Steric and Electronic Requirements in the Synthesis of 2,3-Dihydro-4(1*H*)-quinolinones by the Tandem Michael-S_NAr Reaction

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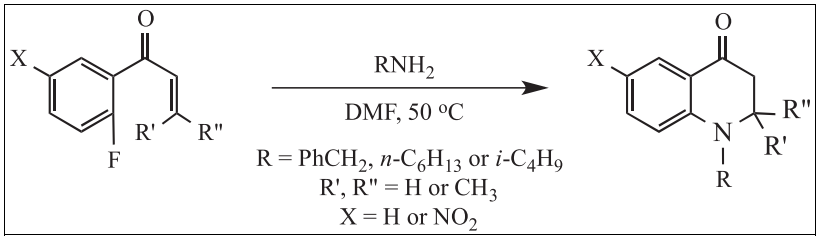

The steric and electronic requirements have been investigated for the synthesis of 2,3-dihydro-4(1*H*)-quinolinones by the tandem Michael-S_NAr reaction. Substrates bearing a single methyl group at the β-enone carbon gave excellent yields of the title compounds from both the *E* and *Z* isomers with X═H or NO_2. Substrates with β,β-dimethyl substitution at the Michael terminus gave low yields of heterocyclic products in molecules having monoactivated S_NAr aromatic acceptor rings (X═H) and very good yields for diactivated systems (X═NO_2). For these hindered substrates, success in the final cyclization hinges on the ability of the aromatic acceptor to capture the pendant nitrogen nucleophile of the initial Michael adduct before this intermediate can revert to starting materials.

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INTRODUCTION

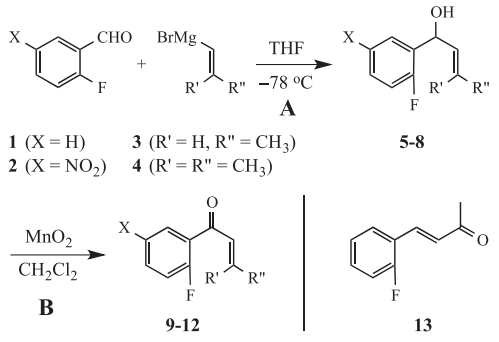
We have recently described several synthetic approaches to substituted 2,3-dihydro-4(1*H*)-quinolines [1–3]. Additionally, numerous schemes have been developed by others for the preparation of these heterocycles and many are cited in our earlier reports [1–3]. The 2,3-dihydro-4(1*H*)-quinoline scaffold is a common structural component in many biologically active compounds. Members of this compound family are valuable building blocks for the construction of drugs to treat pain [4], Alzheimer's disease [5], cancer [6], and central nervous system disorders [7]. Other derivatives have demonstrated activity as potassium channel blockers [8], steroid receptor modulators [9], cholesterol ester transfer protein inhibitors [10], and agents for the treatment of inflammation-based diseases such as asthma [11]. The current work is an extension of a previous study from our laboratory [1], which disclosed a tandem Michael-S_NAr strategy for the preparation of simple derivatives of this ring system and delineated the steric requirements of the starting amine for successful ring closure [12]. The current project sought to further define the steric and electronic demands of this reaction with respect to the acceptor substrate.

RESULTS AND DISCUSSION

Reactive substrates for the current study were prepared by a modification of our earlier synthesis [1] (Fig. 1). Treatment of 2-fluorobenzaldehyde (**1**) and 2-fluoro-5-nitrobenzaldehyde [13] (**2**) with vinylmagnesium bromides **3** and **4** afforded the allylic alcohols **5–8** in 86–88% yields. However, conversion of these alcohols to the corresponding ketones **9–12** using chromic acid [14] in aqueous acetone, as in our original report [1,15], proved troublesome. Under these conditions, oxidation of **5** afforded the 1,3-carbonyl transposition product **13** in 58% yield, along with only 9% of the desired ketone **9** [16]. Fortunately, this difficulty could be circumvented by using activated manganese(IV) dioxide [17] as the oxidizing agent. This method gave clean conversion to the desired products **9–12** in 65–84% yields with no rearrangement.

Our results, from reactions of **9** and **10** with amines **a–c**, are shown in Figure 2. These substrates each possess one alkyl group at the β-enone carbon and differ only in the number of activating (electron-withdrawing) substituents at C2 and C4 relative to the fluoro substituent on the S_NAr aromatic acceptor ring. Based on the yields of **14** and **15**, it can be seen that the reaction proceeds well for compounds having both one and two activating groups, with the diactivated substrate **10** providing slightly higher yields of the heterocyclic products. As previously described, the mechanism of this reaction is consistent with an initial Michael reaction followed by an S_NAr ring closure [1].

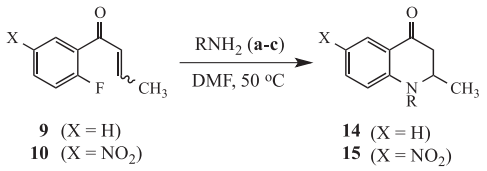
Substrates **11** and **12** (Fig. 3) have increased steric demand for the initial Michael reaction because of the presence of a second methyl group at the Michael terminus. Reaction of monoactivated substrate **11** with amines **a–c** furnished only meager yields of the Michael-S_NAr products **20a–c**, along with recovered starting material.



X	R'	R"	A Yield (%)	B Yield (%)
H	H	CH_3	**5** (88)	**9** (65)[a]
NO_2	H	CH_3	**6** (86)	**10** (68)[a]
H	CH_3	CH_3	**7** (87)	**11** (84)
NO_2	CH_3	CH_3	**8** (88)	**12** (81)

[a]The products isolated were a *ca* 3:1 mixture of *E*:*Z* isomers

Figure 1. Synthesis of cyclization substrates.

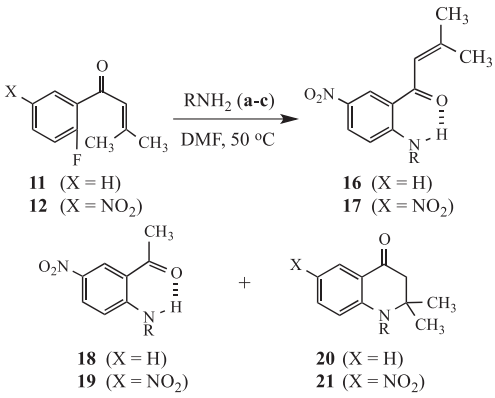


Substrate	R	Product	Yield (%)
9	**a** $PhCH_2NH_2$	**14a**	80
	b *n*-C_6H_{13}	**14b**	86
	c *i*-C_4H_9	**14c**	78
10	**a** $PhCH_2NH_2$	**15a**	97
	b *n*-C_6H_{13}	**15b**	98
	c *i*-C_4H_9	**15c**	92

Figure 2. Cyclizations with **9** and **10**.

Other possible products, such as **16** from a simple S_NAr addition and **18** from an S_NAr-Michael-reverse aldol sequence (*vide infra*), were not observed. On the other hand, doubly activated substrate **12** afforded three products from each amine including the S_NAr adduct **17**, the S_NAr-Michael-retro-aldol acetophenone **19**, and the desired heterocycle **21** as the major product.

The β,β-dimethyl substitution on the side chain enone in **11** and **12** resulted in a noticeable decrease in yield of the desired heterocycle. Reaction of substrate **11**, with a single activating group on the S_NAr acceptor ring, led to significant recovery of starting material. In this system, the Michael addition would be slow and reversible due to steric crowding at the β-enone carbon [18], and thus, the adduct produced could revert to starting material or cyclize to product. For compound **11**, the reverse reaction predominated because the ring was not strongly activated



Substrate	R	Product (%) 11	16	18	20
11	**a** $PhCH_2NH_2$	67	0	0	5
	b *n*-C_6H_{13}	52	0	0	12
	c *i*-C_4H_9	56	0	0	7

Substrate	R	Product (%) 12	17	19	21
12	**a** $PhCH_2NH_2$	0	28	3	65
	b *n*-C_6H_{13}	0	19	4	68
	c *i*-C_4H_9	0	18	6	69

Figure 3. Cyclizations with **11** and **12**.

toward nucleophilic attack. In our earlier study [1], which explored this transformation using substrates lacking β-enone substitution, the Michael addition was relatively fast and less reversible, leading to adducts that cyclized even with weakly activated rings. The intramolecular nature of the final S_NAr ring closure through a chair-like conformation [19], aided in the current case by the Thorpe–Ingold effect [20], appears to be important for cyclizations of minimally activated systems [21] (Fig. 4).

By using substrate **12**, which has two activating substituents on the S_NAr acceptor ring, the reaction proceeded smoothly to give very good yields of the target heterocycles. The cyclized products most likely resulted from the normal Michael-S_NAr process *via* **22**, with the ring being sufficiently active to capture the initial Michael adduct before it could revert to starting materials (Fig. 4 and Scheme 1). The additional formation of **19** from **12** could conceivably arise from an alternative pathway initiated by an S_NAr reaction to give **17**' [22]. This pathway should occur competitively with Michael addition for **12**, due to the β-enone disubstitution, resulting in partial reordering of the reaction sequence. Once addition to the aromatic acceptor occurs to give **17**', steric interaction between the added amine and the side chain would cause rotation of the enone moiety away from the amine to give the six-centered, hydrogen bond-stabilized rotamer **17** [23], which cannot undergo cyclization. Subsequent Michael addition of excess amine to **17** would then give **23**, and

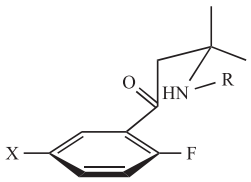
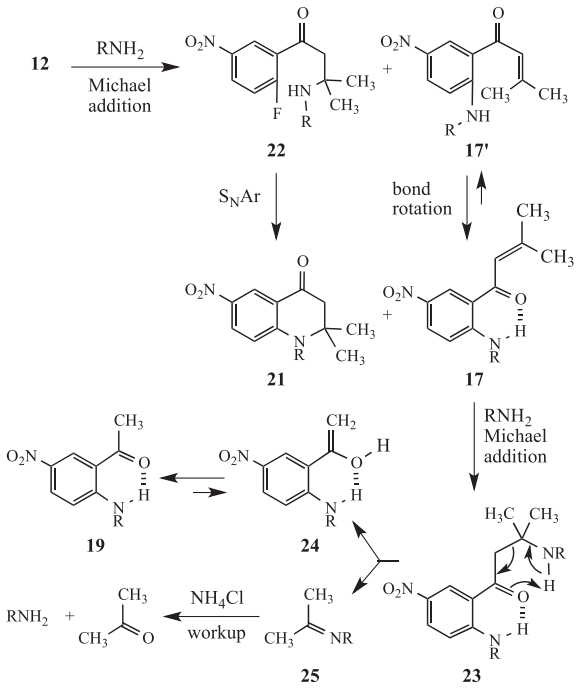


Figure 4. Chair-like conformation for cyclization of **11** (X=H) and **12** (X=NO_2). [R=$PhCH_2$, *n*-C_6H_{13} or *i*-C_4H_9].

Scheme 1. Proposed mechanisms.



reverse aldol reaction would finally produce the acetophenone derivative **19**, *via* enol **24**, along with imine **25**. This imine would presumably hydrolyze to acetone and the amine during workup and be lost from the product mixture.

CONCLUSIONS

We have explored the steric and electronic requirements for the synthesis of 2,3-dihydro-4(1*H*)-quinolinones by the tandem Michael-S_NAr reaction. The current work demonstrates that the steric environment at the β carbon of the Michael acceptor and the activation of S_NAr acceptor ring have a major impact on the reaction outcome. With a single alkyl substituent at the Michael terminus, the reaction proceeded cleanly and in high yield from both the *E* and the *Z* isomers for all cases. Additional substitution at this site, however, slowed addition to the enone and generated an adduct that could partition between two reaction pathways: (1) a reverse Michael reaction or (2) ring closure to the heterocycle. Success in the cyclization step correlated predictably with the electronics of the S_NAr acceptor moiety. In monoactivated substrates, the reverse Michael pathway predominated and significant quantities of starting materials were recovered. For diactivated substrates, however, capture of the tethered nitrogen nucleophile by the aromatic ring was more efficient, and ring closures were observed. Moreover, the increased steric bulk at the Michael terminus resulted in perturbation of the normal reaction sequence to yield simple S_NAr adducts, which assumed a six-centered, hydrogen bond-stabilized conformation that could not cyclize. Further addition to the enone in these products then led to 2-alkylamino-5-nitroacetophenone derivatives *via* a retro-aldol process.

EXPERIMENTAL

All reactions were run under dry nitrogen in oven-dried glassware. Grignards **3** and **4** in THF as well as anhydrous DMF were purchased from Sigma-Aldrich. Reactions were monitored by thin layer chromatography on silica gel GF plates (Analtech, No. 21521). Preparative separations were performed by one of the following methods: (1) column chromatography on silica gel (grade 62, 60–200 mesh) containing UV-active phosphor (Sorbent Technologies, No. UV-05) packed into quartz columns or (2) preparative thin layer chromatography (PTLC) on 20 cm × 20 cm silica gel GF plates (Analtech, No. 02015). Band elution for all chromatographic methods was monitored using a hand-held UV lamp. Melting points were uncorrected. IR spectra were run as thin films on NaCl disks. ^{1}H-NMR and ^{13}C-NMR spectra were measured in $CDCl_3$ using $(CH_3)_4Si$ as the internal standard; coupling constants (*J*) are given in Hertz. Unless otherwise indicated, low-resolution mass spectra (electron impact/direct probe) were obtained at 70 eV.

Representative Grignard addition procedure

(±)-(E)- and (±)-(Z)-1-(2-Fluorophenyl)-2-buten-1-ol (5). The general procedure of Danishefsky and co-workers was used [14]. To a −78°C solution of 1.86 g (15.0 mmol) of 2-fluorobenzaldehyde (**1**) in 75 mL of anhydrous THF was added 45 mL of 0.5 *M* 1-propenylmagnesium bromide (**3**, 22.5 mmol) in THF. The reaction mixture was stirred for 3.5 h at −78°C, then quenched by addition of 50 mL of saturated aqueous NH_4Cl and extracted with ether (3 × 50 mL). The combined ether extracts were washed with water (three times), saturated aqueous NaCl (one time), dried ($MgSO_4$), filtered, and concentrated under vacuum to give 2.19 g (88%) of **5** (ca. 3:1 *E*/*Z*) as a viscous yellow oil. Product **5** decomposed slightly on attempted chromatography and was used without further purification. The spectral data for the mixture were IR: 3347, 1616, 1242 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.49 (overlapping td, 1H, *J* = 7.4, 1.6 Hz), 7.24 (m, 1H), 7.14 (td, 1H, *J* = 7.4, 1.6 Hz), 7.01 (ddd, 1H, *J* = 10.4, 9.3, 1.1 Hz), 5.83 and 5.63 (2d, 1H, *J* = 7.1, 5.0 Hz), 5.73 (m, ~0.5H), 5.61 (m, ~1.5H), 2.18 (br s, 1H), 1.77 and 1.70 (2d, 3H, *J* = 4.9 and 5.4 Hz); ^{13}C-NMR (75 MHz): δ 159.9 (d, *J* = 246.2 Hz), 132.1, 131.4, 130.6 (d, *J* = 13.2 Hz), 129.0 (d, *J* = 8.3 Hz), 128.4 (d, *J* = 8.3 Hz), 127.6, 127.4 (d, *J* = 4.3 Hz), 126.9, 124.3 (d, *J* = 3.4 Hz), 115.3 (d, *J* = 21.8 Hz), 69.2 (d, *J* = 2.2 Hz), 64.1 (d, *J* = 3.4 Hz), 17.6, 13.2; ms: *m/z* 123 ($M^+ - C_3H_7$).

(±)-(E)- and (±)-(Z)-1-(2-Fluoro-5-nitrophenyl)-2-buten-1-ol (6). This compound (1.81 g, ca. 3:1 *E*/*Z*, 86%) was prepared from

1.69 g (10.0 mmol) of 2-fluoro-5-nitrobenzaldehye (**2**) [13] and 30 mL of 0.5 *M* 1-propenylmagnesium bromide (**3**) in THF (**3**, 15.0 mmol), and was isolated as viscous yellow oil. Product **6** decomposed slightly on attempted chromatography and was used without further purification. IR: 3378, 1629, 1530, 1350, 1247 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.49 and 8.46 (dd, 1H, *J* = 6.1, 2.7 Hz), 8.16 (m, 1H), 7.16 (t, 1H, *J* = 9.2 Hz), 5.84 (m, 1H), 5.68 (m, 1H), 5.51 (m, 1H), 2.55 (br s, 1H), 1.82 (dm, ~1.5H, *J* = 6.8 Hz), 1.72 (dd, ~1.5H, *J* = 6.4, 0.8 Hz); ^{13}C-NMR (75 MHz): δ 163.2 (d, *J* = 262.8 Hz), 163.1 (d, *J* = 262.8 Hz), 144.8, 132.6 (d, *J* = 15.5 Hz), 132.4 (d, *J* = 15.5 Hz), 131.0, 130.2, 129.1, 128.5, 124.7 (d, *J* = 3.7 Hz), 124.6 (d, *J* = 3.7 Hz), 123.6 (d, *J* = 6.6 Hz), 116.3 (d, *J* = 25.0 Hz), 68.4, 63.3, 17.6, 13.2; ms: *m/z* 168 ($M^+ - C_3H_7$).

(±)-1-(2-Fluorophenyl)-3-methyl-2-buten-1-ol (7). This compound (2.35 g, 87%) was prepared from 1.86 g (15.0 mmol) of **1** and 45 mL of 0.5 *M* 2-methyl-1-propenylmagnesium bromide (**4**, 22.5 mmol) in THF, and was isolated as a light yellow solid, mp 37–39°C. Product **7** was pure by ^{1}H-NMR analysis and was used without further purification. IR: 3353, 1618, 1224 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.50 (td, 1H, *J* = 7.7, 1.6 Hz), 7.22 (m, 1H), 7.14 (td, 1H, *J* = 7.1, 1.1 Hz), 7.01 (m, 1H), 5.73 (dd, 1H, *J* = 8.8, 3.3 Hz), 5.40 (dq, 1H, *J* = 8.8, 1.1 Hz), 1.95 (d, 1H, *J* = 3.3 Hz), 1.80 (s, 3H), 1.74 (s, 3H); ^{13}C-NMR (75 MHz): δ 159.9 (d, *J* = 245.9 Hz), 135.9, 131.1 (d, *J* = 13.2 Hz), 128.7 (d, *J* = 8.0 Hz), 127.3 (d, *J* = 4.6 Hz), 126.2, 124.2 (d, *J* = 3.4 Hz), 115.3 (d, *J* = 21.8 Hz), 65.4 (d, *J* = 3.1 Hz), 25.8, 18.2; ms: *m/z* 123 ($M^+ - C_4H_9$). *Anal.* Calcd for $C_{11}H_{13}FO$: C, 73.33; H, 7.22. Found: C, 73.57; H, 7.24.

(±)-1-(2-Fluoro-5-nitrophenyl)-3-methyl-2-buten-1-ol (8). This compound (1.98 g, 88%) was prepared from 1.69 g (10.0 mmol) of **2** and 30 mL of 0.5 *M* 2-methyl-1-propenylmagnesium bromide (**4**, 15.0 mmol) in THF, and was isolated as a viscous yellow oil. Product **8** was pure by ^{1}H-NMR analysis and was used without further purification. IR: 3372, 1626, 1531, 1350, 1248 cm^{-1}; ^{1}H-NMR (400 MHz): δ 8.49 (dd, 1H, *J* = 6.2, 2.9 Hz), 8.15 (ddd, 1H, *J* = 9.0, 4.3, 2.9 Hz), 7.15 (t, 1H, *J* = 9.0 Hz), 5.77 (d, 1H, *J* = 9.0 Hz), 5.30 (d, 1H, *J* = 9.0 Hz), 2.13 (br s, 1H), 1.84 (s, 3H), 1.76 (s, 3H); ^{13}C-NMR (100 MHz): δ 163.1 (d, *J* = 257.7 Hz), 144.5, 137.7, 133.1 (d, *J* = 14.7 Hz), 125.1, 124.5 (d, *J* = 10.3 Hz), 123.6 (d, *J* = 7.4 Hz), 116.3 (d, *J* = 24.2 Hz), 64.7 (d, *J* = 2.9 Hz), 25.8, 18.2 (d, *J* = 1.5 Hz); ms: *m/z* 168 ($M^+ - C_4H_9$). *Anal.* Calcd for $C_{11}H_{12}FNO_3$: C, 58.67; H, 5.33; N, 6.22. Found: C, 58.78; H, 5.45; N, 6.08.

Representative oxidation using manganese(IV) oxide

(E)- and (Z)-1-(2-Fluorophenyl)-2-buten-1-one (9). To a solution of 1.00 g (6.02 mmol) of *E*/*Z*-**5** in 25 mL of dichloromethane was added 10.0 g of manganese(IV) oxide [17]. The reaction was stirred vigorously for 4–8 h at 23°C, then filtered through a plug of Celite®. The Celite® was washed thoroughly with dichloromethane, and the solvent was removed to give 620 mg of a mixture of the *E* and *Z* enones. The products were purified on a 40 cm × 2.0 cm silica gel column eluted with increasing concentrations of ether in hexanes to give two bands. Band 1 gave 127 mg (13%) of (*Z*)-**9** as a viscous yellow oil. IR: 1669, 1614, 1215 cm^{-1}; ^{1}H-NMR (400 MHz): δ 7.78 (td, 1H, *J* = 7.7, 1.6 Hz), 7.49 (m, 1H), 7.22 (t, 1H, *J* = 7.7 Hz), 7.11 (dd, 1H, *J* = 11.0, 8.2 Hz), 6.75 (dq, 1H, *J* = 11.2, 1.6 Hz), 6.44 (dq, 1H, *J* = 11.2, 7.1 Hz), 2.19 (dd, 3H, *J* = 7.1, 1.6 Hz); ^{13}C-NMR (100 MHz): δ 189.8, 161.1 (d, *J* = 253.9 Hz), 144.5, 133.8 (d, *J* = 8.9 Hz), 130.8 (d, *J* = 2.6 Hz), 128.2 (d, *J* = 6.0 Hz), 127.7 (d, *J* = 13.2 Hz), 124.4 (d, *J* = 3.4 Hz), 116.5 (d, *J* = 23.5 Hz), 16.4; ms: *m/z* 123 ($M^+ - C_3H_5$). *Anal.* Calcd for $C_{10}H_9FO$: C, 73.17; H, 5.49. Found: C, 73.12; H, 5.51.

Band 2 gave 516 mg (52%) of (*E*)-**9** as a viscous yellow oil. IR: 1667, 1619, 1215 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.70 (td, 1H, *J* = 7.7, 1.6 Hz), 7.48 (m, 1H), 7.22 (t, 1H *J* = 7.7 Hz), 7.12 (dd, 1H, *J* = 11.0, 8.2 Hz), 6.99 (m, 1H), 6.76 (dq, 1H, *J* = 15.4, 1.1 Hz), 1.98 (dd, 3H, *J* = 6.6, 1.1 Hz); ^{13}C-NMR (75 MHz): δ 189.5, 160.9 (d, *J* = 253.1 Hz), 145.6, 135.5 (d, *J* = 8.6 Hz), 131.1 (d, *J* = 5.7 Hz), 130.7 (d, *J* = 2.9 Hz), 127.0 (d, *J* = 13.5 Hz), 124.3 (d, *J* = 3.4 Hz), 116.4 (d, *J* = 23.2 Hz), 18.5; ms: *m/z* 123 ($M^+ - C_3H_5$). *Anal.* Calcd for $C_{10}H_9FO$: C, 73.17; H, 5.49. Found: C, 73.15; H, 5.47.

Attempts to oxidize **5** with chromic acid [1,14,15] on the same scale led to a mixture of 90 mg (9%) of (*E*)-**9** and 572 mg (58%) of the 1,3-carbonyl transposition [16] product (*E*)-4-(2-fluorophenyl)-3-buten-1-one (**13**) as a light yellow solid, mp 42–43°C. The spectral data for **13** were IR: 1672, 1612, 1221, 980 cm^{-1}; ^{1}H-NMR (400 MHz): δ 7.67 (d, 1H, *J* = 16.6 Hz), 7.57 (t, 1H, *J* = 7.4 Hz), 7.37 (m, 1H), 7.17 (t, 1H, *J* = 7.4 Hz), 7.11 (dd, 1H, *J* = 9.9, 9.1 Hz), 6.78 (d, 1H, *J* = 16.6 Hz), 2.40 (s, 3H); ^{13}C-NMR (100 MHz): δ 198.3, 161.2 (d, *J* = 254.0 Hz), 135.5 (d, *J* = 3.7 Hz), 131.9 (d, *J* = 8.8 Hz), 129.1 (d, *J* = 5.2 Hz), 128.6 (d, *J* = 2.9 Hz), 124.5 (d, *J* = 3.7 Hz), 122.4 (d, *J* = 11.8 Hz), 116.1 (d, *J* = 22.1 Hz), 27.4; ms: *m/z* 164 (M^+). *Anal.* Calcd for $C_{10}H_9FO$: C, 73.17; H, 5.49. Found: C, 73.13; H, 5.51.

(E)- and (Z)-1-(2-Fluoro-5-nitrophenyl)-2-buten-1-one (10). These compounds (0.67 g, ca. 3:1 *E*:*Z* mixture, 68%) were prepared from 1.00 g (4.74 mmol) of *E*/*Z*-**6** and 10.0 g of manganese(IV) oxide in 25 mL of dichloromethane. The products were purified on a 40 cm × 2.0 cm silica gel column eluted with increasing concentrations of ether in hexanes to give 2 bands. Band 1 gave 138 mg (14%) of (*Z*)-**10** as a light yellow solid, mp 43–45°C. IR: 1675, 1621, 1532, 1355, 1246 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.69 (dd, 1H, *J* = 6.0, 2.7 Hz), 8.38 (dt, 1H, *J* = 9.3, 3.8 Hz), 7.31 (t, 1H, *J* = 9.3 Hz), 6.74 (dq, 1H, *J* = 11.5, 1.6 Hz), 6.57 (dq, 1H, *J* = 11.5, 7.1 Hz), 2.24 (d, 3H, *J* = 7.1 Hz); ^{13}C-NMR (75 MHz): δ 186.8, 163.9 (d, *J* = 264.0 Hz), 147.5, 144.5, 128.7 (d, *J* = 10.9 Hz), 128.6 (d, obscured), 127.1 (d, *J* = 4.9 Hz), 126.8 (d, *J* = 6.3 Hz), 118.0 (d, *J* = 26.1 Hz), 16.7; ms: *m/z* 168 ($M^+ - C_3H_5$). *Anal.* Calcd for $C_{10}H_8FNO_3$: C, 57.42; H, 3.83; N, 6.70. Found: C, 57.49; H, 3.86; N, 6.64.

Band 2 gave 555 mg (56%) of (*E*)-**10** as a light yellow solid, mp 43–45°C. IR: 1674, 1623, 1532, 1350, 1246 cm^{-1}; ^{1}H-NMR (400 MHz): δ 8.60 (dd, 1H, *J* = 6.0, 2.7 Hz), 8.37 (ddd, 1H, *J* = 9.3, 3.8, 2.7 Hz), 7.32 (t, 1H, *J* = 9.3 Hz), 7.07 (m, 1H), 6.74 (dq, 1H, *J* = 15.4, 1.6 Hz), 2.03 (dd, 3H, *J* = 7.1, 1.6 Hz); ^{13}C-NMR (100 MHz): δ 186.8, 163.8 (d, *J* = 263.4 Hz), 148.0, 144.3, 130.1 (d, *J* = 5.1 Hz), 128.5 (d, *J* = 10.9 Hz), 127.9 (d, *J* = 16.6 Hz), 126.9 (d, *J* = 4.9 Hz), 117.9 (d, *J* = 25.8 Hz), 18.7; ms: *m/z* 168 ($M^+ - C_3H_5$). *Anal.* Calcd for $C_{10}H_8FNO_3$: C, 57.42; H, 3.83; N, 6.70. Found: C, 57.46; H, 3.85; N, 6.65.

1-(2-Fluorophenyl)-3-methyl-2-buten-1-one (11). This compound was prepared from 1.00 g (5.56 mmol) of **7** and 10.0 g of manganese(IV) oxide in 25 mL of dichloromethane. The product was purified on a 25 cm × 2.0 cm silica gel column eluted with increasing concentrations of ether in hexanes to give 0.83 g (84%) of **11** as a yellow oil. IR: 1667, 1614, 1228 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.74 (td, 1H, *J* = 7.7, 1.6 Hz), 7.44 (m, 1H), 7.20 (td, 1H, *J* = 8.2, 1.1 Hz), 7.09 (dd, 1H, *J* = 11.0, 8.2 Hz), 6.64 (m, 1H), 2.25 (s, 3H), 2.00 (s, 3H); ^{13}C-NMR (75 MHz): δ 189.1, 160.8 (d, *J* = 252.8 Hz), 157.5,

133.3 (d, $J = 8.9$ Hz), 130.7 (d, $J = 2.9$ Hz), 128.5 (d, $J = 13.2$ Hz), 124.4 (d, $J = 6.6$ Hz), 124.2 (d, $J = 3.7$ Hz), 116.3 (d, $J = 23.5$ Hz), 28.0, 21.4; ms: *m/z* 123 ($M^+ - C_4H_7$). *Anal*. Calcd for $C_{11}H_{11}FO$: C, 74.16; H, 6.18. Found: C, 74.22; H, 6.21.

1-(2-Fluoro-5-nitrophenyl)-3-methyl-2-buten-1-one (12). This compound was prepared from 1.00 g (4.39 mmol) of **8** and 10.0 g of manganese(IV) oxide in 25 mL of dichloromethane. The product was purified on a 25 cm × 2.0 cm silica gel column eluted with increasing concentrations of ether in hexanes to give 0.80 g (81%) of **12** as a light yellow solid, mp 54–55°C. IR: 1667, 1624, 1532, 1350, 1252 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.64 (dd, 1H, $J = 6.0$, 2.7 Hz), 8.35 (ddd, 1H, $J = 9.3$, 3.8, 2.7 Hz), 7.29 (t, 1H, $J = 9.3$ Hz), 6.62 (q, 1H, $J = 1.1$ Hz), 2.30 (s, 3H), 2.06 (s, 3H); ^{13}C-NMR (75 MHz): δ 186.1, 163.9 (d, $J = 263.4$ Hz), 161.1, 144.4, 129.4, 128.2 (d, $J = 10.9$ Hz), 127.0 (d, $J = 5.2$ Hz), 123.1 (d, $J = 5.7$ Hz), 117.9 (d, $J = 26.3$ Hz), 28.3, 21.8; ms: *m/z* 168 ($M^+ - C_4H_7$). *Anal*. Calcd for $C_{11}H_{10}FNO_3$: C, 59.19; H, 4.48; N, 6.28. Found: C, 59.22; H, 4.49; N, 6.25.

Representative procedure for the tandem Michael-S_NAr reaction

(±)-1-Benzyl-2,3-dihydro-2-methyl-4(1H)-quinolinone (14a). To a solution of 66 mg (0.40 mmol) of (*E*)-**9** in 3 mL of anhydrous DMF was added 51 mg (0.052 mL, 0.48 mmol) of benzylamine, and the solution was heated at 50°C for 24 h. The reaction mixture was cooled, added to 25 mL of saturated aqueous NaCl and extracted with ether (3 × 50 mL). The combined ether extracts were washed with water (one time), saturated aqueous NaCl (one time), dried ($MgSO_4$), filtered, and concentrated under vacuum to afford a yellow oil. The product was purified on a 20 cm × 20 cm PTLC plate using 50–70% ether in hexanes to afford 78 mg (80%) of **14a** as a light yellow solid, mp 88–90°C. IR: 1673 cm^{-1}; ^{1}H-NMR (400 MHz): δ 7.90 (dd, 1H, $J = 7.9$, 1.7 Hz), 7.39–7.25 (complex, 6H), 6.69 (apparent t, 1H, $J = 7.4$ Hz), 6.57 (d, 1H, $J = 8.6$ Hz), 4.69 (d, 1H, $J = 16.6$ Hz), 4.37 (d, 1H, $J = 16.6$ Hz), 3.83 (m, 1H), 3.06 (dd, 1H, $J = 16.0$, 6.1 Hz), 2.55 (dd, 1H, $J = 16.0$, 3.3 Hz), 1.22 (d, 3H, $J = 6.6$ Hz); ^{13}C-NMR (100 MHz): δ 193.3, 149.4, 137.7, 135.7, 128.8, 127.6, 127.4, 126.4, 119.2, 116.4, 113.5, 54.7, 53.3, 44.3, 15.4; ms: *m/z* 160 ($M^+ - C_7H_7$). *Anal*. Calcd for $C_{17}H_{17}NO$: C, 81.27; H, 6.77; N, 5.58. Found: C, 81.28; H, 6.77; N, 5.59. This same reaction, using, (*Z*)-**9**, gave **14a** in 82% yield.

(±)-1-Hexyl-2,3-dihydro-2-methyl-4(1H)-quinolinone (14b). This compound was prepared, as described for **14a**, from 66 mg (0.40 mmol) of (*E*)-**9** and 49 mg (0.063 mL, 0.48 mmol) of hexylamine. Following purification by PTLC, 0.84 mg (86%) of **14b** was isolated as a viscous yellow oil. IR: 1674 cm^{-1}; ^{1}H-NMR (400 MHz): δ 7.86 (dd, 1H, $J = 8.2$, 1.7 Hz), 7.35 (ddd, 1H, $J = 8.8$, 7.2, 1.7 Hz), 6.63 (d, 1H, $J = 8.8$ Hz), 6.62 (t, 1H, $J = 7.2$ Hz), 3.72 (m, 1H), 3.49 (dt, 1H, $J = 14.8$, 7.2 Hz), 3.07 (dt, 1H, $J = 15.0$, 7.4 Hz), 2.93 (dd, 1H, $J = 15.8$, 6.1 Hz), 2.47 (dd, 1H, $J = 16.0$, 3.1 Hz), 1.67 (quintet, 2H, $J = 7.2$ Hz), 1.45–1.29 (complex, 6H), 1.16 (d, 3H, $J = 6.6$ Hz), 0.91 (distorted t, 3H, $J = 6.8$ Hz); ^{13}C-NMR (100 MHz): δ 193.2, 149.1, 135.6, 127.7, 118.6, 115.3, 112.6, 54.5, 49.6, 44.0, 31.6, 27.9, 26.8, 22.6 15.6, 14.0; ms: *m/z* 174 ($M^+ - C_5H_{11}$). *Anal*. Calcd for $C_{16}H_{23}NO$: C, 78.37; H, 9.39; N, 5.71. Found: C, 78.41; H, 9.42; N, 5.67.

(±)-2,3-Dihydro-1-isobutyl-2-methyl-4(1H)-quinolinone (14c). This compound was prepared, as described for **14a**, from 66 mg (0.40 mmol) of (*E*)-**9** and 29 mg (0.040 mL, 0.48 mmol) of isobutylamine. Following purification by PTLC, 68 mg (78%) of **14c** was isolated as a viscous yellow oil. IR: 1674 cm^{-1}; ^{1}H-NMR (400 MHz): δ 7.87 (dd, 1H, $J = 7.8$, 1.8 Hz), 7.34 (ddd, 1H, $J = 8.6$, 7.0, 1.8 Hz), 6.63 (apparent t, 1H, $J = 7.8$ Hz), 6.59 (d, 1H, $J = 8.6$ Hz), 3.70 (quintet of d, 1H, $J = 6.6$, 2.3 Hz), 3.44 (dd, 1H, $J = 14.4$, 5.1 Hz), 2.99 (dd, 1H, $J = 15.9$, 6.1 Hz), 2.64 (dd, 1H, $J = 14.4$, 9.6 Hz), 2.48 (dd, 1H, $J = 15.9$, 2.3 Hz), 2.04 (m, 1H), 1.13 (d, 3H, $J = 6.6$ Hz), 1.04 (d, 3H, $J = 6.6$ Hz), 0.99 (d, 3H, $J = 6.8$ Hz); ^{13}C-NMR (100 MHz): δ 193.2, 149.1, 135.6, 127.7, 118.6, 115.4, 112.7, 57.7, 55.5, 43.7, 27.3, 20.4, 20.0, 14.6; ms: *m/z* 174 ($M^+ - C_3H_7$). *Anal*. Calcd for $C_{14}H_{19}NO$: C, 77.42; H, 8.76; H, 6.45. Found: C, 77.45; H, 8.78; N, 6.38.

(±)-1-Benzyl-2,3-dihydro-2-methyl-6-nitro-4(1H)-quinolinone (15a). This compound was prepared, as described for **14a**, from 84 mg (0.40 mmol) of (*E*)-**10** and 51 mg (0.052 mL, 0.48 mmol) of benzylamine. Following purification by PTLC, 115 mg (97%) of **15a** was isolated as a light yellow solid, mp 118–120°C. IR: 1688, 1506, 1317 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.75 (d, 1H, $J = 2.7$ Hz), 8.09 (dd, 1H, $J = 9.3$, 2.7 Hz), 7.44–7.26 (complex, 5H), 6.64 (d, 1H, $J = 9.3$ Hz), 4.84 (d, 1H, $J = 16.8$ Hz), 4.55 (d, 1H, $J = 16.8$ Hz), 3.98 (quintet of d, 1H, $J = 6.4$, 2.7 Hz), 3.08 (dd, 1H, $J = 15.9$, 6.0 Hz), 2.64 (dd, 1H, $J = 15.9$, 2.7 Hz), 1.28 (d, 3H, $J = 6.9$ Hz); ^{13}C-NMR (75 MHz): δ 191.1, 152.5, 137.6, 135.7, 130.2, 129.1, 128.0, 126.2, 124.5, 117.5, 113.4, 55.0, 53.6, 43.3, 16.2; ms: *m/z* 205 ($M^+ - C_7H_7$). *Anal*. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.92; H, 5.41; N, 9.46. Found: C, 68.88; H, 5.42; N, 9.43.

(±)-1-Hexyl-2,3-dihydro-2-methyl-6-nitro-4(1H)-quinolinone (15b). This compound was prepared, as described for **14a**, from 84 mg (0.40 mmol) of (*E*)-**10** and 49 mg (0.063 mL, 0.48 mmol) of hexylamine. Following purification by PTLC, 114 mg (98%) of **15b** was isolated as a viscous yellow oil. IR: 1688, 1510, 1315 cm^{-1}; ^{1}H-NMR (400 MHz): δ 8.72 (d, 1H, $J = 2.8$ Hz), 8.17 (dd, 1H, $J = 9.6$, 2.8 Hz), 6.67 (d, 1H, $J = 9.6$ Hz), 3.88 (quintet of d, 1H, $J = 6.6$, 2.4 Hz), 3.63 (dt, 1H, $J = 14.7$, 7.2 Hz), 3.23 (dt, 1H, $J = 14.7$, 7.6 Hz), 2.98 (dd, 1H, $J = 16.0$, 6.2 Hz), 2.59 (dd, 1H, $J = 16.0$, 2.5 Hz), 1.73 (quintet, 2H, $J = 7.4$ Hz), 1.46–1.32 (complex, 6H), 1.23 (d, 3H, $J = 6.8$ Hz), 0.91 (distorted t, 3H, $J = 6.9$ Hz); ^{13}C-NMR (100 MHz): δ 191.2, 152.0, 136.9, 130.2, 124.8, 117.0, 112.5, 54.9, 50.4, 43.2, 31.4, 27.8, 26.6, 22.5, 16.2, 13.9; ms: *m/z* 219 ($M^+ - C_5H_{11}$). *Anal*. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.21; H, 7.59; N, 9.66. Found: C, 66.26; H, 7.62; N, 9.58.

(±)-2,3-Dihydro-1-isobutyl-2-methyl-6-nitro-4(1H)-quinolinone (15c). This compound was prepared, as described for **14a**, from 84 mg (0.40 mmol) of (*E*)-**10** and 29 mg (0.040 mL, 0.48 mmol) of isobutylamine. Following purification by PTLC, 96 mg (92%) of **15c** was isolated as a light yellow solid, mp 120–121 °C. IR: 1687, 1511, 1316 cm^{-1}; ^{1}H-NMR (400 MHz): δ 8.74 (d, 1H, $J = 2.8$ Hz), 8.16 (dd, 1H, $J = 9.4$, 2.8 Hz), 6.66 (d, 1H, $J = 9.4$ Hz), 3.85 (quintet of d, 1H, $J = 6.6$, 2.1 Hz), 3.59 (dd, 1H, $J = 14.5$, 5.3 Hz), 3.01 (dd, 1H, $J = 16.0$, 6.1 Hz), 2.84 (dd, 1H, $J = 14.5$, 9.6 Hz), 2.60 (dd, 1H, $J = 16.0$, 2.0 Hz), 2.10 (m, 1H), 1.20 (d, 3H, $J = 6.8$ Hz), 1.08 (d, 3H, $J = 6.6$ Hz), 1.04 (d, 3H, $J = 6.6$ Hz); ^{13}C-NMR (100 MHz): δ 191.1, 152.2, 137.0, 130.1, 124.9, 117.1, 112.7, 57.8, 55.7, 42.9, 27.5, 20.2, 20.0, 15.5; ms: *m/z* 219 ($M^+ - C_3H_7$). *Anal*. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.12; H, 6.87; N, 10.69. Found: C, 64.15; H, 6.89; N, 10.64.

Cyclizations of 11. By using the procedure given for the preparation of **14a**, a solution of 71 mg (0.40 mmol) of **11** and 0.48 mmol of the amine in 2.5 mL of dry DMF was heated at 50°C for 48 h. Workup and purification by PTLC showed two major bands.

With benzylamine. Band 1 gave 48 mg of recovered **11** (67%) as a light yellow oil. Band 2 gave 5 mg (5%) of 1-benzyl-2,3-dihydro-2,2-dimethyl-4(1*H*)-quinolinone (**20a**) as a light yellow solid, mp 114–115°C. IR 1676, 1605, 1364 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.90 (dd, 1H, *J* = 7.7, 1.6 Hz), 7.36 (apparent d, 3H, *J* = 4.4 Hz), 7.27 (m, 3H), 6.70 (t, 1H, *J* = 7.7 Hz), 6.50 (d, 1H, *J* = 8.2 Hz), 4.54 (s, 2H), 2.77 (s, 2H), 1.34 (s, 6H); ^{13}C-NMR (75 MHz): δ 193.8, 150.7, 138.9, 135.7, 128.8, 127.1, 127.0, 125.8, 119.5, 116.5, 114.3, 58.4, 51.8, 49.5, 29.7, 24.8 (2C); ms: *m/z* 250 ($M^+ - CH_3$). *Anal* Calcd $C_{18}H_{19}NO$: C, 81.51; H, 7.17; N, 5.28. Found: C, 81.45; H, 7.15; N, 5.33.

With hexylamine. Band 1 gave 37 mg of recovered **11** (52%) as a light yellow oil. Band 2 gave 12 mg (12%) of 1-hexyl-2,3-dihydro-2,2-dimethyl-4(1*H*)-quinolinone (**20b**) as a viscous yellow oil. IR 1680, 1604, 1361 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.87 (dd, 1H, *J* = 7.7, 1.6 Hz), 7.38 (ddd, 1H, *J* = 8.8, 7.1, 1.6 Hz), 6.67 (t, 1H, *J* = 7.1 Hz), 6.66 (d, 1H, *J* = 8.4 Hz), 3.24 (t, 2H, *J* = 7.7 Hz), 2.60 (s, 2H), 1.66 (m, 2H), 1.37 (m, 6H), 1.30 (s, 6H), 0.93 (distorted t, 3H, *J* = 6.6 Hz); ^{13}C-NMR (75 MHz): δ 193.9, 150.4, 135.6, 127.4, 119.2, 115.6, 113.2, 57.9, 51.8, 45.6, 31.6, 29.5, 26.7, 24.9 (2C), 22.7, 14.0; ms: *m/z* 188 ($M^+ - C_5H_{11}$). *Anal* Calcd $C_{17}H_{25}NO$: C, 78.76; H, 9.65; N, 5.41. Found: C, 78.90; H, 9.67; N, 5.32.

With isobutylamine. Band 1 gave 40 mg of recovered **11** (56%) as a light yellow oil. Band 2 gave 6 mg (7%) of 1-isobutyl-2,3-dihydro-2,2-dimethyl-4(1*H*)-quinolinone (**20c**) as a viscous yellow oil. IR 1679, 1604, 1366 cm^{-1}; ^{1}H-NMR (300 MHz): δ 7.91 (dd, 1H, *J* = 7.7, 1.6 Hz), 7.37 (ddd, 1H *J* = 8.8, 7.1, 1.6 Hz), 6.71 (d, 1H, *J* = 8.4 Hz), 6.71 (t, 1H, *J* = 7.1 Hz), 3.04 (d, 2H, *J* = 7.7 Hz), 2.64 (s, 2H), 2.07 (nonet, 1H, *J* = 7.1 Hz), 1.28 (s, 6H), 1.02 (d, 6H, *J* = 6.6 Hz); ^{13}C-NMR (75 MHz): δ 194.0, 151.3, 135.4, 127.5, 120.0, 116.2, 114.4, 58.6, 52.2, 52.1, 27.7, 25.1 (br, 2C), 20.5 (2C); ms: *m/z* 188 ($M^+ - C_3H_7$). *Anal* Calcd $C_{15}H_{21}NO$: C, 77.92; H, 9.09; N, 6.06. Found: C, 77.99; H, 9.12; N, 5.97.

Cyclizations of 12. By using the procedure given for the preparation of **14a**, a solution of 89 mg (0.40 mmol) of **12** and 0.48 mmol of the amine in 2.5 mL of dry DMF was heated at 50°C for 24 h. Workup and purification by PTLC showed three major bands.

With benzylamine. Band 1 gave 35 mg (28%) of 1-(2-benzylamino-5-nitrophenyl)-3-methyl-2-buten-1-one (**17a**) as a light yellow solid, mp 92–94°C. IR: 3265, 1644, 1609, 1505, 1328 cm^{-1}; ^{1}H-NMR (300 MHz): δ 10.1 (br s, 1H), 8.77 (d, 1H, *J* = 2.7 Hz), 8.13 (dd, 1H, *J* = 9.4, 2.7 Hz), 7.42–7.28 (complex, 5H), 6.73 (s, 1H), 6.68 (d, 1H, *J* = 9.4 Hz), 4.55 (d, 2H, *J* = 5.5 Hz), 2.13 (s, 3H), 2.05 (s, 3H); ^{13}C-NMR (75 MHz): δ 193.9, 155.9, 154.9, 136.8, 135.6, 129.5, 129.1, 128.9, 127.7, 127.0, 121.6, 117.4, 111.8, 47.0, 27.8, 21.1; ms: *m/z* 219 ($M^+ - C_7H_7$). *Anal*. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.68; H, 5.81; N, 9.03. Found: C, 69.77; H, 5.80; N, 8.96.

Band 2 gave 3 mg (3%) of 2-benzylamino-5-nitroacetophenone (**19a**) as a light yellow solid, mp 85–88°C. IR: 3282, 1648, 1504, 1328 cm^{-1}; ^{1}H-NMR (300 MHz): δ 10.0 (br s, 1H), 8.76 (d, 1H, *J* = 2.7 Hz), 8.16 (dd, 1H, *J* = 9.3, 2.7 Hz), 7.42–7.27 (complex, 5H), 6.69 (d, 1H, *J* = 9.3 Hz), 4.55 (d, 2H, *J* = 6.0 Hz), 2.69 (s, 3H); ^{13}C-NMR (75 MHz): δ 200.6, 154.5, 136.6, 130.0, 129.8, 129.0, 127.8, 127.0, 116.2, 112.0, 47.0, 29.7, 27.9; ms: *m/z* 179 ($M^+ - C_7H_7$). *Anal*. Calcd for $C_{15}H_{14}N_2O_3$: C, 66.67; H, 5.19; N, 10.37. Found: C, 66.70; H, 5.21; N, 10.32.

Band 3 gave 81 mg (65%) of 1-benzyl-2,3-dihydro-2,2-dimethyl-6-nitro-4(1*H*)-quinolinone (**21a**) as a light yellow solid, mp 137–138°C. IR: 1691, 1506, 1323 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.77 (d, 1H, *J* = 2.7 Hz), 8.08 (dd, 1H, *J* = 9.4, 2.7 Hz), 7.44–7.26 (complex, 5H), 6.57 (d, 1H, *J* = 9.4 Hz), 4.71 (s, 2H), 2.83 (s, 2H), 1.40 (s, 6H); ^{13}C-NMR (75 MHz): δ 191.7, 153.9, 137.9, 136.7, 130.1, 129.1, 127.6, 125.5, 124.0, 118.2, 114.4, 59.2, 51.1, 49.5, 25.1 (2C); ms: *m/z* 295 ($M^+ - CH_3$). *Anal*. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.68; H, 5.81; N, 9.03. Found: C, 69.72; H, 5.79; N, 9.01.

With hexylamine. Band 1 gave 23 mg (19%) of 1-(2-hexylamino-5-nitrophenyl)-3-methyl-2-buten-1-one (**17b**) as a yellow oil that crystallized on standing, mp 44–46°C. IR: 3262, 1644, 1610, 1505, 1327 cm^{-1}; ^{1}H-NMR (300 MHz): δ 9.72 (br s, 1H), 8.74 (d, 1H *J* = 2.7 Hz), 8.18 (dd, 1H, *J* = 9.4, 2.7 Hz), 6.69 (d, 1H, *J* = 9.4 Hz), 6.69 (s, 1H), 3.30 (dt, 2H, *J* = 7.1, 5.5 Hz), 2.12 (d, 3H, *J* = 1.1 Hz), 2.04 (s, 3H), 1.73 (quintet, 2H, *J* = 7.1 Hz), 1.50–1.22 (complex, 6H), 0.91 (distorted t, 3H, *J* = 6.8 Hz); ^{13}C-NMR (75 MHz): δ 194.0, 155.2, 155.1, 135.0, 129.6, 129.4, 121.8, 117.1, 111.2, 43.1, 31.4, 28.8, 27.7, 26.7, 22.5, 21.0, 14.0; ms: *m/z* 233 ($M^+ - C_5H_{11}$). *Anal*. Calcd for $C_{17}H_{24}N_2O_3$: 67.11; H, 7.89; N, 9.21. Found: C, 67.15; H, 7.93; N, 9.16.

Band 2 gave 4 mg (4%) of 2-hexylamino-5-nitroacetophenone (**19b**) as a yellow oil that crystallized on standing, mp 46–48°C. IR: 3276, 1648, 1502, 1329 cm^{-1}; ^{1}H-NMR (300 MHz): δ 9.66 (br s, 1H), 8.73 (d, 1H, *J* = 2.7 Hz), 8.20 (dd, 1H, *J* = 9.4, 2.7 Hz), 6.71 (d, 1H, *J* = 9.4 Hz), 3.30 (dt, 2H, *J* = 7.1, 5.5 Hz), 2.67 (s, 3H), 1.72 (quintet, 2H, *J* = 7.1 Hz), 1.51–1.24 (complex, 6H), 0.91 (distorted t, 3H, *J* = 6.6 Hz); ^{13}C-NMR (75 MHz): δ 200.4, 154.7, 135.0, 130.1, 130.0, 115.6, 111.5, 43.0, 31.4, 28.7, 27.8, 26.7, 22.5, 14.0; ms: *m/z* 193 ($M^+ - C_5H_{11}$). *Anal*. Calcd for $C_{14}H_{20}N_2O_3$: C, 63.64; H, 7.58; N, 10.61. Found: C, 63.71; H, 7.62; N, 10.54.

Band 3 gave 83 mg (68%) of 1-hexyl-2,3-dihydro-2,2-dimethyl-6-nitro-4(1*H*)-quinolinone (**21b**) as a light yellow solid, mp: 78–79°C. IR: 1691, 1503, 1322 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.74 (d, 1H, *J* = 2.8 Hz), 8.19 (dd, 1H, *J* = 9.4, 2.8 Hz), 6.70 (d, 1H, *J* = 9.4 Hz), 3.39 (distorted t, 2H, *J* = 8.2 Hz), 2.68 (s, 2H), 1.71 (quintet, 2H, *J* = 7.7 Hz), 1.48–1.34 (complex, 6H), 1.38 (s, 6H), 0.94 (distorted t, 3H, *J* = 6.8 Hz); ^{13}C-NMR (75 MHz): δ 191.7, 153.3, 137.2, 130.1, 124.4, 117.8, 113.2, 58.7, 51.5, 45.9, 31.4, 29.1, 26.6, 25.3 (2C), 22.6, 13.9; ms: *m/z* 289 ($M^+ - CH_3$). *Anal*. Calcd for $C_{17}H_{24}N_2O_3$: C, 67.11; H, 7.89; N, 9.21. Found: C, 67.16; H, 7.92; N, 9.13.

With isobutylamine. Band 1 gave 20 mg (18%) of 1-(2-isobutylamino-5-nitrophenyl)-3-methyl-2-buten-1-one (**17c**) as a light yellow solid, mp 75–77°C. IR: 3258, 1643, 1610, 1506, 1327 cm^{-1}; ^{1}H-NMR (300 MHz): δ 9.85 (br s, 1H), 8.74 (d, 1H, *J* = 2.7 Hz), 8.17 (dd, 1H, *J* = 9.3, 2.7 Hz), 6.70 (s, 1H), 6.68 (d, 1H, *J* = 9.3 Hz), 3.13 (t, 2H, *J* = 6.6 Hz), 2.12 (s, 3H), 2.04 (s, 3H), 2.03 (septet, 1H, *J* = 6.6 Hz), 1.06 (d, 6H, *J* = 6.6 Hz); ^{13}C-NMR (75 MHz): δ 194.1, 155.3, 155.2, 134.9, 129.5, 129.4, 121.8, 117.1, 111.2, 50.7, 28.0, 27.7, 21.0, 20.4 (2C); ms: *m/z* 233 ($M^+ - C_3H_7$). *Anal*. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.22; H, 7.25; N, 10.14. Found: C, 65.19; H, 7.23; N, 10.15.

Band 2 gave 6 mg (6%) of 2-isobutylamino-5-nitroacetophenone (**19c**) as a yellow oil that crystallized on standing, mp 44–45°C. IR: 3273, 1652, 1509, 1328 cm^{-1}; ^{1}H-NMR (300 MHz): δ 9.78 (br s, 1H), 8.74 (d, 1H, *J* = 2.7 Hz), 8.20 (dd, 1H, *J* = 9.4, 2.7 Hz), 6.70 (d, 1H, *J* = 9.4 Hz), 3.13 (t, 2H, *J* = 6.6 Hz), 2.67 (s, 3H), 2.01

(septet, 1H, $J = 6.6$ Hz), 1.05 (d, 6H, $J = 7.0$ Hz); ^{13}C-NMR (75 MHz): δ 200.5, 154.9, 135.0, 130.1, 130.0, 115.7, 111.5, 50.7, 28.0, 27.8, 20.3 (2C); ms: *m/z* 193 ($M^+ - C_3H_7$). *Anal*. Calcd for $C_{12}H_{16}N_2O_3$: C, 61.02; H, 6.78; N, 11.86. Found: C, 61.11; H, 6.81; N, 11.78.

Band 3 gave 76 mg (69%) of 2,3-dihydro-1-isobutyl-2,2-dimethyl-6-nitro-4(1*H*)-quinolinone (**21c**) as a light yellow solid, mp 126–127°C. IR: 1690, 1506, 1322 cm^{-1}; ^{1}H-NMR (300 MHz): δ 8.70 (s, 1H, $J = 2.7$ Hz), 8.17 (dd, 1H, $J = 9.3$, 2.7 Hz), 6.79 (d, 1H, $J = 9.3$ Hz), 3.24 (d, 2H, $J = 7.7$ Hz), 2.71 (s, 2H), 2.12 (septet, 1H, $J = 6.6$ Hz), 1.37 (s, 6H), 1.05 (d, 6H, $J = 6.6$ Hz); ^{13}C-NMR (75 MHz): δ 191.8, 154.3, 137.5, 129.7, 124.4, 118.5, 114.5, 59.3, 52.2, 51.3, 28.0, 25.3 (br, 2C), 20.3 (2C); ms: *m/z* 233 ($M^+ - C_3H_7$). *Anal*. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.22; H, 7.25; N, 10.14. Found: C, 65.34; H, 7.25; N, 10.05.

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REFERENCES AND NOTES

[1] Bunce, R. A.; Nago, T. J Heterocycl Chem 2009, 46, 623. Some of the nomenclature given in the Experimental Section of this paper was incorrect in omitting 2,3-dihydro from the names of the final products. These compounds should all have been named as 2,3-dihydro-4(1*H*)-quinolinone derivatives.

[2] Bunce, R. A.; Nammalwar, B. J Heterocycl Chem 2011, 48, 613.

[3] Bunce, R. A.; Nammalwar, B. Org Prep Proced Int 2010, 42, 557.

[4] (a) Bayburt, E. K.; Daanen, J. F.; Gomtsyan, A. R.; Latshaw, S. P.; Lee, C.-H.; Schmidt, R. G. US Pat 20080153871, 2008; Chem Abstr 2008, 149, 104611; (b) Glamkowski, E. J.; Hammer, R. R. L. US Pat 4,786,644, 1988; Chem Abstr 1989, 110, 135097.

[5] (a) Hom, R.; Tucher, J.; Varghese, J.; Shah, N. World Pat WO 2005095326, 2005; Chem Abstr 2005, 143, 386930; (b) Varghese, J.; Maillard, M.; Fang, L.; Tucker, J.; Brogley, L.; Aquino, J.; Bowers, S.; Probst, G.; Tung, J. World Pat WO 2005087714, 2005; Chem Abstr 2005, 143, 326226.

[6] (a) Vicker, N.; Day, J. M.; Bailey, H. V.; Heaton, W.; Gonzalez, A. M. R.; Sharland, C. M.; Reed, M. J.; Purohit, A.; Potter, B. V. L. World Pat WO 2007003934, 2007; Chem Abstr 2007, 146, 142281; (b) Xia, Y.; Yang, Z.-Y.; Bastow, K. F.; Tachibana, Y.; Kuo, S.-C.; Hamel, E.; Hackl, T.; Lee, K.-L. J Med Chem 1998, 41, 1155.

[7] (a) Campbell, D.; Duron, S. G.; Vollrath, B.; Wade, W. World Pat WO 2011156775, 2011; Chem Abstr 2011, 156, 65610; (b) Galley, G.; Groebke Zbinden, K. G.; Norcross, R.; Stalder, H. World Pat WO 2007085558, 2007; Chem Abstr 2007, 147, 841292; (c) Kakihana, M.; Kato, K.; Mori, M.; Yamashita, T. World Pat 2001076629, 2001; Chem Abstr 2001, 135, 313624.

[8] Gerlach, U.; Brendel, J.; Lang, H. J.; Weidmann, K. Eur Pat EP 857,724, 1998; Chem Abstr 1998, 129, 175447.

[9] (a) Roach, S. L.; Hudson, A. R.; Valdez, L. J.; Higuchi, R. I.; Zhi, L.; Vassar, A. C.; Landry-Bayle, A.; Adams, M. E.; Rowley, C. V.; Lamer, R. B.; Grant, V. H. S. World Pat WO 2009103007, 2009; Chem Abstr 2009, 151, 288987; (b) Jones, T. K.; Goldman, M. E.; Pooley, C. L. F.; Winn, D. T.; Edwards, J. E.; West, S. J.; Tegley, C. M.; Zhi, L.; Lawrence, G.; Farmer, L. J.; Davis, R. J. World Pat WO 9619458, 1996; Chem Abstr 1996, 125, 142697.

[10] (a) DeNinno, M. P.; Mularski, C. J.; Ruggeri, R. B.; Wester, R. T. World Pat WO 2000017166, 2000; Chem Abstr 2000, 132, 251081; (b) DeNinno, M. P.; Magnus-Aryitey, G. T.; Ruggeri, R. B.; Wester, R. T. World Pat WO 2000017165, 2000; Chem Abstr 2000, 132, 236999; (c) DeNinno, M. P.; Magnus-Aryitey, G. T.; Ruggeri, R. B.; Wester, R. T. World Pat WO 2000017164, 2000; Chem Abstr 2000, 132, 251080.

[11] Liu, J.; Wang, Y.; Ying, S.; Marshall, D.; Miao, S.; Tonn, G.; Anders, P.; Tocker, J.; Tang, L.; Medina, J. Bioorg Med Chem Lett 2009, 19, 6840.

[12] For a similar approach to 2,3-dihydro-1,8-naphthyridine-4(1*H*)-ones, see Bunce, R. A.; Squires, S. T.; Nammalwar, B. J Org Chem 2013, 78, 2144.

[13] Gale, D. J.; Wilshire, J. F. K. Aust J Chem 1970, 23, 1063.

[14] For a procedure to prepare chromic acid, see Eisenbraun, E. J. In Organic Syntheses; Baumgarten, H. G., Ed.; J Wiley and Sons: New York, 1973; Coll. Vol 5, pp. 310–314.

[15] Use of Jones conditions for unhindered substrates was reported earlier by Shen, W.; Coburn, C. A.; Bornmann, W. G.; Danishefsky, S. J. J Org Chem 1993, 58, 611.

[16] A similar 1,3-transposition has been also been reported from tertiary allylic alcohols using PCC, see Dauben, W. G.; Michno, D. J Org Chem 1977, 42, 682.

[17] (a) Attenburrow, J.; Cameron, A. F. B.; Chapman, J. H.; Evans, R. M.; Hems, B. A.; Jansen, A. B. A.; Walker, T. J Chem Soc 1952, 1094; This same reaction also proceeded using 15 wt% of nano-MnO_2, see (b) Nammalwar, B.; Fortenberry, C.; Bunce, R. A.; Lageshetty, S. K.; Ausman, K. D. Tetrahedron Lett 2013, 54, 2010.

[18] Bergmann, E. D.; Ginsberg, D.; Pappo, R. Org React 1959, 10, 179.

[19] Bunce, R. A.; Nago, T.; Sonobe, N.; Slaughter, L. M. J Heterocycl Chem 2008, 45, 551.

[20] Eliel, E. L.; Wilen, S. H.; Mander, L. N. Stereochemistry of Organic Compounds; Wiley-Interscience: New York, 1994; pp. 682–684.

[21] A control experiment with 2-fluoroacetophenone was not reactive toward intermolecular S_NAr-type addition by alkylamines at 50°C, even after 5 days, while 2-fluoro-5-nitroacetophenone gave facile addition at 50°C after 1 h, Bunce, R. A.; Nago, T., unpublished results.

[22] This reversal of reaction steps has been observed in other hindered substrates, see Bunce, R. A.; Lee, E. J. J Heterocycl Chem 2010, 47, 1176.

[23] Stabilization of a hydrogen-bonded adduct following an initial S_NAr addition has been observed in a previous report, see Bunce, R. A.; Grant, M. T. Org Prep Proced Int 2011, 43, 265.