Enaminones Acylation: Competitive Formation of Quinolin-4-one and Isoquinolin-1-one Derivatives

Magali Valès, Vladimir Lokshin, Gérard Pèpe, André Samat,* Robert Guglielmetti

Université de la Méditerranée, Faculté des Sciences de Luminy, UMR 6114 CNRS Case 901, 13288 Marseille Cedex 9, France
Fax +33(4)91829301; E-mail: samat@luminy.univ-mrs.fr

Received 27 July 2001; revised 27 September 2001

Abstract: The reaction of enaminones with some *o*-halogenobenzoyl chlorides allows the preparation of 3-acyl-2-alkylquinolin-4-one and/or 4-acyl-3-alkylisoquinolin-1-one derivatives depending on the structure of the starting materials. Due to their easy availability the compounds prepared are attractive precursors for further synthesis of polycondensed heterocycles.

Key words: acylation, enaminones, heterocycles, quinolines, isoquinolines

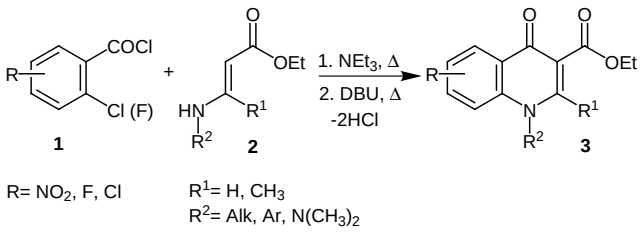
The β-enaminones (or β-keto enamines) defined by Greenhill[1] as monoenamines of 1,3-diketones or 3-keto esters are an important class of organic synthetic intermediates. These highly reactive compounds usually react as ambident nucleophiles at the nitrogen or (and) C_α-atom.

Application of enaminones as synthetic intermediates especially in heterocyclic chemistry is well documented.[2] One illustration is the approach to the pharmacologically important 4-quinolone-3-carboxylic esters elaborated by Grohe et al.[3,4] (Scheme 1).

In this reaction, the first step is a selective C_α-acylation of the enamino ester **2** (for instance the acylated product can be isolated for R^1 = H), followed by the nucleophilic substitution of the halogen atom which is activated by the presence of electron-withdrawing groups on the aromatic ring.[3,4] Recently this approach has been used to prepare heterocyclic compounds such as **3** in which R^1 = Ar.[5]

We decided to extend the field of application of this reaction, using enaminones obtained from 1,3-diketones. Results of our study are reported in this paper.

The reaction of 2,4,5-trifluorobenzoyl chloride (**4a**) or 2-chloro-5-nitrobenzoyl chloride (**4b**) with a set of enaminones **5** was investigated using experimental conditions described in reference[5] which are very close to those previously reported by Grohe et al.[3,4] By refluxing the enaminone with the acid chloride in the presence of triethylamine in toluene for 3 hours followed by the addition of excess of DBU and further heating, the products formed are separated and purified by column chromatography. Under these conditions, besides the expected 3-acyl-2-alkylquinolin-4-ones **6** which can be compared to **3** (Scheme 1), the 4-acyl-3-alkylisoquinolin-1-ones **7** originating from N-acylation of the enaminones (Scheme 2, Table 1) have also been isolated in some cases depending on the molecular structure of the reagents.



Scheme 1

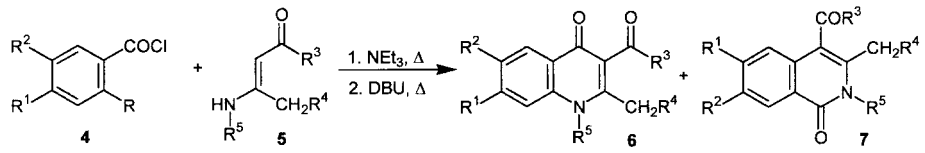
Table 1 Products Formed in the Reaction of **4** with **5**

Entry	**1**	**2**	Products, Yield (%)[a]		
			6	**7**	Others
1	**4a**	**5a**	–[b]		**8** (68)
2	**4a**	**5b**	**6ab** (10)	–	–
3	**4a**	**5c**	**6ac** (34)	–	–
4	**4a**	**5d**	**6ad** (36)	–	–
5	**4a**	**5e**	**6ae** (37)	–	–
6	**4a**	**5f**	**6af** (41)	–	–
7	**4a**	**5g**	**6ag** (19)	–	**9** (17)
8	**4a**	**5h**	**6ah** (32)	–	–
9	**4b**	**5a**	–	**7ba** (71)	–
10	**4b**	**5b**	–	**7bb** (68)	–
11	**4b**	**5c**	–	**7bc** (70)	–
12	**4b**	**5d**	**6bd** (26)	**7bd** (52)	–
13	**4b**	**5e**	**6be** (23)	**7be** (54)	–
14	**4b**	**5f**	**6bf** (40)	**7bf** (14)	–
15	**4b**	**5g**	–	**7bg** (51)	–
16	**4b**	**5h**	–	**7bh** (32)	–

[a] Yield for isolated products.
[b] Not observed.

Synthesis 2001, No. 16, 30 11 2001. Article Identifier:
1437-210X,E;2001,0,16,2419,2426,ftx,en;Z08801SS.pdf.

ISSN 0039-7881



4	R	R^1	R^2
a	F	F	F
b	Cl	H	NO_2

5	R^3	R^4	R^5
a	CH_3	H	n-Pr
b	CH_3	H	Ph
c	Ph	H	n-Pr
d	Ph	H	Ph
e	Ph	Ph	n-Pr
f	Ph	Ph	Ph
g	Ph	H	NMe_2
h	Ph	Ph	NMe_2

Scheme 2

The molecular structure of compounds **6** and **7** have been confirmed by ^{1}H and ^{13}C NMR spectroscopy and elemental analyses (Table 2). Although compounds **6** and **7** have similar ^{1}H NMR spectra, these two structures can be easily differentiated on the basis of the ^{13}C NMR chemical shift of the endocyclic carbonyl group (δ = 173.5–175.5 and 161.0–163.3 for **6** and **7**, respectively). For one compound of each kind (**6bd** and **7bc**), the molecular structure has been confirmed by X-ray cristallography (Figures 1 and 2).

In two cases, compounds having a molecular structure different from that of **6** and **7** have been identified. Especially, the reaction of the acid chloride **4a** with the enaminone **5a** (Table 1, entry 1) leads to N-acylation of the enaminone, the resulting compound **8** being not able to cyclize to **7aa** under the conditions used. This cyclization can be achieved subsequently with sodium hydride in THF as solvent (Scheme 3).

During the reaction of the same acid chloride **4a**, but with the *N*,*N*-dimethylhydrazino derivative of the benzoylacetone **5g** (Table 1, entry 7), another byproduct has been isolated besides the expected quinolone **6ag**. ^{1}H and ^{13}C NMR data as well as crystallographic analysis (Figure 3) allowed to identify this compound as the *N*,*N*-dimethylhydrazine of 3-acetyl-6,7-difluoroflavone **9**.

The existence of a tautomeric equilibrium from the C-acylated intermediate A (Scheme 4) can explain the formation of **9**.

Indeed, according to numerous studies devoted to the tautomerism of nitrogenated derivatives of 1,3-diketones, changing the amino fragment of an enaminone to a *N*,*N*-dimethylhydrazine one, favors unambiguously such an equilibrium.[6,7]

The data gathered in Table 1 show moderate yields of **6** and **7**. This result is certainly due to the weak reactivity of enaminones rather than the formation of byproducts. Indeed variable amounts of starting enaminones have often been isolated during liquid chromatography purification. This behavior has been reported by Cecchetti et al.[5]

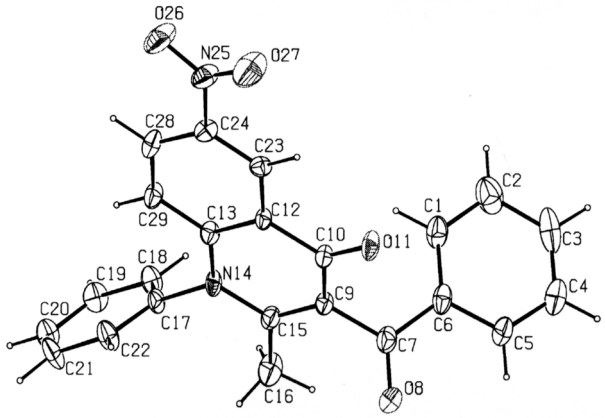


Figure1 Molecular structure of compound **6bd**

Several remarks can be made about the influence of the structure of starting reagents on the course of the reaction. First, the significant influence of the nature of the acid chloride can be highlighted. For instance, while com-

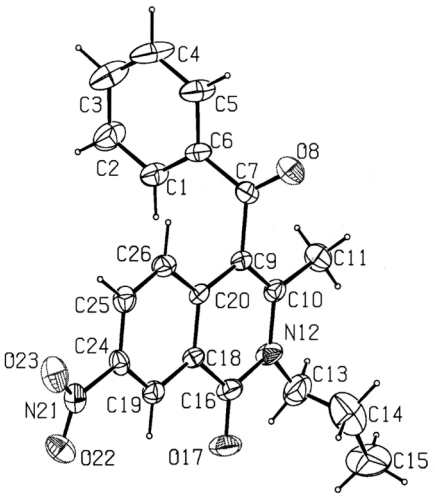
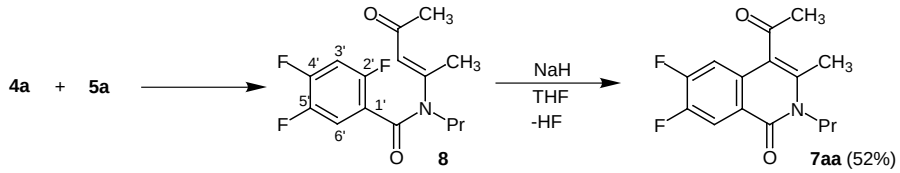
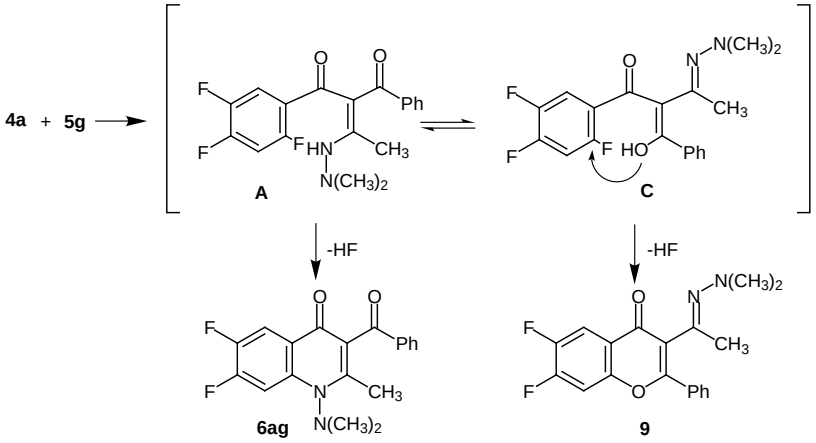


Figure 2 Molecular structure of compound **7bc**



Scheme 3



Scheme 4

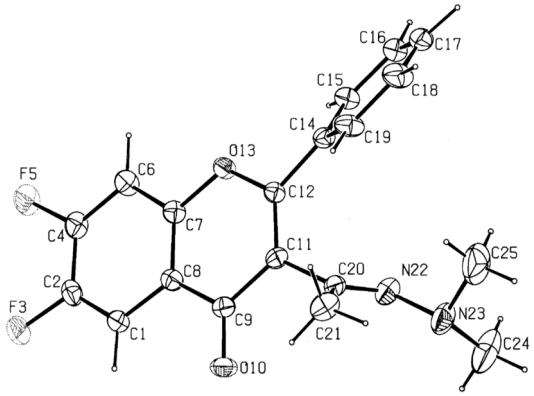


Figure 3 Molecular structure of compound **9**

pound **4a** leads exclusively to quinolones **6**, acid chloride **4b** favors unambiguously the formation of **7**. One can make the assumption that, when **4a** is used, even if the N-acylation reaction is possible (see example of compound **8**), the nucleophilic character of the C_α-atom of the enaminone is not sufficient enough to promote (in the chosen experimental conditions) the substitution of the fluorine atom, itself weakly activated compared to the chlorine atom in the case of compound **4b**.

Secondly, the structure of the enaminone plays also an important role. Indeed, using the same acid chloride **4b**, changing amino esters **2** (Scheme 1) by enamino ketones, modifies completely the direction of the reaction (Table 1, entries 9–16). It clearly appears that the nucleophilic character of the α-carbon atom is weaker for enamino ketones than for enamino esters. This phenomenon, previously observed, is explained by the decrease of the negative charge on this carbon atom due to a higher electron-withdrawing effect of the ketonic carbonyl compared to the carbonyl group of the ester.[8,9]

Finally, the effect of the nature of the amino fragment of enamino ketones has to be taken into account. For instance, the reactivity of the nitrogen atom of compounds (**5b**, **5d**, **5f**), including a *N*-Ph group is weaker than the reactivity of the same atom in molecules bearing a *N*-Pr group. This lower reactivity allows the C_α-acylation followed by cyclization to quinolones, even for acid chloride **4b** which favors generally the N-acylation reaction and the formation of isoquinolones (Table 1, entries 12,14).

In this context, the very low yield observed for the formation of compound **6ab** (C_α- and N-positions on the corresponding enaminone **5b** are unactivated) and the formation of compound **8** (the C_α-position of the enaminone **5a** is unactivated but not the N-position) can be easily explained.

Thus the described method allows the preparation of two different families of functionalized heterocycles depending on the structure of the starting reagents. Despite the moderate yield, the simplicity of this method and the easy accessibility of the precursors make this reaction highly attractive, especially in the frame of polycondensed heterocyclic systems.

Table 2 Physical and Spectroscopic Data of Compounds **6** and **7**[a]

Product	Mp (°C)	R_f[b]	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ, J (Hz)
6ab	132–133	0.1	2.12 (s, 3 H, CH_3), 2.66 (s, 3 H, $COCH_3$), 6,45 (dd, 1 H, *J* = 11.7, 6.5, H-8), 7.33 (m, 2 H, NC_6H_5), 7.70 (m, 3 H, NC_6H_5), 8.13 (dd, 1 H, *J* = 9.0, 9.1)	19.8 (CH_3), 32.4 ($COCH_3$), 107.0 (d, $^2J_{CF}$ = 39.4, C-8), 113.8 (d, $^2J_{CF}$ =18.4, C-5), 123.1 (d, $^3J_{CF}$ = 3.5, C-4a), 123.7 (C-3), 128.8 (CH), 130.7 (CH), 131.3 (CH), 138.6 (CN), 139.2 (d, $^3J_{CF}$ = 9.1, C-8a), 148.0 (q, $^1J_{CF}$ = 252.3, $^2J_{CF}$ = 11.3, C-6), 151.6 (C-2), 153.0 (q, $^1J_{CF}$ = 255.0, $^2J_{CF}$ = 15.2, C-7), 174.2 (CO), 203.7($COCH_3$)
6ac	162–163	0.26	0.93 (t, 3 H, *J* = 7.2, $CH_2CH_2CH_3$), 1.67 (m, 2 H, $CH_2CH_2CH_3$), 2.24 (s, 3 H, CH_3), 3.94(t, 2 H, *J* = 8.0, $CH_2CH_2CH_3$), 7.21–7.30 (m, 3 H, H-8 and H of COC_6H_5), 7.37 (m, 1 H, H of COC_6H_5), 7.74 (m, 2 H , H of COC_6H_5), 7.89 (dd, 1 H, *J* = 9.3, 9.2, H-5)	10.9 ($CH_2CH_2CH_3$), 18.4 (CH_3), 21.9 ($CH_2CH_2CH_3$), 49.1 ($CH_2CH_2CH_3$), 105.4 (d, $^2J_{CF}$ = 22.9, C-8), 113.8 (d, $^2J_{CF}$ = 17.9, C-5), 122.5 (C-3), 123.7 (d, $^3J_{CF}$ = 6.3, C-4a), 128.7 (CH), 129.3 (CH), 133.6 (CH), 137.4 (C), 137.6 (d, $^3J_{CF}$ = 8.3, C-8a), 147.6 (q, $^1J_{CF}$ = 248.0, $^2J_{CF}$ = 13.5, C-6), 149.6 (C-2), 153.5 (q, $^1J_{CF}$ = 252.8, $^2J_{CF}$ = 14.7, C-7), 173.6 (CO), 196.8 (*C*OPh)
6ad	163–164	0.3	2.01 (s, 3 H, CH_3), 6.53 (dd, 1 H, *J* = 13.8, 6.5, H-8), 7.31 (m, 2 H, NC_6H_5), 7.44 (m, 2 H, COC_6H_5), 7.56 (m, 1 H, COC_6H_5), 7.69 (m, 3 H, NC_6H_5), 7.96 (m, 2 H, COC_6H_5), 8.11 (dd, 1 H, *J* = 10.1, 10.0, H-5)	19.6 (CH_3), 107.0 (d, $^2J_{CF}$ = 22.9, C-8), 113.7 (d, $^2J_{CF}$ = 17.9, C-5), 122.2 (C-3), 122.8 (d, $^3J_{CF}$ = 3.8, C-4a), 128.7 (CH), 128.8 (CH), 129.5 (CH), 130.6 (CH), 131.2 (CH), 133.6 (CH), 137.5 (NC), 138.2 (C), 139.5 (d, $^3J_{CF}$ = 9.4, C-8a), 147.9 (q, $^1J_{CF}$ = 252.7, $^2J_{CF}$ = 16.0, C-6), 150.2 (C-2), 153.2 (q, $^1J_{CF}$ = 254.3, $^2J_{CF}$ = 15.7, C-7), 174.1 (CO), 196.4 (*C*OPh)
6ae	149–150	0.53	0.90 (t, 3 H, *J* = 7.4, $CH_2CH_2CH_3$), 1.58 (m, 2 H, $CH_2CH_2CH_3$), 3.95 (t, 2 H, *J* = 7.8, $CH_2CH_2CH_3$), 4.05 (s, 2 H, CH_2), 7.25–7.34 (m, 6 H, H-8 and $CH_2C_6H_5$), 7.39 (m, 2 H, COC_6H_5), 7.51 (m, 1 H, COC_6H_5), 7.90 (m, 2 H, COC_6H_5), 8.20 (dd, 1H, *J* = 9.4, 9.3, H-5)	10.8 ($CH_2CH_2CH_3$), 21.8 ($CH_2CH_2CH_3$), 37.5 (CH_2), 49.2 ($CH_2CH_2CH_3$), 105.1 (d, $^2J_{CF}$ = 23.8, C-8), 114.4 (d, $^2J_{CF}$ = 16.6, C-5), 124.0 (d, $^3J_{CF}$ = 4.9, C-4a), 127.4 (CH), 128.1 (CH), 128.3 (C-3), 128.6 (CH), 129.1 (CH), 129.4 (CH), 133.5 (CH), 135.4 (C), 137.3 (C), 137.8 (d, $^3J_{CF}$ = 9.3, C-8a), 147.9 (q, $^1J_{CF}$ = 250.5, $^2J_{CF}$= 13.0, C-6), 150.4 (C-2), 153.9 (q, $^1J_{CF}$= 254.0, $^2J_{CF}$ = 14.5, C-7), 174.2 (CO), 196.2 (*C*OPh)
6af	171–172	0.45	3.79 (s, 2 H, CH_2), 6.42 (dd, 1 H, *J* = 12.0, 6.4, H-8), 6.74 (m, 2 H, NC_6H_5), 6.93 (m, 2 H, $CH_2C_6H_5$), 7.05 (m, 3 H, $CH_2C_6H_5$), 7.37–7.45 (m, 5 H, NC_6H_5 and COC_6H_5), 7.54 (m, 1 H, COC_6H_5), 7.96 (m, 2 H, COC_6H_5),8.19 (dd, 1 H, *J* = 8.9, 8.8, H-5)	37.7 (CH_2), 106.8 (d, $^2J_{CF}$ = 22.2, C-8), 113.7 (d, $^2J_{CF}$ = 18.5, C-5), 122.8 (d, $^3J_{CF}$ = 4.5, C-4a), 123.6 (C-3), 126.8 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 129.2 (CH), 129.5 (CH), 130.1 (CH), 133.4 (CH), 135.7 (C), 137.39 (NC), 137.45 (C), 139.8 (d, $^3J_{CF}$ =9.5, C-8), 148.1 (q, $^1J_{CF}$ = 250.5, $^2J_{CF}$ = 13.6, C-6), 151.5 (C-2), 153.2 (q, $^1J_{CF}$ = 255.2, $^2J_{CF}$ = 15.6, C-7), 174.6 (CO), 195.8 (*C*OPh)
6ag	188	0.29	2.27 (s, 3 H, CH_3), 3.01 [s, 6 H, $N(CH_3)_2$], 7.29 (m, 2 H, COC_6H_5), 7.42 (m, 2 H, H-8 and COC_6H_5), 7.79 (m, 2 H, COC_6H_5), 7.97 (dd, 1 H, *J* = 9.3, 9.2, H-5)	17.1 (CH_3), 43.5 [$N(CH_3)_2$], 105.5 (d, $^2J_{CF}$ = 23.2, C-8), 114.6 (d, $^2J_{CF}$ = 20.2, C-5), 122.2 (C-3), 123.8 (d, $^3J_{CF}$ = 4.1, C-4a), 128.9 (CH), 129.5 (CH), 133.7 (CH), 137.4 (C), 138.5 (d, $^3J_{CF}$ = 8.7, C-8a), 148.2 (q, $^1J_{CF}$ =246.3, $^2J_{CF}$ = 13.2, C-6), 153.7 (q, $^1J_{CF}$ = 258.6, $^2J_{CF}$ = 16.2, C-7), 153.8 (C-2), 173.5 (CO), 196.2 (*C*OPh)
6ah	161–162	0.33	2.63 [s, 6 H, $N(CH_3)_2$], 3.80 (s, 2 H, CH_2), 7.06 (m, 6 H, H-8 and $CH_2C_6H_5$), 7.22 (m, 2 H, COC_6H_5), 7.34 (m, 1 H, COC_6H_5), 7.69 (m, 2 H, COC_6H_5), 8.00 (dd, 1H, *J* = 9.2, 9.1, H-5)	41.4 (CH_2), 43.3 [$N(CH_3)_2$], 104.5 (d, $^2J_{CF}$ = 23.0, C-8), 115.7 (d, $^2J_{CF}$ = 23.9, C-5), 124.1 (d, $^3J_{CF}$ = 4.7, C-4a), 125.1 (C-3), 127.7 (CH), 128.1 (CH), 128.6 (CH),129.0 (CH), 130.6 (CH), 133.7 (CH), 135.9 (C), 136.6 (C), 137.3 (d, $^3J_{CF}$ = 8.9, C-8a), 147.6 (q, $^1J_{CF}$ = 214.0, $^2J_{CF}$ = 12.1, C-6), 151.6 (C-2), 153.0 (q, $^1J_{CF}$ = 254.4, $^2J_{CF}$ = 13.7, C-7), 174.6 (CO), 194.1 (*C*OPh)
6bd	217–218	0.13	1.93 (s, 3 H, CH_3), 6.75 (d, 1 H, *J* = 9.4, H-8), 7.28–7.43 (m, 4 H, NC_6H_5 and COC_6H_5), 7.45 (m, 1 H, COC_6H_5), 7.57 (m, 3 H, NC_6H_5), 7.84 (m, 2 H, COC_6H_5), 8.06 (dd, 1 H, *J* = 9.4, 2.7, H-7), 9.06 (d, 1 H, *J* = 2.7, H-5)	19.1 (CH_3), 119.6 (C-8), 122.8 (C-7), 123.8 (C-4a), 125.2 (C-3), 126.2 (C-5), 128.7 (CH), 128.9 (CH), 129.5 (CH), 130.8 (CH), 131.3 (CH), 133.9 (CH), 137.1 (C), 137.9 (C), 143.5 (C-6), 145.7 (C-8a), 150.8 (C-2), 174.7 (CO), 195.7 (*C*OPh)

Table 2 Physical and Spectroscopic Data of Compounds **6** and **7**[a] (continued)

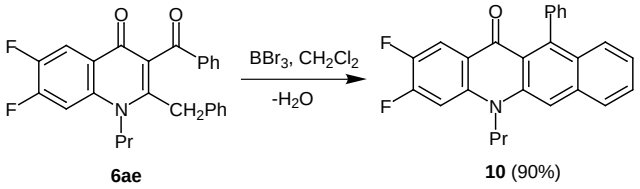
Product	Mp (°C)	R_f[b]	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ, J (Hz)
6be	141–142	0.4	0.80 (t, 3 H, *J* = 7.3, $CH_2CH_2CH_3$), 1.46 (m, 2 H, $CH_2CH_2CH_3$), 4.02 (m, 4 H, $CH_2CH_2CH_3$ and CH_2), 7.17 (m, 5 H, $CH_2C_6H_5$), 7.25 (m, 2 H, COC_6H_5), 7.41 (m, 1H, COC_6H_5), 7.55 (d, 1 H, *J* = 9.5, H-8), 7.78 (m, 2H, COC_6H_5), 8.29 (dd, 1 H, *J* = 9.4, 2.7, H-7), 9.10 (d, 1 H, *J* = 2.7, H-5)	11.0 ($CH_2CH_2CH_3$), 22.2 ($CH_2CH_2CH_3$), 37.9 (CH_2), 49.5 ($CH_2CH_2CH_3$), 118.2 (C-8), 123.6 (C-4a), 125.9 (C-3), 126.6 (C-7), 126.9 (C-5), 127.8 (CH), 128.4 (CH), 128.9 (CH), 129.5 (CH), 129.7 (CH), 134.0 (CH), 135.2 (C), 137.1 (C), 143.6 (C-6), 144.5 (C-8a), 151.3 (C-2), 175.4 (CO), 195.8 (*C*OPh)
6bf	208–209	0.29	3.82 (s, 2 H, CH_2), 6.75 (m, 3 H, H-8 and NC_6H_5), 6.95 (m, 2 H, $CH_2C_6H_5$), 7.06 (m, 3 H, $CH_2C_6H_5$), 7.42 (m, 4 H, NC_6H_5 and COC_6H_5), 7.53 (m, 2 H, COC_6H_5), 7.99 (m, 2 H, COC_6H_5), 8.16 (m, 1 H, H-7), 9.22 (m, 1 H, H-5)	38.1 (CH_2), 119.8 (C-8), 123.1 (C-4a), 125.5 (C-3), 126.5 (C-7), 127.2 (C-5), 128.7 (CH), 128.9 (CH), 129.4 (CH), 129.7 (CH), 130.5 (CH), 134.0 (CH), 135.5 (C), 137.2 (NC), 137.3 (C), 143.6 (C-6), 146.2 (C-8a), 152.4 (C-2), 175.5 (CO), 195.5 (*C*OPh)
7ba	101–102	0.28	1.05 (t, 3 H, *J* = 7.4, $CH_2CH_2CH_3$), 1.78 (m, 2 H, $CH_2CH_2CH_3$), 2.49 (s, 3 H, CH_3), 2.65 (s, 3 H, $COCH_3$), 4.10 (t, 2 H, *J* = 7.7, $CH_2CH_2CH_3$), 7.40 (d, 1 H, *J* = 9.0, H-5), 8.33 (dd, 1 H, *J* = 9.0, 2.2, H-6), 9.10 (d, 1 H, *J* = 2.1, H-8)	11.4 ($CH_2CH_2CH_3$), 17.9 (CH_3), 21.9 ($CH_2CH_2CH_3$), 33.2 ($COCH_3$), 46.3 ($CH_2CH_2CH_3$), 118.8 (C-4), 124.0 (C-8a), 124.2 (C-8), 124.6 (C-6), 126.4 (C-5), 137.4 (C-4a), 140.9 (C-7), 145.4 (C-3), 161.0 (CO), 203.3 ($COCH_3$)
7bb	196–197	0.26	2.04 (s, 3 H, CH_3), 2.65 (s, 3 H, $COCH_3$), 7.27 (m, 2 H, NC_6H_5), 7.43–7.60 (m, 4 H, H-5 and NC_6H_5), 8.38 (dd, 1 H, *J* = 8.9, 2.4, H-6), 9.09 (d, 1 H, *J* = 2.4, H-8)	19.5 (CH_3), 33.1 ($COCH_3$), 118.6 (C-4), 124.5 (C-8), 124.6 (C-8a), 124.7 (C-6), 126.9 (C-5), 128.1 (CH), 129.4 (CH), 130.1 (CH), 137.6 (C), 138.0 (C-4a),141.5 (C-7), 145.6 (C-3), 161.4 (CO), 202.9 ($COCH_3$)
7bc	157	0.33	1.08 (t, 3 H, *J* = 7.3, $CH_2CH_2CH_3$), 1.80 (m, 2 H, $CH_2CH_2CH_3$), 2.36 (s, 3 H, CH_3), 4.14 (t, 2 H, *J* = 7.3, $CH_2CH_2CH_3$), 7.28 (d, 1 H, *J* = 9.0, H-5), 7.51 (m, 2 H, COC_6H_5), 7.67 (1 H, m, COC_6H_5), 7.91 (m, 2 H, COC_6H_5), 8.23 (dd, 1 H, *J* = 9.0, 2.3, H-6), 9.24 (d, 1 H, *J* = 2.3, H-8)	11.4 ($CH_2CH_2CH_3$), 18.6 (CH_3), 22.0 ($CH_2CH_2CH_3$), 46.3 ($CH_2CH_2CH_3$), 115.7 (C4), 124.1 (C-8a), 124.7 (C-8), 125.2 (C-6), 126.4 (C-5), 129.3 (CH), 129.8 (CH), 134.7 (CH), 137.2 (C), 138.8 (C-4a), 142.2 (C-7), 145.6 (C-3), 161.3 (CO), 195.9 (*C*OPh)
7bd	120–121	0.3	1.92 (s, 3 H, CH_3), 7.2 (m, 2 H, NC_6H_5), 7.32 (d, 1 H, *J* = 9.0, H-5), 7.49–7.58 (m, 5 H, NC_6H_5 and COC_6H_5), 7.67 (m, 1 H, COC_6H_5), 7.96 (m, 2 H, COC_6H_5), 8.29 (dd, 1 H, *J* = 9.0, 2.4, H-6), 9.21 (d, 1 H, *J* = 2.4, H-8)	20.0 (CH_3), 115.5 (C-4), 124.6 (C-8a), 124.7 (C-8), 125.3 (C-6), 126.8 (C-5), 128.1 (CH), 129.3 (CH), 129.4 (CH), 129.7 (CH), 130.1 (CH), 134.7 (CH), 137.0 (C), 137.5 (C), 139.4 (C-4a), 142.7 (C-7), 145.7 (C-3), 161.6 (CO), 195.5 (*C*OPh)
7be	125–126	0.63	0.76 (t, 3 H, *J* = 7.2, $CH_2CH_2CH_3$), 1.43 (m, 2 H, $CH_2CH_2CH_3$), 3.85 (m, 4-H, $CH_2CH_2CH_3$ and CH_2), 7.08 (m, 5 H, $CH_2C_6H_5$), 7.16 (d, 1 H, *J* = 8.9, H-5), 7.29 (m, 2 H, COC_6H_5), 7.45 (m, 1 H, COC_6H_5), 7.75 (m, 2 H, COC_6H_5), 8.08 (dd, 1 H, *J* = 8.9, 2.4, H-6), 9.10 (d, 1 H, *J* = 2.3, H-8)	11.4 ($CH_2CH_2CH_3$), 22.0 ($CH_2CH_2CH_3$), 37.5 (CH_2), 46.8 ($CH_2CH_2CH_3$), 117.6 (C-4), 124.7 (C-8), 125.7 (C-6), 126.5 (C-5), 127.5 (C-8a), 128.1 (CH), 129.2 (CH), 129.3 (CH), 129.9 (CH), 134.8 (CH), 135.8 (C), 137.1 (C), 138.9 (C-4a), 143.6 (C-7), 145.9 (C-3), 161.7 (CO), 195.7 (*C*OPh)
7bf	144–146	0.69	3.52 (s, 2 H, CH_2), 6.49 (m, 2 H, NC_6H_5), 6.72 (m, 2 H, $CH_2C_6H_5$), 6.87 (m, 3 H, $CH_2C_6H_5$), 7.12 (m, 3 H, NC_6H_5), 7.21 (d, 1 H, *J* = 9.0, H-5), 7.31 (m, 2 H, COC_6H_5), 7.47 (m, 1 H, COC_6H_5), 7.75 (m, 2 H, COC_6H_5), 8.13 (dd, 1 H, *J* = 9.0, 2.7, H-6), 9.05 (d, 1 H, *J* = 2.4, H-8)	38.7 (CH_2), 118.0 (C-4), 125.6 (C-8), 125.9 (C-6), 126.7 (C-5), 127.7 (C-8a), 127.8 (CH), 129.0 (CH), 129.1 (CH), 129.6 (CH), 129.8 (CH), 130.0 (CH), 130.1 (CH), 130.7 (CH), 135.6 (CH), 136.2 (C), 137.7 (C), 137.9 (C), 140.2 (C-4a), 145.1 (C-7), 146.9 (C-3), 162.8(CO), 196.1 (*C*OPh)
7bg	163–164	0.45	2.31 (s, 3 H, CH_3), 3.12 [s, 6 H, $N(CH_3)_2$], 7.33 (d, 1H, *J* = 9.0, H-5), 7.52 (m, 2 H, COC_6H_5), 7.69 (m, 1 H, COC_6H_5), 7.99 (m, 2 H, COC_6H_5), 8.30 (dd, 1 H, *J* = 8.9, 2.4, H 6), 9.07 (d 1 H, *J* = 2.2, H-8)	18.3 (CH_3), 42.9 [$N(CH_3)_2$], 115.2 (C-4), 124.1 (C-8), 125.8 (C-6), 126.7 (C-8a), 126.8 (C-5), 129.8 (CH), 130.3 (CH), 134.9 (CH), 138.1 (C), 139.6 (C-4a), 145.8 (C-7), 147.3 (C-3), 161.4 (CO), 195.4 (*C*OPh)

Table 2 Physical and Spectroscopic Data of Compounds **6** and **7**[a] (continued)

Product	Mp (°C)	R_f[b]	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ, J (Hz)
7bh	161–162	0.63	2.70 [s, 6 H, $N(CH_3)_2$], 3.92 (s, 2 H, CH_2), 7.24 (m, 5 H, $CH_2C_6H_5$), 7.32 (d, 1 H, *J* = 8.9, H 5), 7.50 (m, 2 H, COC_6H_5), 7.65 (m, 1 H, COC_6H_5), 7.95 (m, 2 H, COC_6H_5), 8.25 (dd, 1 H, *J* = 8.9, 2.3, H-7), 9.19 (d, 1 H, *J* = 2.1, H-8)	37.4 (CH_2), 42.9 [$N(CH_3)_2$], 116.8 (C-4), 124.2 (C-8), 125.7 (C-6), 126.4 (C-8a), 126.5 (C-5), 128.4 (CH), 128.6 (CH), 129.2 (CH), 129.9 (CH), 134.7 (CH), 137.1 (C), 137.8 (C), 138.8 (C-4a), 145.6 (C-7), 147.8 (C-3), 161.4 (CO), 195.1 (*C*OPh)
7aa	104–105	0.33	0.90 (t, 3 H, *J* = 7.8, $CH_2CH_2CH_3$), 1.61 (m, 2 H, $CH_2CH_2CH_3$), 2.32 (s, 3 H, CH_3), 2.58 (s, 3 H, $COCH_3$), 3.92 (m, 2 H, $CH_2CH_2CH_3$), 6.97 (dd, 1 H, *J* = 11.5, 6.7, H-5), 7.97 (dd, 1 H, *J* = 9.2, 9.1, H-8)	11.2 ($CH_2CH_2CH_3$), 17.5 (CH_3), 22.0 ($CH_2CH_2CH_3$), 32.9 ($COCH_3$), 45.9 ($CH_2CH_2CH_3$), 110.7 (d, $^2J_{CF}$ = 19.3, C-5), 116.1 (d, $^2J_{CF}$ = 18.4, C-8), 118.3 (C-4), 121.4 (d, $^3J_{CF}$ = 4.7, C-8a), 137.3 (d, $^3J_{CF}$ = 2.3, C-4a), 149.2 (q, $^1J_{CF}$ = 250.7, $^2J_{CF}$ = 14.2, C-7), 153.6 (q, 149.2 (q, $^1J_{CF}$ = 250.7, $^2J_{CF}$ = 14.2, C-7), 153.6 (q, $^1J_{CF}$ = 245.7, $^2J_{CF}$ = 15.0, C-6), 160.5 (C-3), 163.3 (CO), 203.3 ($COCH_3$)

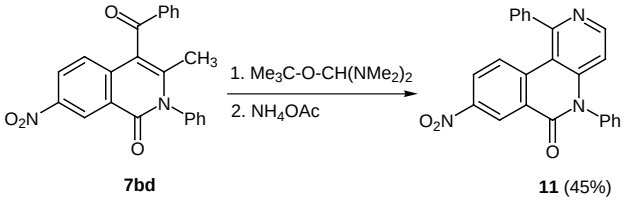
[a] Satisfactory microanalyses obtained: C ±0.12; H ±0.11; N±0.08.
[b] TLC was carried out on Merck $60F_{254}$ silica gel sheets, eluent: cyclohexane–EtOAc (8:2).

Indeed, the *ortho*-position of alkyl groups and ketonic groups in compounds **6** and **7** opens the way to various cyclization reactions. Two examples of this kind of transformations (based on known methods[10,11]) are given on Schemes 5 and 6.



6ae **10** (90%)

Scheme 5



7bd **11** (45%)

Scheme 6

More details concerning different cyclization reactions of compounds **6** and **7** will be communicated in the near future.

All reactions were conducted under argon with magnetic stirring. All solvents (Carlo Erba Company, France) for the reactions were purified before use and were dried, if necessary. THF was distilled under N_2 from sodium benzophenone ketyl and used immediately. Column liquid chromatography were carried out on Merck silica gel 60 (70–230 mesh). Melting points were determined on a Büchi 510 apparatus in open glass capillaries and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 250 spectrometer (250 MHz and 62.5 MHz, respectively) in $CDCl_3$ as solvent with tetramethylsilane as the internal standard. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are in Hz. Elemental analyses were performed using a Perkin-Elmer EA 240 instrument.

Acid chlorides **4a** (Aldrich), **4b** (Lancaster) and *tert*-butoxybis(dimethylamino)methane (Bredereck's reagent) (Aldrich) are commercially available. Enaminones **5** were prepared from corresponding 1,3-diketones and primary amines according to a standard procedure.[12] Compounds **5a**,[13] **5b**,[14] **5c**,[15] **5d**,[12] **5f**,[16] and **5g**[17] were previously described.

1,4-Diphenyl-3-propylaminobut-2-en-1-one (5e)
Yellow oil; yield: 90%.

^{1}H NMR: δ = 0.90 (t, 3 H, *J* = 7.4 Hz, $CH_2CH_2CH_3$), 1.61 (m, 2 H, $CH_2CH_2CH_3$), 3.12 (m, 2 H, $CH_2CH_2CH_3$), 3.69 (s, 2 H, CH_2), 5.69 (s, 1 H, CH), 7.09–7.34 (m, 5 H, $CH_2C_6H_5$), 7.41 (m, 3 H, COC_6H_5), 7.84 (m, 2 H, COC_6H_5), 11.49 (s, 1 H, NH).

3-(2,2-Dimethylhydrazino)-1,4-diphenylbut-2-en-1-one (5h)
Yield: 82%; yellow solid; mp 68–69 °C.

^{1}H NMR: δ = 2.51 [s, 6 H, $N(CH_3)_2$], 3.82 (s, 2 H, CH_2), 5.64 (s, 1 H, CH), 7.21–7.35 (m, 5 H, $CH_2C_6H_5$), 7.43 (m, 3 H, COC_6H_5), 7.82 (m, 2 H, COC_6H_5), 11.63 (s, 1 H, NH).

3-Acyl-2-alkylquinolin-4-ones (6) and 4-Acyl-3-alkylisoquinolin-1-ones (7); General Procedure
A solution of the acid chloride **4** (5 mmol) in anhyd toluene (8 mL) was added to a mixture of enaminone **5** (3.2 mmol) and anhyd Et_3N (10 mmol) in anhyd toluene (7 mL). The resulting mixture was refluxed for 3 h, then DBU (10 mmol) was added and refluxing was maintained for 3 h more. The solvent was evaporated to dryness and the residue was dissolved in CH_2Cl_2 (25 mL). The organic phase was washed with aq sat. NH_4Cl solution and then with brine, dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, cyclohexane–EtOAc, 8:2) to afford compounds **6** or (and) **7** (Table 2).

4-[*N*-Propyl-*N*-(2,4,5-trifluorobenzoyl)amino]pent-3-en-2-one (8)
Compound **8** was prepared from **4a** and **5a** using the above general procedure.

Yellow oil; yield: 68% (650 mg); R_f 0.5 (cyclohexane–EtOAc, 8:2).

^{1}H NMR: δ = 1.02 (t, 3 H, *J* = 6.6 Hz, $CH_2CH_2CH_3$), 1.61 (m, 2 H, $CH_2CH_2CH_3$), 2.02 (s, 3 H, CH_3), 2.34 (s, 3 H, $COCH_3$), 3.76 (t, 2 H, *J* = 7.5 Hz, $CH_2CH_2CH_3$), 5.72 (s, 1 H, H-3), 6.89 (m, 1 H, H-3'), 7.4 (m, 1 H, H-6').

^{13}C NMR: δ = 11.4 ($CH_2CH_2CH_3$), 18.4 (CH_3), 21.5 ($CH_2CH_2CH_3$), 32.0 ($COCH_3$), 47.9 ($CH_2CH_2CH_3$), 106.2 (d, $^2J_{CF}$ = 20.0, $^2J_{CF}$ = 20.0 Hz, C-3'), 118.0 (ddd, $^2J_{CF}$ = 20.0, $^3J_{CF1}$ = $^3J_{CF2}$ = 4.5 Hz, C-6'), 120.2 (d, $^1J_{CF}$ = 257.0 Hz, C-2), 121.6 (dd, $^2J_{CF}$ = 20.0, $^3J_{CF}$ = 2.7 Hz, C-1'), 124.5 (C-3), 151.4 (dd, $^1J_{CF}$ = 264.1, $^2J_{CF}$ = 24.5 Hz, C-4'), 153.6 (dd, $^1J_{CF}$ = 242.6, $^2J_{CF}$ = 23.9 Hz, C-5'), 152.5 (C-4), 163.5 (C=O), 197.1 ($COCH_3$).

(6,7-Difluoro-4-oxo-2-phenyl-[4*H*-1]benzopyran-3-yl)methyl Ketone Dimethylhydrazone (9)

Compound **9** was prepared from **4a** and **5g** using the above general procedure.

Yield: 17% (174 mg); white solid; mp 156–157 °C; R_f 0.25 (cyclohexane–EtOAc, 8:2).

^{1}H NMR: δ = 2.09 (s, 3 H, CH_3), 2.19 [s, 6 H, $N(CH_3)_2$], 7.21 (dd, 1 H, *J* = 9.8, 6.2 Hz, H-8), 7.31 (m, 3 H, C_6H_5), 7.52 (m, 2 H, C_6H_5), 7.83 (dd, 1 H, *J* = 9.6, 9.5 Hz, H-5).

^{13}C NMR: δ = 19.4 (CH_3), 46.5 [$N(CH_3)_2$], 107.1 (d, $^2J_{CF}$ = 21.2 Hz, C-8), 113.0 (d, $^2J_{CF}$ = 21.2 Hz, C-5), 120.6 (d, $^3J_{CF}$ = 4.8 Hz, C-4a), 122.5 (C-3), 128.4 (CH), 128.8 (CH), 131.0 (CH), 148.6 (dd, $^1J_{CF}$ = 250.7, $^2J_{CF}$ = 13.4 Hz, C-6), 152.2 (d, $^3J_{CF}$ = 9.8 Hz, C-8a), 154.0 (dd, $^1J_{CF}$ = 258.6, $^2J_{CF}$ = 15.5 Hz, C-7), 160.2 (C-2), 163.1 (C=N), 175.7 (C=O).

4-Acetyl-6,7-difluoro-3-methyl-2-propyl-2*H*-isoquinolin-1-one (7aa)

To a stirred suspension of NaH (80 mg, 3.3 mmol) in anhyd THF (5 mL) was added slowly a solution of **8** (900 mg, 3 mmol) in anhyd THF (5 mL). The mixture was refluxed for 4 h and the solvent was evaporated in vacuo. The resulting oil was dissolved in cold H_2O. The aqueous phase was acidified with 10% HCl to pH 5–6 and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with H_2O (30 mL) and brine, dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, cyclohexane–EtOAc, 8:2) to afford compound **7aa** (435 mg, 52%) as a white solid.

2,3-Difluoro-11-phenyl-5-propyl-5*H*-benzo[*b*]acridin-12-one (10)

A 1.0 M solution of BBr_3 in CH_2Cl_2 (3 mL, 3 mmol) was added slowly to a stirred solution of quinolone **6ae** (313 mg, 0.75 mmol) in CH_2Cl_2 (30 mL) at –78 °C under dry argon. The solution was allowed to warm to r.t., stirred overnight and poured into H_2O (30 mL). The organic phase was washed with H_2O (30 mL) and brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, CH_2Cl_2) to afford compound **10** (270 mg, 90%) as a yellow solid; mp 218–219 °C.

^{1}H NMR: δ = 1.19 (t, 3 H, *J* = 7.5 Hz, CH_3), 2.03 (m, 2 H, CH_2), 4.21 (t, 2 H, *J* = 7.8 Hz, NCH_2), 7.01 (dd, 1 H, *J* = 12.8, 6.1 Hz, H-4), 7.23 (m, 3 H, H-7,8,9), 7.39–7.52 (m, 5 H, C_6H_5), 7.79 (s, 1 H, H-6), 7.91 (m, 1 H, H-10), 8.1 (dd, 1 H, *J* = 9.5, 9.6 Hz, H-1).

^{13}C NMR: δ = 11.3 ($CH_2CH_2CH_3$), 19.9 ($CH_2CH_2CH_3$), 49.1 ($CH_2CH_2CH_3$), 102.7 (d, $^2J_{CF}$ = 23.0 Hz, C-4), 110.9 (C-6), 116.0 (d, $^2J_{CF}$ = 15.5 Hz, C-1), 118.9 (d, $^3J_{CF}$ = 3.1 Hz, C-1a), 119.0 (C-11a), 124.7 (C-9), 126.8 (C-7), 127.0 (C-8), 128.0 (CH), 128.2 (CH), 128.5 (CH), 128.6 (C-10), 128.9 (C-10a), 135.8 (C-6a), 139.4 (C), 139.7 (d, $^3J_{CF}$ = 9.7 Hz, C-4a), 141.2 (C-11), 144.2 (C-5a), 145.3 (dd, $^1J_{CF}$ = 242.9, $^2J_{CF}$ = 16.9 Hz, C-2), 154.7 (dd, $^1J_{CF}$ = 263.2, $^2J_{CF}$ = 15.1 Hz, C-3), 177.8 (C-12).

1,5-Diphenyl-8-nitro-5*H*-benzo[*c*][1,6]naphthyridin-6-one (11)

To a stirred solution of **7bd** (384 mg, 1 mmol) in 1,4-dioxane (5 mL) was added Bredereck's reagent (191 mg, 1.1 mmol). The resulting mixture was heated under reflux for 5 h. After cooling to r.t., the solution was poured into H_2O (5 mL). The red precipitate was filtered, washed with H_2O and dried (170 mg, 39%). This product was added without purification to a stirred solution of NH_4Ac (154 mg, 2 mmol) in DMF (5 mL). The mixture was heated at 95–100 °C for 5 h. The resulting solution was allowed to cool to r.t. and then poured into H_2O (5 mL). The precipitate formed was filtered, washed with H_2O, and dried to provide **11** (170 mg, 45%); white solid; mp 244–246 °C.

^{1}H NMR: δ = 6.32 (d, 1 H, *J* = 5.7 Hz, H-4), 7.17 (d, 1 H, *J* = 8.4 Hz, H-10), 7.37 (m, 5 H, C_6H_5), 7.41–7.51 (m, 5 H, NC_6H_5), 7.89 (dd, 1 H, *J* = 9.0, 2.4 Hz, H 9), 8.26 (d, 1 H, *J* = 6.0 Hz, H-3), 9.06 (d, 1 H, *J* = 2.7 Hz, H-7).

^{13}C NMR: δ = 110.6 (C-4), 113.1 (C-1a), 125.1 (C-7), 126.2 (C-9), 128.6 (C-6a), 129.4 (CH), 129.6 (CH), 129.7 (C-10), 130.3 (CH), 130.4 (CH), 130.5 (CH), 131.4 (CH), 137.4 (C), 139.1 (C), 142.5 (C-10a), 147.5 (C-4a), 147.7 (C-8), 149.4 (C-3), 160.3 (CO), 161.1 (C-1).

Crystallographic Data for Compounds 6bd, 7bc and 9[18].

Crystals suitable for X-ray analysis were obtained by recrystallization from MeOH. For all compounds the probability of the thermal ellipsoids is 50%.

Data for **6bd**: $C_{23}H_{16}N_2O_4$ (384.4). Crystal size 0.4 × 0.2 × 0.2 mm; monoclinic, space group $P2_1/n$: a = 12.812(2), b = 8.464(2), c = 17.229(3) Å; β = 90.83(2)°; V = 1868.1(6) Å^3; Z = 4; D_c = 1.367 Mg m^{-3}; F(000) = 800; T = 293(2) K; θ = 0°–27.14°, –16 < h < 16, 0 <k < 13, 0 < l < 22. Reflections collected 4141, independent reflections 4141, reflections having I > 2σ(I) 2039. Full matrix least-squares refinement led to the final convergence with R = 0.0490.

Data for **7bc**: $C_{20}H_{18}N_2O_4$ (350.4). Crystal size 0.6 × 0.3 × 0.3 mm; monoclinic, space group $P2_1/n$: a = 11.798(2), b = 7.5320(10), c = 20.092(4) Å; β = 96.29(5)°; V = 1774.7(5) Å^3; Z = 4; D_c = 1.311 Mg m^{-3}; F(000) = 736; T = 293(2) K; θ = 0°–27.14°, –15 < h < 14, 0 <k < 9, 0 < l < 25. Reflections collected 3932, independent reflections 3932, reflections having I > 2σ(I) 1626. Full matrix least-squares refinement led to the final convergence with R = 0.0420.

Data for **9**: $C_{19}H_{16}F_2N_2O_2$ (342.3). Crystal size 0.5 × 0.5 × 0.2 mm; monoclinic, space group $P2_1/a$: a = 12.161(2), b = 8.799(10), c = 16.126(3) Å; β = 97.94(2)°; V = 1709.0(5) Å^3; Z = 4; D_c = 1.311 Mg m^{-3}; F(000) = 712; T = 293(2) K; θ = 0°–27.14°, –15 < h < 15, 0 <k < 11, 0 < l < 20. Reflections collected 3792, independent reflections 3792, reflections having I > 2σ(I) 1584. Full matrix least-squares refinement led to the final convergence with R = 0.0417.

References

(1) Greenhill, J. V. *Chem. Soc. Rev.* **1977**, *6*, 277.
(2) (a) Kucklander, U. *In The Chemistry of Enamines*; Rappoport, Z., Ed.; Wiley: Chichester, **1994**, Chap. 10, 523. (b) Stille, J. R.; Barta, N. S. *Stud. Nat. Prod. Chem.* **1996**, *18*, 315. (c) Lue, P.; Greenhill, J. V. *Adv. Heterocycl. Chem.* **1997**, *67*, 207. (d) Granik, V. G.; Makarov, V. A.; Parkanyi, C. *Adv. Heterocycl. Chem.* **1999**, *72*, 283. (e) Katritzky, A. R.; Fang, Y.; Donkor, A.; Xu, J. *Synthesis* **2000**, 2029; and references cited therein..
(3) Grohe, K.; Heitzer, H. *Liebigs Ann. Chem.* **1987**, 29.
(4) Grohe, K.; Heitzer, H. *Liebigs Ann. Chem.* **1987**, 871.
(5) Cecchetti, V.; Fravolini, A.; Sabatini, S.; Tabarrini, O.; Xin, T. *Eur. J. Med. Chem.* **1998**, *33*, 899.
(6) Yakimovich, S. L.; Zelenin, K. N. *Russ. J. Gen. Chem.* **1995**, *65*, 637.

(7) Yakimovich, S. L.; Zerova, I. V. *J. Org. Chem. USSR* **1991**, *27*, 1427.
(8) Zelenin, A. K.; Ershov, B. A.; Zelenin, K. N. *Russ. J. Gen. Chem.* **1991**, *64*, 636.
(9) Wang, M. X.; Miao, W. S.; Cheng, Y.; Huang, Z. T. *Tetrahedron* **1999**, *55*, 14611.
(10) Singh, B.; Bacon, E. R.; Lesher, G. Y.; Robinson, S.; Pennock, P. O.; Bode, D. C.; Pagani, E. D.; Bentley, R. G.; Connell, M. J.; Hamel, L. T.; Silver, P. J. *J. Med. Chem.* **1995**, *38*, 2546.
(11) Wrobel, J.; Sredy, J.; Moxham, C.; Dietrich, A.; Li, Z.; Sawick, D. R.; Seestaller, L.; Wu, L.; Katz, A.; Sullivan, D.; Tio, C.; Zhang, Z. *J. Med. Chem.* **1999**, *42*, 3199.
(12) Maroni, P.; Cazaux, L.; Tisnes, P.; Zambetti, M. *Bull. Soc. Chim. Fr.* **1980**, *2*, 179.
(13) Dabrowski, J.; Kamienska-Trela, K. *J. Am. Chem. Soc.* **1976**, *98*, 2826.
(14) Braibante, M. E. F.; Braibante, H. S.; Missio, L.; Andricopulo, A. *Synthesis* **1994**, 898.
(15) Nishio, T.; Omote, Y. *Synthesis* **1980**, 390.
(16) Bol'shedvorskaya, R. L.; Pavlova, G. A.; Gavrilov, L. D.; Alekseeva, N. V.; Vereshchagin, L. I. *Zh. Org. Chem.* **1972**, *8*, 1879; Chem. Abstr. 1973, 78, 15707.
(17) Turner, J. A.; Jacks, W. S. *J. Org. Chem.* **1989**, *54*, 4229.
(18) The crystallographic data have been deposited at the Cambrige Crystallographic Data Center. The registration numbers are: 171351(**6bd**), 171352(**7bc**), and 171353(**9**).