Substituted 4-Oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic Esters by a Tandem Imine Addition-S_NAr Reaction

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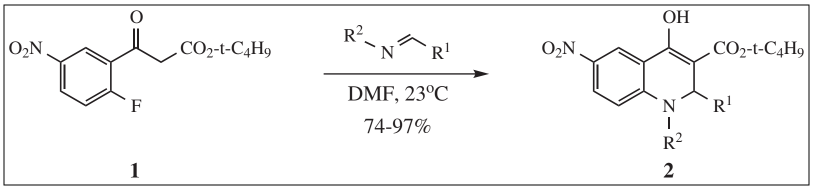

A tandem imine addition-S_NAr annulation reaction has been developed as a new approach to the synthesis of 4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic esters. A series of these structures has been generated by reacting selected imines with *tert*-butyl 2-fluoro-5-nitrobenzoylacetate. Structural variations in the final products are accomplished by changing the substituents on the imine and the alkyl group of the ester. The title compounds are isolated as their enols in 55–97% yield without the need for added base or catalysts. The synthesis of the starting materials as well as mechanistic studies and further synthetic conversions of the products are presented.

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INTRODUCTION

Our recent work has described two new approaches to the synthesis of 4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic esters and related structures using tandem Michael-S_NAr [1,2] and Michael addition-elimination-S_NAr processes [3,4]. In the current study, it was envisioned that highly substituted 4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic esters could be prepared by reacting *tert*-butyl 2-fluoro-3-nitrobenzoyl acetate (**1**) with a series of imines via a tandem imine addition-S_NAr reaction. These heterocycles have potential as cannabinoid CB_2 receptor ligands [5] and as glycogen synthase kinase-3 (GSK-3) inhibitors [6]. The cannabinoid CB_2 receptors are believed to be important in the alleviation of pain [7] and inflammation [8] as well as for treating certain cancers [9]. GSK-3 inhibition has been investigated as a possible treatment for Alzheimer's disease [6].

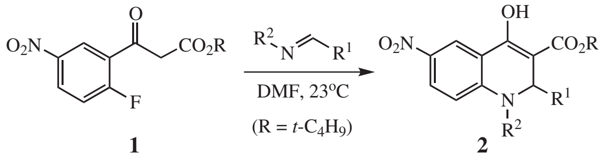
Tandem reactions using imines are relatively rare in the literature and, generally, require the use of catalysts to facilitate the reaction. Additions to imines have been key steps in tandem processes used to prepare chiral piperidinones [10], fused-ring pyridines [11], 2-alkylidene-1,2,3,4-tetrahydropyrimidines [12], and 2,3-disubstituted cyclopentanones [13]. The current reaction proposes to utilize a selection of imines in a tandem sequence to prepare (±)-1,2-dialkyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic esters.

A number of synthetic routes to 1-alkyl-4-oxo-1,4-dihydroquinoline-3-carboxylic esters and 1,2-dialkyl-4-oxo-1,4-dihydroquinoline-3-carboxylic esters have been described [14–18], but approaches to 1,2-dialkyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic esters have been limited. To date, the latter structures have been the subject of only one report involving addition of a cuprate to 1-alkyl-4-oxo-1,4-dihydroquinoline-3-carboxylates, and this afforded the target heterocycles in 44–88% yields [19]. The current procedure, involving a tandem imine addition-S_NAr sequence, represents a fundamentally new approach to this important ring system.

RESULTS AND DISCUSSION

tert-Butyl 2-fluoro-5-nitrobenzoylacetate (**1**) was prepared by modification of a previously reported method [17]. [*Note*: The ethyl and methyl β-ketoesters were also prepared and reacted, but the *tert*-butyl ester proved more synthetically versatile for subsequent transformations.] As with other tandem processes involving S_NAr reactions [1,3], the aromatic moiety of the β-ketoester required appropriate substitution to activate it toward nucleophilic addition. The method was envisioned to begin with the preparation of the imine, followed immediately by reaction with the β-ketoester, all in dry DMF solvent. The annulation sequence would proceed by addition of the enol (without base) or enolate (with base) of the β-ketoester to the imine followed by capture of the resulting secondary amine in an S_NAr reaction.

The results of our cyclization study are summarized in Figure 1. The reactions were performed by generating the imine in DMF [20], adding β-ketoester **1**, and stirring at 23°C for 6 h. Two entries (**j** and **k**) required heating for complete conversion to the imine. In these cases, the amine and the aldehyde were refluxed in benzene for 12 h, the solvent was replaced by DMF, and the cyclization was carried out using the standard protocol. Our exploratory



Entry	R^1	R^2	Method [a]	Product	Yield (%)
a	Ph	$PhCH_2$	A	**2a**	92
b	Ph	n-C_6H_{13}	A	**2b**	93
c	Ph	i-C_4H_9	A	**2c**	95
d	Ph	c-C_3H_5	A	**2d**	80
e	Ph	C_3H_5	A	**2e**	75
f	Ph	Ph	A	**2f**	74
g	4-CH_3OPh	$PhCH_2$	A	**2g**	82
h	4-FPh	$PhCH_2$	A	**2h**	97
i	4-CF_3Ph	$PhCH_2$	A	**2i**	92
j	3,4-(CH_2O_2)Ph	$PhCH_2$	B	**2j**	74
k	PhCH=CH	$PhCH_2$	B	**2k**	74
l	CH_3	$PhCH_2$	C	**2l**	92
m	CH_3	n-C_6H_{13}	C	**2m**	97
n	CH_3	i-C_4H_9	C	**2n**	81
o	CH_3	c-C_3H_5	C	**2o**	75
p	CH_3	C_3H_5	C	**2p**	74

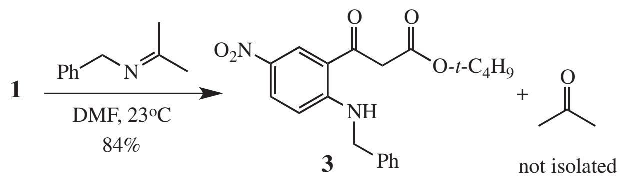
[a] Method A: The imine was generated from the aldehyde and the amine in DMF at 23°C for 6 h; Method B: The imine was formed in refluxing benzene and the solvent was changed to DMF prior to cyclization; Method C: The same as Method A with 4-Å molecular sieves added to facilitate imine formation.

Figure 1. Cyclizations by tandem imine addition-SNAr reaction.

studies determined that neither base nor heat was necessary for the annulation reaction. Isolation of products **2a–2k** from aromatic aldehydes was accomplished by extractive work up followed by trituration of the crude product in ether. Heterocycles **2l–2p**, derived from aliphatic aldehydes, required chromatography prior to trituration.

We began our study using the *N*-benzylimine of benzaldehyde since this imine is stabilized by conjugation [21]. Subsequent studies looked at a series of imines derived from other aromatic aldehydes as well as acetaldehyde. Imines derived from aromatic aldehydes formed readily in DMF at 23°C, whereas those prepared from acetaldehyde required the addition of powdered 4-Å molecular sieves to ensure complete conversion [22,23]. The annulation was successful for all of the aldimines employed, but attempts to extend this process to the *N*-benzylimine of acetone failed, even when the imine was isolated and purified [24]. Presumably, steric hindrance in the ketimine prevented the initial addition, and the annulation could not occur. The only product isolated from this reaction was the benzylamine addition product **3** (keto form) in 84% yield (Scheme 1). This product could arise from reversion of the ketimine back to the starting materials and S_NAr of the free amine with the aromatic moiety of the ketoester. Although every

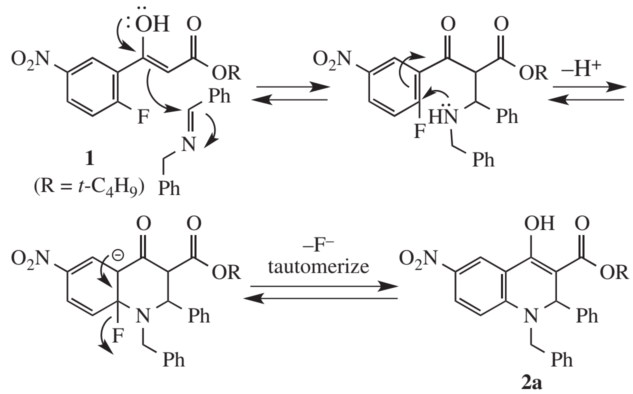
Scheme 1



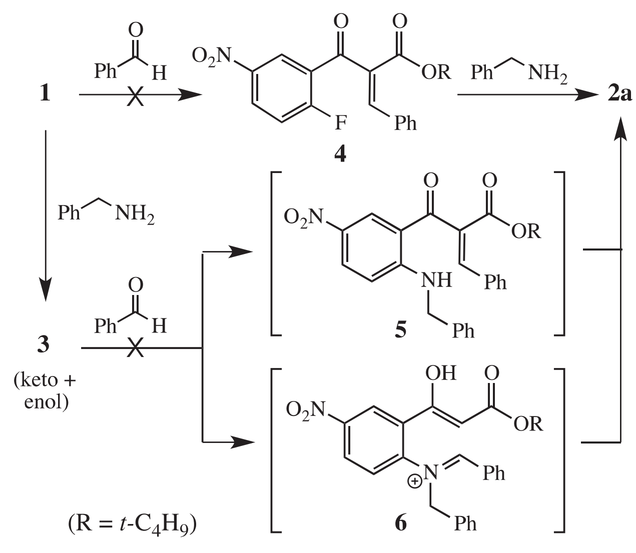
effort was made to maintain anhydrous conditions, there was apparently sufficient water associated with the β-ketoester to promote conversion of the imine back to the starting materials.

The mechanism of the reaction was assumed to involve attack of enol ester **1** on the imine followed by addition of the resulting amine to the activated aromatic ring (Scheme 2), but three other scenarios involving hydrolysis of the imine and recombination by alternate sequences were also possible (Scheme 3). In the first, benzaldehyde would undergo condensation with the ketoester to give **4**, followed by sequential

Scheme 2



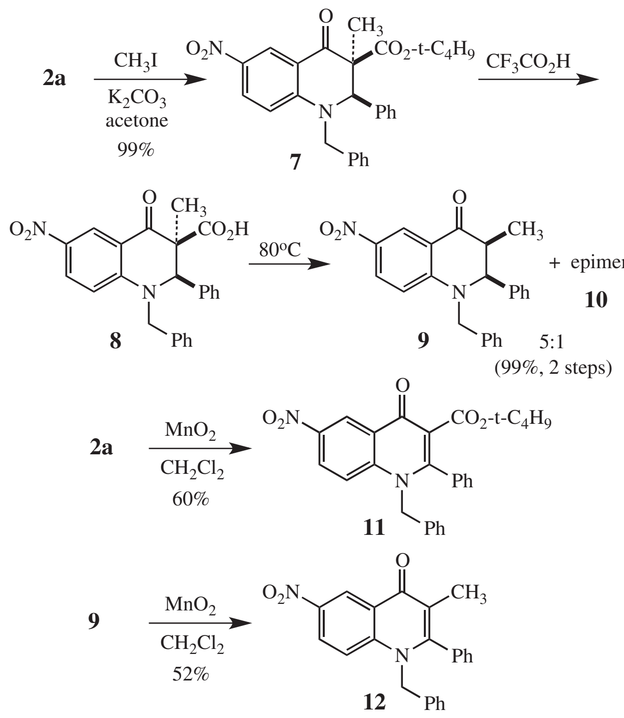
Scheme 3



addition of the amine to the enone and the aromatic ring. This possibility was discounted by considering that the aldol is slow relative to addition of the amine to the doubly activated aromatic ring and that the Michael-S_NAr sequence typically requires mild heating [1,2]. The remaining options were similar to each other but differed in the sequence of events. In one, addition of the amine to the aromatic ring and condensation of benzaldehyde with the ketoester would give **5**, which could then cyclize by an intramolecular conjugate addition to the polarized double bond. In the second, benzaldehyde would condense with the nitrogen of the amine-aromatic addition product **3**, and the enol of the ketoester would add to the resulting iminium intermediate **6**. Both of these routes were ruled out by stirring **3** with benzaldehyde under the standard conditions at 23°C. In each case, the reactants were isolated unchanged from the reaction. Thus, the original formulation for the reaction chronology appears to be correct.

To demonstrate the synthetic potential of this annulation, several transformations of **2a** were explored to elaborate the initial cyclic enol product – alkylation, decarboxylation, and double bond migration. Alkylation of **2a** would be expected to yield the product having a *trans* orientation between the C3 alkyl and the C2 phenyl [25]. Subsequent cleavage of the *tert*-butyl ester and decarboxylation under acidic conditions would then generate the enol intermediate, which should undergo protonation *trans* to the C2 phenyl to yield the *cis*-2,3-disubstituted heterocycle. Finally, double bond migration of the initial enol product to give the conjugated ketone should also be possible (Scheme 4).

Scheme 4



The alkylation was carried out by dissolving 1 equivalent of enol **2a** in acetone, adding 6.6 equivalents of anhydrous potassium carbonate followed by 4.4 equivalents of methyl iodide, and stirring for 1.5 h. The only product observed (in 99% yield) was the C3 alkylation product **7** with the methyl group *trans* to the C2 substituent. Because the alkylation site is quite hindered, other alkylating agents (e.g., allyl bromide and benzyl bromide) yielded 10–20% of the *O*-alkylated product as well. The *O*-alkylation products were difficult to obtain in pure form, but were readily identified by NMR analysis.

Once alkylated, exposure of ester **7** to trifluoroacetic acid gave the corresponding carboxylic acid **8**, which was directly decarboxylated by heating at 80°C for 45 min to give a 5:1 mixture of **9** and **10**. The overall yield for these two steps was nearly 99%. As predicted, the major product **9**, isolated in 74% yield, had the *cis* orientation between the C2 and C3 substituents, and this has been established by X-ray analysis [26] (see Experimental section). The minor product **10** was detected by ^{1}H NMR, but could not be isolated free from contamination by **9**.

Finally, migration of the enol double bond in **2a** to give the enone **11** proved to be more challenging. Standard methods, such as treatment with palladium(II) acetate [27], bromine followed by triethylamine [28], and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone [29] failed to give more than a trace of the desired product. However, treatment of the enol with a 10-fold excess (by weight) of manganese(IV) oxide [20,31] in dichloromethane afforded the enone product in 60% yield after 72 h. It was also found that manganese(IV) oxide could be used to convert **9** to its corresponding enone **12** as well, although we did not explore the use of other reagents for this transformation.

CONCLUSION

We have developed a novel tandem imine addition-S_NAr annulation sequence for the production of highly substituted 4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic esters starting from readily available starting materials. The reaction involved pre-forming the imine and reacting it directly with *tert*-butyl 2-fluoro-5-nitrobenzoylacetate in DMF at 23°C. The annulation was successful with imines derived from aromatic and aliphatic aldehydes, but failed with imines derived from more hindered ketones. Variation at N1 and C2 of the products was possible by altering the imine substituents. Additionally, examination of several alkyl esters revealed the *tert*-butyl ester to be the most versatile for subsequent transformations. Finally, alkylation, dealkoxycarbonylation, and double bond migration studies using **2a** were performed to demonstrate the synthetic potential of the method. We are continuing our work to expand the scope and utility of this reaction.

EXPERIMENTAL

All reactions were run under N_2 (unless otherwise stated) in oven-dried glassware. Anhydrous solvents were used in all reactions. Powdered 4-Å molecular sieves were dried at 300°C under vacuum for 6 h and stored under dry N_2. Flash column chromatography [32] was performed on silica gel (Davisil®, grade 62, 60–200 mesh) containing 2% UV-active phosphor (Sorbent Technologies No. UV-05) packed into quartz columns. Band elution 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 $CDCl_3$ at 300 and 75 MHz, respectively, using tetramethylsilane as the internal standard; coupling constants (*J*) are given in Hertz.

***tert*-Butyl 2-fluoro-5-nitrobenzoylacetate (1).** The general procedure of Domagala [17] was modified. To a solution of 4.76 g (25.7 mmol) of 2-fluoro-5-nitrobenzoic acid in 100 mL of benzene was added 5.35 g (3.28 mL, 45.0 mmol) of thionyl chloride dropwise over 45 min, and the reaction was heated at reflux under a drying tube for 12 h. The reaction was cooled and concentrated under vacuum to give 5.20 g (99%) of the acid chloride as light tan oil that crystallized when stored in the freezer. This acid chloride was used directly in the next step.

A solution of 7.41 g (46.3 mmol) of *tert*-butyl hydrogen malonate and 25 mg of 2,2′-bipyridyl (indicator) in 250 mL of THF was cooled to −30°C using a dry ice-acetonitrile bath. At this temperature, 20.5 mL of 2.25 M *n*-butyllithium in hexanes (46.3 mmol) was added dropwise by syringe over 30 min. Efficient stirring was required to prevent a solid mass from forming. The reaction was warmed to −10°C using an ice-salt water bath and a second 20.5 mL-portion of 2.25 M *n*-butyllithium in hexanes (46.3 mmol) was added dropwise by syringe over 30 min until a red color persisted for 5 min.

The reaction was cooled to −78°C using a dry ice-acetone bath, and a solution of 5.20 g (25.5 mmol) of 2-fluoro-5-nitrobenzoyl chloride in 25 mL of THF was added to the reaction via addition funnel over a 30-min period. The reaction was stirred at −78°C for 30 min and then at −10°C for 30 min. The reaction was poured over approximately 200 g of ice in a 1-L separatory funnel and saturated NH_4Cl was added. The aqueous layer was extracted with dichloromethane (2 × 200 mL), and the combined organic layers were washed once with 5% $NaHCO_3$, once with saturated NaCl, then dried ($MgSO_4$), filtered, and concentrated under vacuum to yield an orange solid. Flash column chromatography on silica gel eluted with 1% ether in hexanes gave 6.84 g (94%) of β-ketoester **1** in its enol form as a white solid, mp 79–81°C. IR: 1613, 1536, 1349 cm^{-1}; ^{1}H NMR: δ 12.9 (br s, 1H), 8.78 (dd, 1H, *J* = 6.6, 2.9), 8.29 (dt, 1H, *J* = 9.5, 3.2), 7.28 (t, 1H, *J* = 9.5), 5.81 (s, 1H), 1.55 (s, 9H); ^{13}C NMR: δ 172.7, 163.6 (d, *J* = 265.1), 162.8, 144.4, 127.0 (d, *J* = 11.2), 125.4 (d, *J* = 4.3), 123.5, 117.6 (d, *J* = 26.1), 95.7 (d, *J* = 14.6), 82.2, 28.2. *Anal.* Calcd for $C_{13}H_{14}FNO_5$: C, 55.07; H, 4.98; N, 4.94. Found: C, 55.08; H, 4.99; N, 4.93.

Representative tandem imine addition-S$_N$Ar reaction with an aromatic imine: *tert*-Butyl (±)-1-benzyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (2a).

Method A. A solution of 0.59 g (0.60 mL, 5.50 mmol) of benzylamine and 0.61 g (0.58 mL, 5.75 mmol) of benzaldehyde in 5 mL of DMF was stirred at 23°C for 6 h. To the resulting mixture was added 1.58 g (5.60 mmol) of solid **1**, resulting in an instantaneous change from colorless to yellow. Stirring at 23°C for an additional 6 h gave a yellow precipitate. The reaction was added to 50 mL of water, and the mixture was extracted with dichloromethane (2 × 15 mL). The combined organic layers were washed once with saturated NaCl, then dried ($MgSO_4$), filtered, and concentrated under vacuum to give a yellow solid. Trituration with a minimum of ether gave 2.32 g (92%) of **2a** as a yellow powder, mp 163–165°C. IR: 1655, 1634, 1505, 1320 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.63 (d, 1H, *J* = 2.6), 7.98 (dd, 1H, *J* = 9.4, 2.6), 7.40–7.18 (complex m, 10H), 6.37 (d, 1H, *J* = 9.4), 5.44 (s, 1H), 4.51 (ABd, 1H, *J* = 16.9), 4.39 (ABd, 1H, *J* = 16.9), 1.36 (s, 9H); ^{13}C NMR: δ 169.8, 160.3, 150.6, 142.0, 137.7, 135.2, 129.0, 128.6, 128.5, 128.4, 127.7, 126.9, 126.4, 121.9, 115.2, 110.9, 98.4, 82.9, 63.0, 52.3, 28.0. *Anal.* Calcd for $C_{27}H_{26}N_2O_5$: C, 70.71; H, 5.71; N, 6.11. Found: C, 70.81; H, 5.74; N, 6.08.

Method B. In some cases, the imine was not completely formed in DMF at 23°C even in the presence of 4-Å molecular sieves. In these cases, the imine was generated by refluxing a solution of 1.00 mmol of the amine with 1.10 mmol of the aldehyde in 15 mL of benzene for 24 h using a Dean–Stark trap to remove water. The reaction was cooled, and the solvent evaporated under vacuum. The resulting imine was dissolved in 3 mL of DMF, 0.75 equivalents of β-ketoester was added, and the reaction was completed as describe for M Method A.

***tert*-Butyl (±)-1-hexyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (2b).** Using Method A, 34 mg (44.4 μL, 0.34 mmol) of hexylamine and 38 mg (36.3 μL, 0.36 mmol) of benzaldehyde were converted to the imine, 82 mg (0.29 mmol) of **1** was added and the mixture was stirred for 6 h. Work up and trituration gave 122 mg (93%) of ester **2b** as a yellow solid, mp 151–152°C. IR: 1653, 1629, 1505, 1317 cm^{-1}; ^{1}H NMR: δ 12.5 (br s, 1H), 8.59 (d, 1H, *J* = 2.9), 8.11 (dd, 1H, *J* = 9.3, 2.9), 7.27 (apparent s, 5H), 6.44 (d, 1H, *J* = 9.3), 5.36 (s, 1H), 3.23 (m, 2H), 1.54 (m, 2H), 1.40 (s, 9H), 1.27 (m, 6H), 0.88 (distorted t, 3H, *J* = 6.8); ^{13}C NMR: δ 169.7, 160.2, 150.2, 142.7, 136.8, 128.7, 128.4, 128.3, 126.8, 122.0, 114.4, 109.8, 98.0, 82.7, 63.2, 49.5, 31.3, 28.0, 26.4, 26.2, 22.4, 13.9. *Anal.* Calcd for $C_{26}H_{32}N_2O_5$: C, 68.94; H, 7.13; N, 6.19. Found: C, 69.07; H, 7.16; N, 6.14.

***tert*-Butyl (±)-1-isobutyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (2c).** Using Method A, 73 mg (99 μL, 1.00 mmol) of isobutylamine and 111 mg (106 μL, 1.05 mmol) of benzaldehyde were converted to the imine, 283 mg (1.00 mmol) of **1** was added, and the mixture was stirred for 6 h. Work up and trituration gave 402 mg (95%) of ester **2c** as a yellow solid, mp 134–135°C. IR: 1652, 1628, 1506, 1321 cm^{-1}; ^{1}H NMR: δ 12.5 (br s, 1H), 8.57 (d, 1H, *J* = 2.9), 8.08 (dd, 1H, *J* = 9.3, 2.9), 7.26 (apparent s, 5H), 6.47 (d, 1H, *J* = 9.3), 5.36 (s 1H), 3.29 (dd, 1H, *J* = 14.6, 5.4), 2.79 (dd, 1H, *J* = 14.6, 9.2), 2.10 (m, 1H), 1.43 (s, 9H), 1.06 (d, 3H, *J* = 6.3), 0.94 (d, 3H, *J* = 6.3); ^{13}C NMR: δ 169.7, 160.4, 150.8, 142.0, 137.0, 128.5, 128.4, 128.2, 126.6, 122.1, 114.7, 110.4, 98.1, 82.8, 63.2, 56.1, 28.1, 26.3, 20.01, 19.96. *Anal.* Calcd for $C_{24}H_{28}N_2O_5$: C, 67.84; H, 6.65; N, 6.60. Found: C, 68.01; H, 6.62; N, 6.64.

***tert*-Butyl (±)-1-cyclopropyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (2d).** Using Method A, 11 mg (13 μL, 0.180 mmol) of cyclopropylamine and 20 mg (19 μL, 0.190 mmol) of benzaldehyde were converted to the imine, 51 mg (0.180 mmol) of **1** was added and the reaction was stirred for 6 h. Work up and trituration gave 59 mg (80%) of ester **2d** as a yellow solid, mp 175–176°C. IR: 1655, 1627, 1494, 1322 cm^{-1}; ^{1}H NMR: δ 12.5 (br s, 1H), 8.58 (d, 1H, *J* = 2.9), 8.11 (dd, 1H, *J* = 9.3, 2.9), 7.26 (apparent s, 5H), 6.95 (d, 1H, *J* = 9.3), 5.37 (s, 1H), 2.18 (m, 1H), 1.38 (s, 9H), 1.05 (m, 1H), 0.97 (m, 2H), 0.73 (m, 1H); ^{13}C NMR: δ 169.9, 160.3, 151.7, 140.8, 138.5, 128.4, 128.2, 128.0, 126.8, 121.3, 116.4, 112.7, 99.2, 82.6, 61.6, 29.8, 28.1, 10.9, 7.9. *Anal.* Calcd for $C_{23}H_{24}N_2O_5$: C, 67.57; H, 5.92; N, 6.86. Found: C, 67.64; H, 5.93; N, 6.81.

***tert*-Butyl (±)-1-allyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (2e).** Using Method A, 11 mg (15 μL, 0.180 mmol) of allylamine and 20 mg (19 μL, 0.190 mmol) of benzaldehyde were converted to the imine, 51 mg (0.180 mmol) of **1** was added and the reaction was stirred for 6 h. Work up and trituration gave 55 mg (75%) of ester **2e** as a yellow solid, mp 155–156°C. IR: 1656, 1633, 1504, 1320 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.59 (d, 1H, *J* = 2.4), 8.07 (dd, 1H, *J* = 9.3, 2.4), 7.27 (apparent s, 5H), 6.45 (d, 1H, *J* = 9.3), 5.57 (ddt, 1H, *J* = 15.6, 10.3, 5.4), 5.38 (s, 1H), 5.19 (d, 1H, *J* = 15.6), 5.18 (d, 1H, *J* = 10.3), 3.93 (ABdd, 1H, *J* = 17.1, 4.9), 3.83 (ABdd, 1H, *J* = 17.1, 4.9), 1.39 (s, 9H); ^{13}C NMR: δ 169.7, 160.2, 150.3, 142.3, 137.5, 131.3, 128.6, 128.5, 128.4, 127.0, 121.9, 117.8, 114.7, 110.5, 98.2, 82.8, 63.0, 51.7, 28.1. *Anal.* Calcd for $C_{23}H_{24}N_2O_5$: C, 67.57; H, 5.92; N, 6.86. Found: C, 67.72; H, 5.95; N, 6.79.

***tert*-Butyl (±)-6-nitro-4-oxo-1,2-diphenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (2f).** Using Method A, 93 mg (91 μL, 1.00 mmol) of aniline and 111 mg (106 μL, 1.05 mmol) of benzaldehyde were converted to the imine, 283 mg (1.00 mmol) of **1** was added and the reaction was stirred for 6 h. Work up and trituration as earlier gave 162 mg (74%) of ester **2f** as a yellow solid, mp 154–156°C. IR: 1652, 1631, 1494, 1319 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.65 (d, 1H, *J* = 2.9), 7.91 (dd, 1H, *J* = 9.3, 2.9), 7.36 (m, 3H), 7.25 (m, 3H), 7.16 (m, 2H), 6.93 (d, 2H, *J* = 6.8), 6.23 (d, 1H, *J* = 9.3), 5.58 (s, 1H), 1.37 (s, 9H); ^{13}C NMR: δ 169.7, 160.2, 150.6, 142.9, 142.7, 138.2, 130.1, 129.2, 128.4, 128.2, 127.8, 126.9, 126.5, 122.0, 115.1, 113.3, 98.3, 82.9, 64.5, 28.0. *Anal.* Calcd for $C_{26}H_{24}N_2O_5$: C, 70.19; H, 5.44; N, 6.30. Found: C, 70.07; H, 5.42; N, 6.23.

***tert*-Butyl (±)-1-benzyl-2-(4-methoxyphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2g).** Using Method A, 27 mg (27 μL, 0.25 mmol) of benzylamine and 36 mg (32 μL, 0.26 mmol) of 4-methoxybenzaldehyde were converted to the imine, 71 mg (0.25 mmol) of **1** was added and the reaction was stirred for 6 h. Work up and trituration gave 100 mg (82%) of ester **2g** as a yellow solid, mp 161–164°C. IR: 2838, 1655, 1633, 1510, 1320 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.61 (d, 1H, *J* = 2.6), 7.98 (dd, 1H, *J* = 9.4, 2.6), 7.32 (d, 2H, *J* = 8.5), 7.30 (m, 2H), 7.20 (m, 3H), 6.80 (d, 2H, *J* = 8.5), 6.36 (d, 1H, *J* = 9.4), 5.39 (s, 1H), 4.49 (ABd, 1H, *J* = 16.9), 4.39 (ABd, 1H, *J* = 16.9), 3.78 (s, 3H), 1.37 (s, 9H); ^{13}C NMR: δ 169.8, 160.1, 159.6, 150.5, 137.7, 135.3, 134.4, 128.9, 128.6, 128.2, 127.7, 126.4, 121.9, 115.1, 113.8, 110.9, 98.6, 82.8, 62.3, 55.3, 52.2, 28.1. *Anal.* Calcd for $C_{28}H_{28}N_2O_6$: C, 68.78; H, 5.78; N, 5.73. Found: C, 68.88; H, 5.82; N, 5.64.

***tert*-Butyl (±)-1-benzyl-2-(4-fluorophenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2h).** Using Method A, 27 mg (27 μL, 0.25 mmol) of benzylamine and 33 mg (28 μL, 0.26 mmol) of 4-fluorobenzaldehyde were converted to the imine, 71 mg (0.25 mmol) of **1** was added and the reaction was stirred for 6 h. Work up and trituration gave 115 mg (97%) of ester **2h** as a yellow solid, mp 165–166°C. IR: 1655, 1632, 1506, 1321 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.63 (d, 1H, *J* = 2.6), 8.00 (dd, 1H, *J* = 9.4, 2.6), 7.42–7.16 (m, 7H), 6.97 (t, 2H, *J* = 8.5), 6.39 (d, 1H, *J* = 9.4), 5.43 (s, 1H), 4.51 (ABd, 1H, *J* = 17.1), 4.37 (ABd, 1H, *J* = 17.1), 1.36 (s, 9H); ^{13}C NMR: δ 169.9, 162.7 (d, *J* = 247.9) 160.4, 150.4, 142.0, 138.0, 135.1, 129.0, 128.6 (d, *J* = 7.7), 127.8, 127.0, 126.4, 122.0, 115.2 (d, *J* = 16.6), 115.1, 111.0, 98.3, 83.0, 62.2, 52.4, 28.1. *Anal.* Calcd for $C_{27}H_{25}FN_2O_5$: C, 67.99; H, 5.29; N, 5.88. Found: C, 68.07; H, 5.27; N, 5.79.

***tert*-Butyl (±)-1-benzyl-2-(4-trifluoromethylphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydro-quinoline-3-carboxylate (2i).** Using Method A, 27 mg (27 μL, 0.25 mmol) of benzylamine and 46 mg (36 μL, 0.26 mmol) of 4-(trifluoromethyl)benzaldehyde were converted to the imine, 71 mg (0.25 mmol) of **1** was added, and the reaction was stirred for 6 h. Work up and trituration gave 120 mg (92%) of ester **2i** as a yellow solid, mp 161–163°C. IR: 1659, 1629, 1506, 1321 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.63 (d, 1H, *J* = 2.4), 8.01 (dd, 1H, *J* = 9.3, 2.4), 7.55 (d, 2H, *J* = 8.3), 7.39 (d, 2H, *J* = 8.3), 7.31 (m, 3H), 7.19 (d, 2H, *J* = 6.8), 6.44 (d, 1H, *J* = 9.3), 5.53 (s, 1H), 4.55 (ABd, 1H, *J* = 17.1), 4.36 (ABd, 1H, *J* = 17.1), 1.38 (s, 9H); ^{13}C NMR: δ 169.4, 160.7, 150.4, 145.7, 138.1, 134.5, 130.6 (q, *J* = 32.6) 129.0, 128.8, 127.9, 127.2, 126.4, 125.6, 123.7 (q, *J* = 260.5), 122.0, 115.1, 111.1, 97.8, 83.3, 62.4, 52.7, 28.1. *Anal.* Calcd for $C_{28}H_{25}F_3N_2O_5$: C, 63.82; H, 4.79; N, 5.32. Found: C, 63.97; H, 4.85; N, 5.25.

***tert*-Butyl (±)-1-benzyl-2-(3,4-methylenedioxyphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydro-quinoline-3-carboxylate (2j).** Using Method B, 107 mg (109 μL, 1.00 mmol) of benzylamine and 158 mg (1.05 mmol) of piperonal were converted to the imine and reacted with 212 mg (0.75 mmol) of **1** for 8 h. Work up and trituration gave 279 mg (74%) of ester **2j** as a yellow solid, mp 154–156°C. IR: 1658, 1633, 1504, 1321 cm^{-1}; ^{1}H NMR: δ 12.6 (br s, 1H), 8.60 (d, 1H, *J* = 2.4), 7.97 (dd, 1H, *J* = 9.3, 2.4), 7.32 (m, 3H), 7.21 (d, 2H, *J* = 6.8), 6.73 (m, 3H), 6.38 (d, 1H, *J* = 9.3), 5.93 (s, 2H), 5.37 (s, 1H), 4.53 (ABd, 1H, *J* = 17.1), 4.42 (ABd, 1H, *J* = 17.1), 1.39 (s, 9H); ^{13}C NMR: δ 169.7, 160.1, 150.4, 147.9, 147.6, 137.7, 136.0, 135.2, 128.9, 128.5, 127.7, 126.4, 121.9, 120.5, 115.0, 110.9, 107.7, 107.1, 101.2, 98.3, 82.9, 62.6, 52.1, 28.1. *Anal.* Calcd for $C_{28}H_{26}N_2O_6$: C, 66.86; H, 5.21; N, 5.57. Found: C, 66.91; H, 5.22; N, 5.52.

***tert*-Butyl (±)-1-benzyl-2-(2-phenylethenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2k).** Using Method B, 107 mg (109 μL, 1.00 mmol) of benzylamine and 139 mg (132 μL, 1.05 mmol) of cinnamaldehyde were converted to the imine and reacted with 212 mg (0.75 mmol) of **1** for 8 h. Work up and trituration gave 269 mg (74%) of ester **2k** as a yellow solid, mp 167–168°C. IR: 1651, 1631, 1501, 1319 cm^{-1}; ^{1}H NMR: δ 12.5 (br s, 1H), 8.58 (d, 1H, *J* = 2.8), 8.01 (dd, 1H, *J* = 9.1, 2.8), 7.42–7.24 (complex m, 10H), 6.46 (d, 1H, *J* = 9.1), 6.42 (d, 1H, *J* = 15.5), 6.16 (dd, 1H, *J* = 15.5, 8.3), 4.98 (d, 1H, *J* = 8.3), 4.69 (ABd, 1H, *J* = 16.6), 4.55 (ABd, 1H, *J* = 16.6), 1.48 (s, 9H); ^{13}C NMR: δ 172.2, 160.9, 150.6, 135.8, 135.5, 131.1, 129.0, 128.7, 128.4, 128.2, 127.8, 126.6, 126.5, 126.3, 122.0, 115.7, 111.4, 100.0, 96.5, 82.7, 61.4, 52.5, 28.3. *Anal.* Calcd for $C_{29}H_{28}N_2O_5$: C, 71.82; H, 5.82; N, 5.78. Found: C, 71.91; H, 5.86; N, 5.65.

Representative tandem imine addition-S_NAr reaction with an aliphatic imine: *tert*-butyl (±)-1-benzyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2l).

Method C. A solution of 107 mg (109 μL, 1.00 mmol) of benzylamine and 53 mg (68 μL, 1.20 mmol) of acetaldehyde in 3 mL of DMF containing 25 mg of 4-Å molecular sieves was stirred at 23°C for 6 h. To the resulting mixture was added 283 mg (1.00 mmol) of solid **1**, resulting in an instantaneous change from colorless to orange. The reaction was stirred for 5 min, the molecular sieves were removed by filtration through a pad of Celite®, the filtrate was added to 50 mL of water, and the mixture was extracted with dichloromethane (2 × 15 mL). The combined organic layers were washed once with saturated NaCl, then dried ($MgSO_4$), filtered, and concentrated under vacuum to give a yellow solid. Purification by flash column chromatography on silica gel using 5–40% ether in hexanes afforded 364 mg (92%) of ester **2l** as a yellow solid, mp 145–147°C. IR: 1655, 1627, 1505, 1317 cm^{-1}; ^{1}H NMR: δ 12.4 (br s, 1H), 8.54 (d, 1H, *J* = 2.4), 7.98 (dd, 1H, *J* = 9.3, 2.4), 7.40–7.22 (complex m, 5H), 6.41 (d, 1H, *J* = 9.3), 4.71 (ABd, 1H, *J* = 16.6), 4.56 (ABd, 1H, *J* = 16.6), 4.52 (q, 1H, *J* = 6.3), 1.52 (s, 9H), 1.26 (d, 3H, *J* = 6.3); ^{13}C NMR: δ 169.6, 160.5, 150.3, 137.6, 135.7, 128.9, 128.0, 127.7, 126.4, 121.7, 115.7, 111.8, 99.1, 82.4, 55.0, 53.3, 28.2, 20.6. *Anal.* Calcd for $C_{22}H_{24}N_2O_5$: C, 66.59; H, 6.10; N, 7.06. Found: C, 66.67; H, 6.15; N, 7.02.

***tert*-Butyl (±)-1-hexyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2m).** Using Method C, 50.5 mg (66 μL, 1.00 mmol) of hexylamine and 53 mg (68 μL, 1.20 mmol) of acetaldehyde were converted to the imine and reacted with 283 mg (1.00 mmol) of **1** for 5 min. Work up and purification gave 378 mg (97%) of ester **2m** as a yellow solid, mp 86–87°C. IR: 1656, 1628, 1505, 1316 cm^{-1}; ^{1}H NMR: δ 12.3 (br s, 1H), 8.50 (d, 1H, *J* = 2.9), 8.08 (dd, 1H, *J* = 9.3, 2.9), 6.49 (d, 1H, *J* = 9.3), 4.43 (q, 1H, *J* = 6.4), 3.53 (dt, 1H, *J* = 14.1, 6.5), 3.23 (dt, 1H, *J* = 15.2, 7.3), 1.66 (m, 2H), 1.56 (s, 9H), 1.35 (m, 6H), 1.21 (d, 3H, *J* = 6.4), 0.91 (distorted t, 3H, *J* = 6.8); ^{13}C NMR: δ 169.6, 160.6, 150.1, 136.9, 128.2, 122.0, 115.2, 110.7, 98.6, 82.3, 54.6, 49.6, 31.4, 28.3, 27.3, 26.5, 22.6, 20.8, 13.9. *Anal.* Calcd for $C_{21}H_{30}N_2O_5$: C, 64.53; H, 7.74; N, 7.17. Found: C, 64.67; H, 7.76; N, 7.05.

***tert*-Butyl (±)-1-isobutyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2n).** Using Method C, 73 mg (100 μL, 1.00 mmol) of isobutylamine and 53 mg (68 μL, 1.20 mmol) of acetaldehyde were converted to the imine and reacted with 283 mg (1.00 mmol) of **1** for 5 min. Work up and purification gave 292 mg (81%) of ester **2n** as a yellow solid, mp 135–136°C. IR: 1651, 1631, 1505, 1317 cm^{-1}; ^{1}H NMR: δ 12.3 (br s, 1H), 8.52 (d, 1H, *J* = 2.9), 8.07 (dd, 1H, *J* = 9.3, 2.9), 6.50 (d, 1H, *J* = 9.3), 4.38 (q, 1H, *J* = 6.4), 3.54 (dd, 1H, *J* = 14.4, 5.1), 2.85 (dd, 1H, *J* = 14.4, 9.5), 2.03 (m, 1H), 1.55 (s, 9H), 1.18 (d, 3H, *J* = 6.4), 1.01 (d, 3H, *J* = 6.8), 0.98 (d, 3H, *J* = 6.8); ^{13}C NMR: δ 169.6, 160.8, 150.4, 136.9, 128.1, 122.1, 115.4, 111.1, 98.6, 82.3, 56.6, 55.1, 28.3, 26.7, 20.1, 19.9. *Anal.* Calcd for $C_{19}H_{26}N_2O_5$: C, 62.91; H, 7.23; N, 7.73. Found: C, 63.07; H, 7.27; N, 7.60.

***tert*-Butyl (±)-1-cyclopropyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2o).** Using Method C, 57 mg (69 μL, 1.00 mmol) of cyclopropylamine and 53 mg (68 μL, 1.20 mmol) of acetaldehyde were converted to the imine and reacted with 283 mg (1.00 mmol) of **1** for 5 min. Work up and purification gave 260 mg (75%) of ester **2o** as a yellow solid, mp 142–143°C. IR: 1654, 1633, 1507, 1322 cm^{-1}; ^{1}H NMR: δ 12.3 (br s, 1H), 8.49 (d, 1H, *J* = 2.4), 8.13 (dd, 1H, *J* = 9.3, 2.4), 7.02 (d, 1H, *J* = 9.3), 4.48 (q, 1H, *J* = 6.4), 2.62 (m, 1H), 1.56 (s, 9H), 1.24 (d, 3H, *J* = 6.4), 1.09 (m, 1H), 0.97 (m, 1H), 0.78 (m, 1H), 0.63 (m, 1H); ^{13}C NMR: δ 169.6, 160.2, 151.9, 138.4, 127,7, 121.2, 116.5, 113.0, 100.2, 82.3, 53.3, 29.4, 28.3, 18.8, 10.5, 7.5. *Anal.* Calcd for $C_{18}H_{22}N_2O_5$: C, 62.36; H, 6.40; N, 8.09; Found: C, 62.32; H, 6.37; N, 8.10.

***tert*-Butyl (±)-1-allyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (2p).** Using Method C, 57 mg (74 μL, 1.00 mmol) of allylamine and 53 mg (68 μL, 1.20 mmol) of acetaldehyde were converted to the imine and reacted with 283 mg (1.00 mmol) of **1** for 5 min. Work up and purification gave 256 mg (74%) of ester **2p** as a yellow solid, mp 99–100°C. IR: 1656, 1631, 1505, 1321 cm^{-1}; ^{1}H NMR: δ 12.3 (br s, 1H), 8.52 (d, 1H, *J* = 2.4), 8.07 (dd, 1H, *J* = 9.3, 2.4), 6.50 (d, 1H, *J* = 9.3), 5.87 (ddt, 1H, *J* = 17.1, 10.3, 5.1), 5.30 (d, 1H, *J* = 17.1), 5.29 (d, 1H, *J* = 10.3), 4.47 (q, 1H, *J* = 6.4), 4.09 (ABdd, 1H, *J* = 17.1, 4.9), 3.97 (ABdd, 1H, *J* = 17.1, 4.9), 1.55 (s, 9H), 1.23 (d, 3H, *J* = 6.4); ^{13}C NMR: δ 169.6, 160.3, 150.2, 137.2, 132.2, 128.0, 121.6, 117.7, 115.2, 111.3, 98.9, 82.4, 54.8, 52.4, 28.2, 21.0. *Anal.* Calcd for $C_{18}H_{22}N_2O_5$: C, 62.36; H, 6.40; N, 8.09. Found: C, 62.47; H, 6.46; N, 7.98.

Attempted addition of *N*-benzylimine of acetone to 1. The imine was prepared on a 10.0-mmol scale as described by Black and Blackman [24], bp 64–67°C at 1.2 mm Hg (lit [24] bp 36°C at 0.07 mm Hg). A solution of 88 mg (0.60 mmol) of the imine in 3 mL of DMF was treated with 142 mg (0.50 mmol) of **1** at 23°C and stirred for 12 h. The crude reaction mixture was added to 50 mL of water and extracted with dichloromethane (2 × 15 mL). The combined organic layers were washed once with saturated NaCl, then dried ($MgSO_4$), filtered, and concentrated under vacuum to give 156 mg (84%) of **5** as a yellow solid, mp 137–138°C. IR: 3297, 1730, 1650, 1504, 1329 cm^{-1}; ^{1}H NMR: δ 9.94 (br t, 1H, *J* = 5.5), 8.71 (d, 1H, *J* = 2.7), 8.16 (dd, 1H, *J* = 9.3, 2.7), 7.41–7.26 (complex m, 5H), 6.72 (d, 1H, *J* = 9.3), 4.56 (d, 2H, *J* = 5.5), 3.98 (s, 2H), 1.49 (s, 9H); ^{13}C NMR: δ 195.2, 166.4, 154.7, 136.4, 135.7, 130.2, 129.5, 129.0, 127.8, 127.0, 115.3, 112.3, 82.5, 48.0, 47.0, 27.9. *Anal.* Calcd for $C_{20}H_{22}N_2O_5$: C, 64.86; H, 5.95; N, 7.57. Found: C, 64.82; H, 5.93; N; 7.61.

***tert*-Butyl (±)-1-benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (7).** In a 100-mL, one-necked, round-bottomed flask, 1.00 g (2.18 mmol) of **2a** in 40 mL of acetone was stirred with 2.00 g (14.4 mmol) of anhydrous potassium carbonate and 1.36 g (0.6 mL, 9.58 mmol) of methyl iodide at 23°C for 1.5 h. The crude reaction mixture was filtered with dichloromethane through a pad of Celite®, 100 mL of water was added to the filtrate, and the mixture was extracted with dichloromethane (2 × 50 mL). The combined organic layers were washed once with saturated NaCl, then dried ($MgSO_4$), filtered, and concentrated to yield 1.01 g (99%) of **7** as a yellow solid, mp 142–144°C. IR: 1723, 1686, 1605, 1508, 1315 cm^{-1}; ^{1}H NMR: δ 8.91 (d, 1H, *J* = 3.0), 8.18 (dd, 1H, *J* = 9.4, 3.0), 7.40–7.32 (m, 4H), 7.31–7.22 (m, 4H), 7.13 (d, 2H, *J* = 7.5), 6.82 (d, 1H, *J* = 9.4), 4.72 (ABd, 1H, *J* = 16.2), 4.51 (s, 1H), 4.25 (ABd, 1H, *J* = 16.2), 1.58 (s, 3H), 1.09 (s, 9H); ^{13}C NMR: δ 189.7, 168.1, 153.0, 138.5, 137.0, 135.3, 130.3, 129.0, 128.8, 128.10, 128.05, 126.9, 125.5, 116.9, 113.4, 82.2, 71.9, 58.5, 53.5, 27.2, 22.8 (one aromatic C unresolved). *Anal.* Calcd for $C_{28}H_{28}N_2O_5$: C, 71.10; H, 5.97; N, 5.93. Found: C, 71.28; H, 6.02; N, 5.81.

(±)-1-Benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (8). In a 50-mL, one-necked, round-bottomed flask, 210 mg (0.44 mmol) of **7** was stirred with 1 mL of trifluoroacetic acid in dichloromethane at 23°C for 1.5 h. The reaction was added to water and extracted with dichloromethane (2 × 15 mL). The organic layer was washed once with saturated NaCl, then dried ($MgSO_4$), filtered, and concentrated to yield 183 mg of **8** as a yellow solid, which was used without purification in the next reaction, mp 78°C (dec). IR: 3500–2417, 1758, 1646, 1510, 1317 cm^{-1}; ^{1}H NMR: δ 12.3 (br s 1H), 8.87 (d, 1H, *J* = 2.6), 8.28 (dd, 1H, *J* = 9.4, 2.6), 7.39 (m 3H), 7.32–7.20 (complex m, 5H), 7.15 (d, 2H, *J* = 7.3), 6.94 (d, 1H, *J* = 9.4), 4.96 (s, 1H), 4.84 (ABd, 1H, *J* = 16.4), 4.31 (ABd, 1H, $J=16.4$), 1.75 (s, 3H); ^{13}C NMR: δ 197.7, 170.5, 153.4, 138.5, 134.9, 134.7, 132.2, 129.6, 129.3, 128.6, 127.6, 126.9, 125.9, 114.7, 113.1, 69.3, 53.9, 53.8, 25.3 (one aromatic C unresolved). *Anal.* Calcd for $C_{24}H_{20}N_2O_5$: C, 69.16; H, 4.84; N, 6.73. Found: C, 69.28; H, 4.86; N, 6.56.

(±)-1-Benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline (9). In a 100-mL, one-necked, round-bottomed flask, 183 mg (0.44 mmol) of acid **8** was heated as a solid at 80°C (oil bath) for 45 min until gas evolution ceased to yield 162 mg (99% for two steps) of a 5:1 mixture of **9** and **10** as a yellow solid. The major product was purified by crystallization from ether-dichloromethane to give 120 mg (74%) of **9** as a yellow solid, mp 159–161°C. IR: 1690, 1509, 1320 cm^{-1}; ^{1}H NMR: δ 8.74 (d, 1H, $J=3.0$), 8.13 (dd, 1H, $J=9.4$, 3.0), 7.44–7.22 (complex m, 8H), 7.07 (d, 2H, $J=7.3$), 6.67 (d, 1H, $J=9.4$), 4.75 (ABd, 1H, $J=17.1$), 4.69 (d, 1H, $J=6.8$), 4.36 (ABd, 1H, $J=17.1$), 3.52 (quintet, 1H, $J=6.8$), 1.05 (d, 3H, $J=6.4$); ^{13}C NMR: δ 193.1, 153.8, 137.7, 135.7, 130.3, 129.2, 129.0, 128.9, 128.0, 127.4, 126.2, 126.0, 124.2, 118.1, 112.2, 68.5, 53.6, 45.2, 10.8. *Anal.* Calcd for $C_{23}H_{20}N_2O_3$: C, 74.11; H, 5.41; N, 7.52. Found: C, 74.42; H, 5.49; N, 7.24. Efforts to purify **10** free from **9** were unsuccessful.

X-ray structure elucidation of (±)-1-benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline (9). Crystals of **9** were obtained as yellow square rods by vapor diffusion of ether into a dichloromethane solution of the compound. A specimen measuring 0.72 × 0.13 × 0.11 mm was mounted on a nylon loop. X-ray intensity data were measured at 296 K on a Bruker SMART APEX II diffractometer (Billerica, MA, 01821 USA). Graphite-monochromated Mo-K(α) radiation (λ = 0.71073 Å, fine-focus sealed tube) was used with the CCD detector placed at 6.0 cm. Data frames were collected in a series of ϕ and ω scans with 0.5° sweeps and 90 s exposure times. Data integration employed the Bruker SAINT software package [26]. Data were corrected for absorption effects using the SADABS multi-scan technique. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using the Bruker SHELXTL software suite. The H atoms were placed in calculated positions and allowed to ride on their carrier atoms with C–H = 0.93–0.96 Å and with $U_{iso} = 1.2\,U\mathrm{eq}(C)$ for CH and CH_2. Refined formula: $C_{23}H_{20}N_2O_3$, $Mr = 372.41$, monoclinic, space group $P2_1/c$, $a = 10.2874(13)$ Å, $b = 14.522(2)$ Å, $c = 13.423(2)$ Å, $\alpha = 90°$, $\beta = 107.823(5)°$, $\gamma = 90°$, $V = 1909.1(4)$ Å^3, $Z=4$, $D_{calcd} = 1.296$ Mg m^{-3}, $\mu = 0.09$ mm^{-1}, $T = 296$ K, 29590 total reflections, 4738 independent reflections ($R_{int} = 0.044$), 3154 reflections with $I > 2\sigma(I)$; Final R $[F^2 > 2\sigma(F^2)] = 0.043$, $wR(F^2) = 0.123$. The ORTEP diagram for **9** is shown in Figure 2. CCDC835949 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

***tert*-Butyl 1-benzyl-6-nitro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (11).** In a 100-mL, one-necked, round-bottomed flask, 298 mg (0.65 mmol) of **2a** was dissolved in 40 mL of dichloromethane. To this was added 3.00 g of manganese(IV) oxide [30], and the reaction was stirred at 23°C for 72 h. The reaction was worked up by filtration through a pad of Celite®, removal of the solvent under vacuum, and flash column chromatography using 30% ether in hexanes to afford 178 mg (60%) of **11** as a yellow powder, mp 89–91°C. IR: 1725, 1630, 1612, 1525, 1343 cm^{-1}; ^{1}H NMR: δ 9.33 (d, 1H, $J=2.9$), 8.30 (dd, 1H, $J=9.3$, 2.9), 7.53–7.26 (complex m, 10H), 6.98 (d, 1H, $J=9.3$), 5.25 (s, 2H), 1.19 (s, 9H); ^{13}C NMR: δ 173.3, 164.0, 152.6, 143.8, 143.6, 134.7, 132.0, 130.3, 129.2, 128.7, 128.5, 128.1, 126.8, 126.6, 125.3, 123.5, 122.2, 118.8, 82.1, 52.5, 27.5. *Anal.* Calcd for $C_{27}H_{24}N_2O_5$: C, 70.97; H, 5.30; N, 6.13. Found: C, 70.88; H, 5.28; N, 6.05.

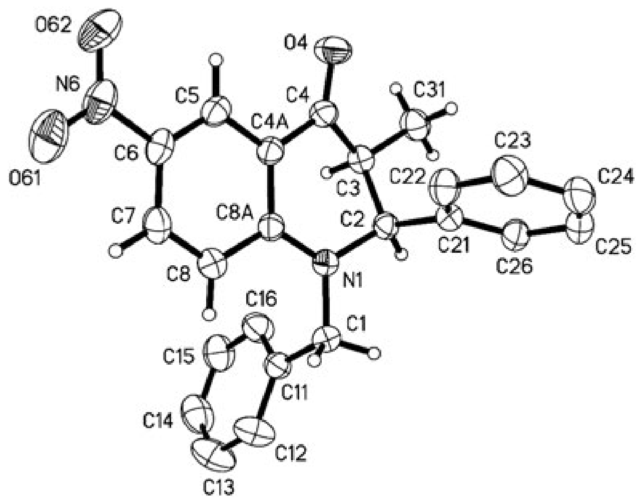


Figure 2. Molecular structure of **9** with 30% probability ellipsoids. The hydrogen atoms on two of the phenyl rings have been removed for clarity.

1-Benzyl-3-methyl-6-nitro-2-phenylquinolin-4(1*H*)-one (12). In a 100-mL, one-necked, round-bottomed flask, 100 mg (0.27 mmol) of **9** was dissolved in 40 mL of dichloromethane. To this was added 1.00 g of manganese(IV) oxide [30], and the reaction was stirred at 23°C for 72 h. The reaction was worked up by filtration through a pad of Celite®, removal of the solvent under vacuum, and flash column chromatography on silica gel using 30% ether in hexanes to afford 52 mg (52%) of **12** as a yellow solid, mp 160–162°C. IR: 1735, 1626, 1608, 1520, 1339 cm^{-1}; ^{1}H NMR: δ 9.36 (d, 1H, $J=2.7$), 8.26 (dd, 1H, $J=9.3$, 2.7), 7.49–7.25 (complex m, 10H), 6.91 (d, 1H, $J=9.3$), 5.22 (s, 2H), 1.87 (s, 3H); ^{13}C NMR: δ 177.0, 152.3, 143.6, 143.0, 135.3, 134.1, 129.7, 129.3, 129.1, 127.9, 127.8, 125.9, 125.2, 124.6, 123.8, 120.7, 118.2, 52.8, 30.3. *Anal.* Calcd for $C_{23}H_{18}N_2O_3$: C, 74.57; H, 4.90; N, 7.57. Found: C, 74.58; H, 4.93; N, 7.52.

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