). Calculation of the heats of formation of the carbonitrilemethylene derivatives showed that the C-4 regioisomer is in both cases the most stable (Table 2).[13] 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 isomerization. MNDO as well as AM1 calculations of the atomic charges for the C-2 adducts led to very similar electron distribution whatever 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 cyanomethyl group compare to trichloromethyl or acetonyl.

Experimental Section

Synthesis grade acetonitrile (Aldrich) was dried on molecular sieves. Commercial cesium and potassium fluoride (Aldrich, reagent ACS) was dried prior to use in a domestic microwave oven. Methiodides **1** and **6** were prepared according to literature procedures[13] by alkylation of the quinoline with methyl iodide in acetone solution. The mixture was maintained at room temperature until the substrate had completely reacted, as monitored by TLC (SiO$_2$; Et$_2$O/CH$_2$Cl$_2$, 30:70 v/v). The precipitated salts were filtered off and crystallized. Data for these compounds are identical to those in the literature.[14]

Flash column chromatography techniques (30 cm × 2 cm column) were employed to purify crude products using 70−230 mesh alumina (activity II−III, CH$_2$Cl$_2$) under positive air pressure. Ultrasound-promoted reactions were carried out in a common ultrasonic laboratory cleaner filled with thermostated water at 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. *J* values are reported in Hz. Elemental analyses were performed by Service Central d'Analyses du CNRS (F-69390 Vernaison).

Typical Procedure for Cyanomethylation. A mixture of quinolinium iodide (7.4 mmol), cesium fluoride (8.1 mmol), and TMSAN (8.1 mmol) in acetonitrile (20 mL) was stirred at reflux or sonicated at 0−5 °C until the starting material completely reacted as monitored by TLC (SiO$_2$, MeOH−Me$_2$CO, 10:90). The reaction mixture was filtered through Celite, and the filtrate was evaporated to dryness. The residue was taken up with 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 chromatographed eluting typically with CH$_2$Cl$_2$ (Al$_2$O$_3$, activity II−III, 70−230 mesh). Yields are given in Table 1. All the solid products were crystallized in C$_6$H$_{12}$/CH$_2$Cl$_2$ (95:5 v/v).

2-Cyanomethyl-1,2-dihydro-1-methylquinoline (2a): colorless liquid; R_f 0.63 (SiO$_2$,CHCl$_3$); δ_H 2.37 and 2.47 (2H, AB part of ABX syst, $J = 16.3$, 6.8, 5.5, CNCH$_2$), 3.01 (3H, s, NCH$_3$), 4.40 (1H, ddd, $J = 6.8$, 5.6, 5.5, H-2), 5.82 (1H, dd, $J = 9.6$, 5.6, H-3), 6.56 (1H, d, $J = 9.5$, H-4), 6.56 (1H, d, $J = 7.6$, H-8), 6.74 (1H, dd, $J = 7.5$, 7.4, H-6), 7.00 (1H, dd, $J = 7.4$, 1.4, H-5), 7.18 (1H, ddd, $J = 7.6$, 7.5, 1.4, H-7); δ_C 21.1 (CN*C*H$_2$), 37.1 (N*C*H$_3$), 57.5 (C-2), 111.4, 117.9, 121.3, 127.4, 127.7, 129.8 (CHsp^2), 117.7 ($C\equiv N$),122.0, 143.1 (Cq); MS *m/z* 184 (M$^+$, 5.8), 144 (M − CH$_2$CN, 100); IR (neat) ν_{max}/cm^{-1} 1640 (C=C), 2240 ($C\equiv N$). Anal. Calcd for C$_{12}$H$_{12}$N$_2$: C, 78.22; H, 6.57; N, 15.21. Found: C, 78.45; H, 6.62; N, 14.89.

2-Cyanomethyl-1,2-dihydro-1,2-dimethylquinoline (2b): colorless liquid; R_f 0.60 (SiO$_2$, CH$_2$Cl$_2$); δ_H 1.67 (3H, s, CH$_3$-2), 2.47 and 2.60 (2H, AB syst, d, $J = 16.4$, CNCH$_2$), 2.91 (3H, s, NCH$_3$), 5.56 (1H, d, $J = 9.7$, H-3), 6.49 (1H, d, $J = 9.7$, H-4), 6.62 (1H, d, $J = 8.2$, H-8), 6.73 (1H, dd, $J = 7.3$, 7.3, H-6), 6.99 (1H, d, $J = 7.3$, H-5), 7.15 (1H, dd, $J = 8.2$, 7.3, H-7); δ_C 26.6 (CH$_3$-2), 27.2 (CN*C*H$_2$), 31.0 (NCH$_3$), 57.7 (C-2), 111.5, 117.9, 126.9, 127.2, 127.3, 129.7 (CHsp^2), 116.5 ($C\equiv N$),120.2, 143.0 (Cq); MS *m/z* 198 (M$^+$, 3.6), 158 (M − CH$_2$CN, 100); IR (neat) ν_{max}/cm^{-1} 1635 (C=C), 2240 ($C\equiv N$). Anal. Calcd for C$_{13}$H$_{14}$N$_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.46; H, 7.01; N, 14.09.

2-Cyanomethyl-1,2-dihydro-1,3-dimethylquinoline (2c): colorless liquid; R_f 0.85 (SiO$_2$, CHCl$_3$); δ_H 1.99 (3H, d, $J = 1.4$, CH$_3$-3), 2.33 and 2.41 (2H, AB part of ABX syst., $J = 16.8$, 5.3, 6.1, CNCH$_2$), 3.08 (3H, s, NCH$_3$), 4.19 (1H, dd, $J = 6.1$, 5.3, H-2), 6.30 (1H, q, $J = 1.4$, H-4), 6.59 (1H, dd, $J = 8.1$, 0.9, H-8), 6.74 (1H, ddd, $J = 7.4$, 7.4, 0.9, H-6), 6.95 (1H, dd, $J = 7.4$, 1.4, H-5), 7.15 (1H, ddd, $J = 8.1$, 7.4, 1.4, H-7); δ_C 18.2 (CN*C*H$_2$), 21.1 (CH$_3$-3), 37.4 (NCH$_3$), 62.1 (C-2), 111.6, 118.1, 123.1, 126.4, 128.7 (CHsp^2), 118.8 ($C\equiv N$),122.4, 130.5, 141.5 (Cq); MS *m/z* 198 (M$^+$, 3.4), 158 (M − CH$_2$CN, 100); IR (neat) ν_{max}/cm^{-1} 2240 ($C\equiv N$). Anal. Calcd for C$_{13}$H$_{14}$N$_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.91; H, 7.23; N, 13.79.

2-Cyanomethyl-1,2-dihydro-1,4-dimethylquinoline (2d): pale yellow solid; mp 68 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$); R_f 0.75 (SiO$_2$, CHCl$_3$); δ_H 2.10 (3H, d, $J = 1.2$, CH$_3$-4), 2.27 and 2.38 (2H, AB part of ABX syst, $J = 16.3$, 6.9, 5.4, CNCH$_2$), 2.95 (3H, s, NCH$_3$), 4.27 (1H, ddd, $J = 6.9$, 5.7, 5.4, H-2), 5.66 (1H, qd, $J = 5.7$, 1.2, H-3), 6.56 (1H, dd, $J = 7.9$, 1.5, H-8), 6.80 (1H, ddd, $J = 7.5$, 7.5, 1.1, H-6), 7.19 (1H, dd, $J = 7.5$, 1.5, H-5), 7.21 (1H, ddd, $J = 7.9$, 7.5, 1.5, H-7); δ_C 18.9 (CH$_3$-4), 20.8 (CN*C*H$_2$), 37.0 (NCH$_3$), 57.3 (C-2), 111.5, 117.6, 119.3, 124.2, 129.5 (CHsp^2), 118.2 ($C\equiv N$),-121.1, 132.6, 143.2 (Cq); MS *m/z* 198 (M$^+$, 2.0), 158 (M − CH$_2$CN, 100); IR (neat) ν_{max}/cm^{-1} 1635 (C=C), 2240 ($C\equiv N$). Anal. Calcd for C$_{13}$H$_{14}$N$_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.59; H, 7.22; N, 13.76.

4-Cyanomethyl-1,4-dihydro-1,2-dimethylquinoline (3b): colorless liquid; R_f 0.56 (SiO$_2$, CH$_2$Cl$_2$); δ_H 1.97 (3H, d, $J = 0.9$, CCH$_3$), 2.32 (2H, d, $J = 6.6$, CNCH$_2$), 3.15 (3H, s, NCH$_3$), 3.74 (1H, dd, $J = 6.6$, 5.6, H-4), 4.59 (1H, dd, $J = 5.6$, 0.9, H-3), 6.81 (1H, d, *J* 8.1), 6.90−7.30 (3H, m). IR (neat) ν_{max}/cm^{-1} 1596, 1635 (C=C), 2240 ($C\equiv N$). Anal. Calcd for C$_{13}$H$_{14}$N$_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.49; H, 7.19; N, 13.78.

9-Cyanomethyl-9,10-dihydro-10-methylacridine (3e): colorless liquid; R_f 0.75 (SiO$_2$, CH$_2$Cl$_2$); δ_H 2.77 (2H, d, $J = 7.3$, CH$_2$), 3.70 (3H, s, NCH$_3$), 4.56 (1H, t, $J = 7.3$, H-9), 7.23 (4H, m), 7.58 (4H, m); δ_C 25.4 (CH$_2$), 33.11 (NCH$_3$), 40.99 (C-9), 112.6, 121.2, 128.9 (2) (CHsp^2), 123.8, 142.2 (Cq), 116.4 (CN); IR (neat) ν_{max}/cm^{-1} 1633, 1595 (C=C), 2193 (CN). Anal. Calcd for C$_{16}$H$_{14}$N$_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.20; H, 5.95; N, 11.70.

***(E)*-2-Cyanomethylidene-1,2-dihydro-1-methylquinoline (4a):** white solid; mp 88 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$); R_f 0.36 (SiO$_2$, CHCl$_3$); δ_H 3.26 (3H, s, NCH$_3$), 3.89 (1H, s, H-9), 7.00−7.50 (6H, m); δ_C 34.0 (N*C*H$_3$), 60.1 (CH-9), 113.3, 121.0, 122.1, 123.8, 128.6, 130.8, 132.0 (CHsp^2), 121.9, 123.8, 140.1, 154.4 (Cq); MS *m/z* 182 (M$^+$, 100); IR (neat) ν_{max}/cm^{-1} 2180 ($C\equiv N$). Anal. Calcd for C$_{12}$H$_{10}$N$_2$: C, 79.10; H, 5.53; N, 15.37. Found: C, 79.21; H, 5.43; N, 15.19.

(*E*)-2-Cyanomethylidene-1,2-dihydro-1,3-dimethylquinoline (4c): pale yellow solid; mp 91 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$); δ_H 2.08 (3H, s, CH$_3$-3), 3.91 (3H, s, NCH$_3$), 4.16 (1H, s, H-9), 7.01 (1H, s, H-4), 7.11 (1H, ddd, $J = 7.6$, 7.6, 0.9, H-6), 7.17 (1H, dd, $J = 8.5$, 0.9, H-8), 7.30 (1H, dd, $J = 7.6$, 1.5, H-5), 7.42 (1H, ddd, $J = 8.5$, 7.6, 1.5, H-7); δ_C 20.1 (CH$_3$-3), 40.1 (NCH$_3$), 59.5 (CH-9), 113.8, 122.3, 127.4, 129.8, 130.4 (CHsp^2), 122.5, 122.6, 129.5, 140.5, 155.2 (Cq); *m/z* 196 (M$^+$, 100); IR (neat) ν_{max}/cm^{-1} 2180 ($C\equiv N$). Anal. Calcd for C$_{13}$H$_{12}$N$_2$: C, 79.57; H, 6.16; N, 14.27. Found: C, 79.41; H, 6.23; N, 14.09.

(*E*)-2-Cyanomethylidene-1,2-dihydro-1,4-dimethylquinoline (4d): pale yellow solid; mp 158 °C (C$_6$H$_{12}$/CH$_2$Cl$_2$); R_f 0.5 (SiO$_2$, CH$_2$Cl$_2$); δ_H 2.34 (3H, s, CH$_3$-4), 3.34 (3H, s, NCH$_3$), 3.88 (1H, s, H-9), 7.02 (1H, s, H-3), 6.16 (1H, d, $J = 8.3$, H-8), 7.13 (1H, dd, $J = 7.8$, 7.8, H-6), 7.43 (1H, ddd, $J = 8.3$, 7.8, 1.5, H-7), 7.50 (1H, dd, $J = 7.8$, 1.5, H-5); δ_C 18.9 (CH$_3$-4), 34.0 (NCH$_3$), 58.8 (CH-9), 113.5, 120.2, 122.0, 125.0, 130.5 (CHsp^2), 122.4, 123.1, 139.1, 140.2, 154.5 (Cq); MS *m/z* 196 (M$^+$, 100); IR (neat) ν_{max}/cm^{-1} 2180 ($C\equiv N$). Anal. Calcd for C$_{13}$H$_{12}$N$_2$: C, 79.57; H, 6.16; N, 14.27. Found: C, 79.44; H, 6.21; N, 14.11.

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[13] 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.

[14] (a) Doebner, O.; Miller, W. *Ber.* **1883,** *16*, 2464. (b) Duffin, C. F. *Adv. Heterocycl. Chem.* **1964**, *3*, 1.

(*E*)-4-Cyanomethylidene-1,4-dihydro-1,2-dimethylquinoline (5b): colorless solid; mp 152 °C (C_6H_{12}/CH_2Cl_2); R_f 0.35 (SiO_2, CH_2Cl_2); δ_H 2.30 (3H, s, CH_3-2), 3.50 (3H, s, NCH_3), 4.66 (1H, s, H-9), 6.35 (1H, s, H-3), 7.13 (1H, ddd, $J = 8.2$, 8.1, 1.2, H-6), 7.20 (1H, dd, $J = 8.5$, 1.2, H-8), 7.46 (1H, ddd, $J = 8.5$, 8.2, 1.1, H-7), 7.66 (1H, dd, $J = 8.1$, 1.1, H-5); δ_C 21.7 (CH_3-2), 34.0 (NCH_3), 64.6 (CH-9), 106.4, 115.2, 123.1, 123.7, 131.2 ($CHsp^2$), 121.1, 122.8, 139.4, 143.6, 149.6 (Cq); MS *m/z* 196 (M^+, 100); IR (neat) ν_{max}/cm^{-1} 2180 (C≡N). Anal. Calcd for $C_{13}H_{12}N_2$: C, 79.57; H, 6.16; N, 14.27. Found: C, 79.63; H, 6.05; N, 14.05.

(*Z*)-4-Cyanomethylidene-1,4-dihydro-1,3-dimethylquinoline (5c): pale yellow solid; mp 148 °C (C_6H_{12}/CH_2Cl_2); R_f 0.1 (SiO_2, CH_2Cl_2); δ_H 1.91 (3H, s, CH_3-3), 3.56 (3H, s, NCH_3), 4.39 (1H, s, H-9), 6.72 (1H, s, H-2), 7.16 (1H, dd, $J = 8.6$, 1.2, H-8), 7.26 (1H, ddd, $J = 8.2$, 8.2, 1.2, H-6), 7.51 (1H, ddd, $J = 8.6$, 8.2, 1.5, H-7), 9.10 (1H, dd, $J = 8.2$, 1.5, H-5); δ_C 17.7 (CH_3-3), 40.1 (NCH_3), 67.0 (CH-9), 114.2, 122.9, 126.9, 130.6, 134.4 ($CHsp^2$), 112.3, 121.4, 148.8, 151.7 (Cq); MS *m/z* 196 (M^+, 100); IR (neat) ν_{max}/cm^{-1} 2180 (C≡N). Anal. Calcd for $C_{13}H_{12}N_2$: C, 79.57; H, 6.16; N, 14.27. Found: C, 79.49; H, 6.23; N, 14.05.

1-Cyanomethyl-1,2-dihydro-2-methylisoquinoline (7a): liquid; R_f 0.59 (SiO_2, CH_2Cl_2); δ_H 2.46 and 2.63 (2H, AB part of ABX syst, $J = 16.4$, 6.7, 6.1, $CNCH_2$), 3.02 (3H, s, NCH_3), 4.69 (1H, dd, $J = 6.7$, 6.1, H-1), 5.40 (1H, d, $J = 7.3$, H-3), 6.04 (1H, d, $J = 7.3$, H-4), 6.90−7.40 (4H, m); δ_C 19.2 ($CNCH_2$), 40.9 (NCH_3), 59.4 (C-1), 98.3, 125.3, 126.0, 126.2, 132.0, 135.2 ($CHsp^2$), 118,7, 126.9, 132.1 (Cq); MS *m/z* 184 (M^+, 8.9), 144 (M − CH_2CN, 100); IR (neat) ν_{max}/cm^{-1} 1625 (C═C), 2320 (C≡N). Anal. Calcd for $C_{13}H_{12}N_2$: C, 79.57; H, 6.16; N, 14.27. Found: C, 79.41; H, 6.05; N, 14.38.

6-Cyanomethyl-5,6-dihydro-5-methylphenanthridine (7b): oil; R_f 0.85 (SiO_2, CH_2Cl_2); δ_H 2.38 and 2.60 (2H, AB part of ABX syst., $J = 16.4$, 7.6, 5.7, CH_2), 3.17 (3H, s, NCH_3), 4.71 (1H, dd, $J = 7.6$, 5.7, H-6), 6.77 (1H, d, $J = 8.1$), 6.93 (1 H, t, $J = 7.0$), 7.30−7.46 (4H, m), 7.79 (1 H, d, $J = 7.75$); δ_C 19.6 (CH_2), 37.8 (NCH_3), 61.2 (C-6), 113.6, 119.2, 123.0, 123.6, 126.3, 127.5, 128.8, 129.8 ($CHsp^2$), 118.4, 121.7, 130.4, 132.8 142.4 (Cq). IR (neat) ν_{max}/cm^{-1} 1604 (C═C), 2248 (C≡N). Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.19; H, 5.99; N, 11.75.

(*E*)-1-Cyanomethylidene-1,2-dihydro-2-methylisoquinoline (8a): yellow solid; mp 78 °C (C_6H_{12}/CH_2Cl_2); R_f 0.5 (SiO_2, CH_2Cl_2); δ_H 2.28 (3H, s, NCH_3), 4.01 (1H, s, H-9), 6.70 (1H, d, $J = 7.3$, H-3), 6.15 (1H, d, $J = 7.3$, H-4), 6.90−7.50 (3H, m), 9.10 (d, 1H, $J = 8.2$, H-8); δ_C 42.5 (NCH_3), 57.0 (CH-9), 106.3, 126.2, 126.6, 126.9, 131.2, 133.5 ($CHsp^2$), 123.5, 125.2, 133.7, 152.9 (Cq); *m/z* 182 (M^+, 100). Anal. Calcd for $C_{12}H_{10}N_2$: C, 79.10; H, 5.53; N, 15.37. Found: C, 79.21; H, 5.39; N, 15.21.

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