CSIRO PUBLISHING

Aust. J. Chem. **2012**, *65*, 409–416
http://dx.doi.org/10.1071/CH12025

Full Paper

A New and Efficient Procedure for Friedländer Synthesis of Quinolines in Low Melting Tartaric Acid-Urea Mixtures

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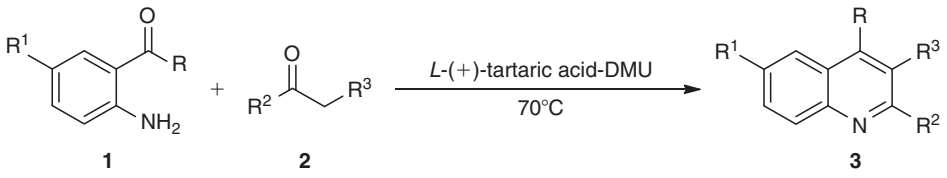
A general, efficient and green method for the synthesis of quinoline derivatives via the Friedländer heteroannulation reaction of 2-aminoaryl ketones and α-methylene ketones has been developed, employing low melting mixtures of *L*-(+)-tartaric acid and urea derivatives as an inexpensive, non-toxic, easily biodegradable reaction medium. The melt acts as both the reaction medium and catalyst, furnishing quinolines in high to excellent yields.

Manuscript received: 19 January 2012.
Manuscript accepted: 24 February 2012.
Published online: 27 March 2012.

Introduction

Quinolines have attracted much attention for their various biological and medicinal properties. Many quinoline derivatives are used as anticancer,[1] antimicrobial,[2] antitubercular,[3] antimalarial,[4] antiviral,[5] radiosensitizing,[6] antibacterial and antifungal agents,[7] as well as selective glucocorticoid receptor agonists.[8] In addition to the medical applications, quinoline derivatives have been employed in the synthesis of fungicides, virucides, biocides, alkaloids, rubber chemicals and flavouring agents. Additionally, they are also used as polymers, catalysts, corrosion inhibitors, preservatives, and as solvent for resins and terpenes. Furthermore, these compounds find applications in chemistry of transition-metal catalyst for uniform polymerization and luminescence chemistry. Quinoline derivatives also act as antifoaming agent in refineries.[9] Therefore, the importance of this heterocyclic motif has promoted the development of practical and diversified synthesis methods.[10] Among them, the Friedländer reaction is still one of the simplest and most powerful tools for the synthesis of quinolines.[11] In its most general and classical form, the Friedländer reaction involves condensation of an aromatic 2-amino-substituted carbonyl compound with an appropriately substituted carbonyl derivative containing a reactive α-methylene group followed by cyclodehydration. Numerous catalysts for the Friedländer reaction have been developed successfully, including ZrO_2,[12] $Cu_3(BTC)_2$ (BTC = benzene-1,3,5-tricarboxylate),[13] cuprous triflate,[14] $Mg(NTf_2)_2$,[15] proline,[16] sulfuric acid-modified PEG-6000,[17] sulfonic acid functionalized ionic liquid,[18] cerium(IV) ammonium nitrate,[19] nanoporous cage-type aluminosilicate AlKIT-5,[20] $GdCl_3 \cdot 6H_2O$,[21] silica gel-supported sodium hydrogen sulfate,[22] 1-butyl-3-methylimidazolium hydrogen sulfate,[23] peptide coupling agent propylphosphonic anhydride (T3P®),[24] *o*-benzenedisulfonimide,[25] $Yb(OTf)_3$,[26] $KHSO_4$,[27] or neodymium(III) nitrate hexahydrate.[28] Unfortunately, these approaches are associated with one or more disadvantages such as the use of harmful organic solvents, harsh reaction conditions, unsatisfactory yields of the products, long reaction times, or non-available and costly reagents.

The application of environmentally friendly solvents such as water,[29] ionic liquids,[30] supercritical fluids,[31] polyethylene glycol,[32] glycerol,[33] and perfluorinated solvents[34] is one of the most important areas of green chemistry. Recently, a low melting eutectic mixture consisting of urea, carbohydrates and inorganic salts has been introduced as a new alternative sustainable solvent for organic transformations.[35] Some organic reactions such as the Stille,[36] Diels-Alder,[37] Heck, or cycloaddition reactions,[38] and the synthesis of 5-hydroxymethylfurfural,[39] and glycosyl ureas[40] have been reported to proceed in these low melting mixtures with excellent yield and selectivity. The peculiar physical and chemical properties of low melting mixtures, such as polarity, low toxicity, non-volatility, biodegradability, low cost, and ready availability from bulk renewable resources without any further modification, prompted us to extend their use as green solvents in organic synthesis. In 2011, Gore et al. introduced *L*-(+)-tartaric acid-DMU (*N,N*-dimethylurea) as a novel and green reaction medium for the synthesis of 3,4-dihydropyrimidin-2-ones.[41] To the best of our knowledge, there are no previous reports for the synthesis of quinoline derivatives by using this eutectic mixture as a reaction medium. As a continuation of our interest in developing efficient and environmentally benign synthetic methodologies,[42] we describe here the use of this eutectic mixture as a green solvent for the synthesis of quinoline derivatives via the Friedländer



Scheme 1. Synthesis of quinoline derivatives in *L*-(+)-tartaric acid-DMU.

reaction of 2-aminoaryl ketones and α-methylene ketones (Scheme 1).

Results and Discussion

The first trials were performed using the model reaction of 2-aminobenzophenone and acetylacetone in various low melting mixtures under catalyst-free conditions. Unfortunately, no reaction proceeded in *D*-(−)-fructose-DMU, lactose-DMU-NH_4Cl, glucose-urea-$CaCl_2$, glucose-urea-NaCl, sucrose-choline chloride, and glucose-guanidinium HCl at their minimal melting temperature. It is also observed that only a trace amount of product was detected under solvent-free conditions at 100°C. Bearing in mind that the Friedländer reaction worked well under acidic or base conditions, we focussed on the melt systems consisting of an organic acid as one of the melt components. Fortunately, the desired condensation reaction eventually took place in *L*-(+)-tartaric acid-choline chloride, giving the corresponding quinoline product in 80 % yield. Further studies showed that the yield could be increased to as high as 92 % when *L*-(+)-tartaric acid-DMU was used. Thus, the use of *L*-(+)-tartaric acid-DMU as the reaction medium not only avoids the disadvantages of conventional organic solvents, such as volatility, inflammability, and potential pollution hazards, but it also results in greatly enhanced reactivity. Moreover, this simple procedure allowed easy scale-up of the reaction, whereby 90 % yield was obtained in the 50-mmol-scale reaction, indicating that the reaction can be successfully performed at large scales without significant loss of the yield.

Based on the above results, this process was then extended to other structurally varied α-methylene ketones to investigate its scope and generality. Representative results are shown in Table 1. It can be seen that under similar conditions, a wide range of ketones containing a reactive α-methylene group can undergo easy condensation with 2-aminobenzophenone to give substituted quinolines with fast reaction times and in high yields. The α-methylene carbonyl compounds used for the preparation of these quinolines include cycloalkanones, 1,3-diketones, and 1,4-diketones. Interestingly, cyclic ketones such as cyclopentanone, cyclohexanone, cycloheptanone, cyclododecanone, 1*H*-inden-2(3*H*)-one and dimedone gave the respective polycyclic quinoline in high yields. When an unsymmetrical 1,3-diketone such as 1-benzoylacetone was used, excellent regioselectivity was obtained (Table 1, entry 2). It is interesting to note that the reaction tolerated an acid sensitive ketal functional group (Table 1, entry 8) and afforded the expected quinoline (**3h**) in good yield. Acyclic β-keto esters such as methyl acetoacetate, ethyl acetoacetate, *iso*-butyl acetoacetate, *tert*-butyl acetoacetate, allyl acetoacetate, and 2-methoxyethyl acetoacetate were examined. The alkoxy moiety present had little influence on the reaction, and generally good yields were obtained.

In addition, when 2-aminobenzophenone was replaced by 1-(2-aminophenyl)ethanone, the reaction also led to the formation of the desired fused quinolines in high yields (Table 1, entries 32–36). The reaction is very clean and free of side products, which are generally formed by self-condensation of ketones under basic conditions.

In conclusion, we have developed an innovative, general, highly efficient, and environmentally-benign method for the Friedländer synthesis of polysubstituted and polycyclic quinolines using low melting mixtures of *L*-(+)-tartaric-DMU as a novel and green reaction medium. This approach presented herein avoids the use of hazardous acids or base, toxic organic solvents, and harsh reaction conditions.

Experimental

Melting points were measured on an X-4 melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FTIR-8900 spectrophotometer. The ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker DRX-500 spectrometer using $CDCl_3$ as solvent and TMS as internal standard. Elemental analyses were carried out on a Vario EL III CHNOS elemental analyzer. All reagents were purchased from commercial suppliers and used without further purification.

*General Procedure for the Preparation of Quinoline Derivatives (**3**)*

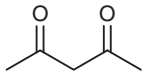
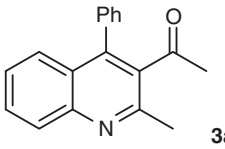
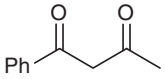
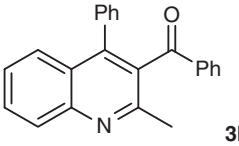
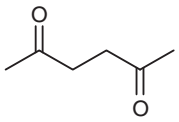
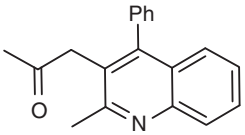
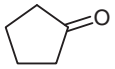
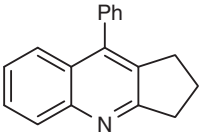
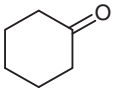
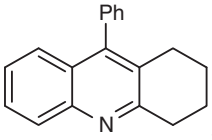
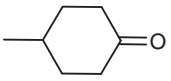
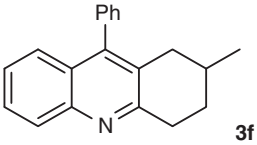
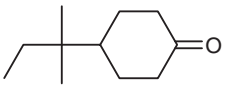
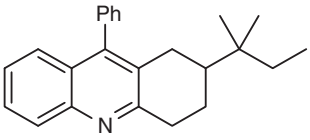
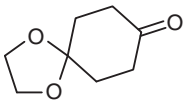
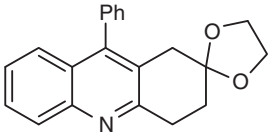
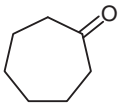
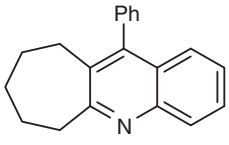
A mixture of 2-aminoaryl ketone (1.0 mmol) and α-methylene ketone (1.0 mmol) in 1.5 g *L*-(+)-tartaric acid-DMU (30 : 70) was stirred at 70°C. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and water was added. The solid product that precipitated out was filtered off, washed with water, and dried to afford the quinolines in good purity. The oily products were extracted with ethyl acetate (2 × 10 mL), and the combined phase was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced vacuum. The residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate) to afford the pure product.

The spectroscopic data (IR, ^1H NMR, ^{13}C NMR) and elemental analytical data of all new compounds are given below.

*2-Methyl-9-phenyl-1,2,3,4-tetrahydroacridine (**3f**)*

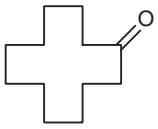
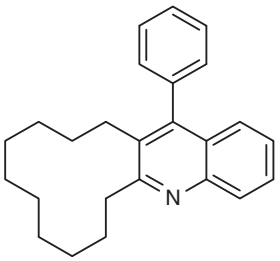
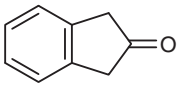
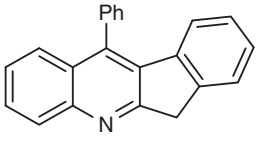
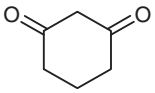
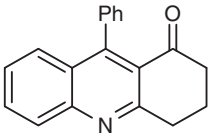
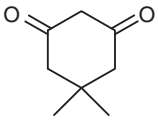
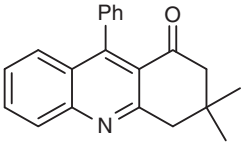
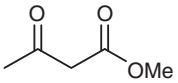
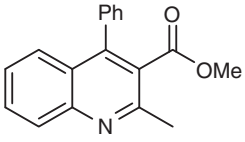
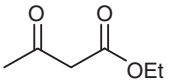
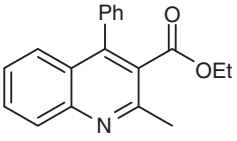
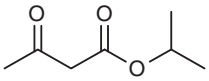
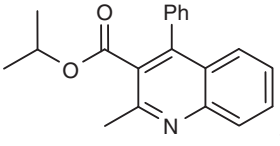
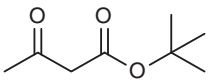
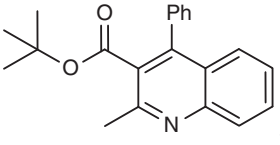
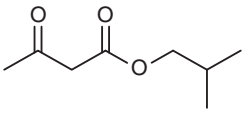
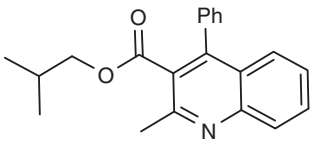
ν_{max} (KBr)/cm^{-1} 3060, 2923, 1610, 1569, 1558, 1485, 1398, 1355, 1153, 1029, 761. δ_H (500 MHz, $CDCl_3$) 1.01(d, *J* 6.5, 3H), 1.54–1.63 (m, 1H), 1.82–1.92 (m, 1H), 2.03–2.07 (m, 1H), 2.65 (ddd, *J* 17.0, 5.0, 2.0, 1H), 2.20–2.26 (m, 1H), 3.14–3.21 (m, 1H), 3.30 (ddd, *J* 17.0, 5.0, 3.5, 1H), 7.23 (t, *J* 8.0, 2H), 7.31 (d, *J* 9.0, 2H), 7.48 (t, *J* 7.5, 1H), 7.51–7.55 (m, 2H), 7.58–7.62 (m, 1H), 8.01 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 21.9, 29.3, 31.2, 33.9, 36.5, 125.4, 125.8, 126.6, 127.7, 127.9, 128.3, 128.4, 128.6, 129.1, 137.1, 146.4, 158.8. Anal. Calc. for $C_{20}H_{19}N$: C 87.87, H 7.01, N 5.12. Found: C 88.05, H 6.86, N 4.93 %.

Table 1. Synthesis of quinoline derivatives in *L*-(+)-tartaric acid-DMU

Entry	R	R^1	Ketone **2**	Product **3**	Time [h]	Yield [%][A]	mp [°C]
1	Ph	H		 **3a**	30	92	113–114 111–112[19]
2	Ph	H		 **3b**	60	95	135–136 135–138[17]
3	Ph	H		 **3c**	25	90	114–115 115[21]
4	Ph	H		 **3d**	45	92	131–132 131–133[12]
5	Ph	H		 **3e**	50	70	139–140 137[20]
6	Ph	H		 **3f**	90	91	129–130
7	Ph	H		 **3g**	50	96	126–128
8	Ph	H		 **3h**	70	95	158–159
9	Ph	H		 **3i**	60	91	130–131 131–132[19b]

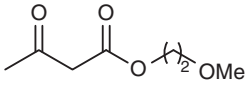
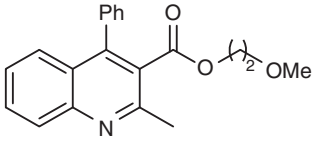
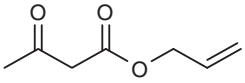
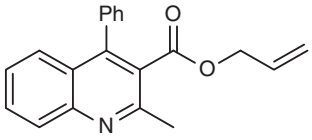
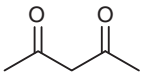
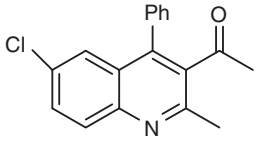
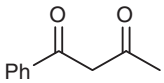
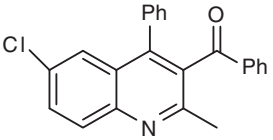
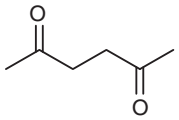
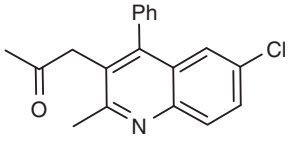
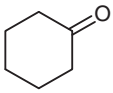
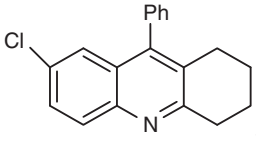
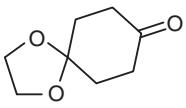
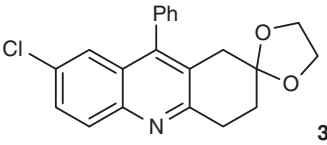
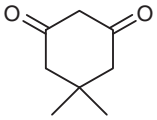
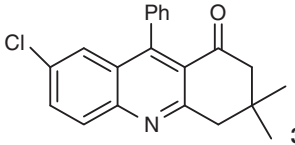
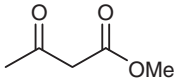
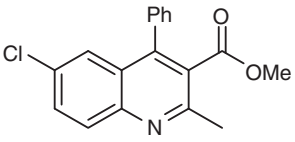
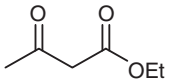
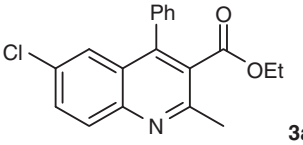
(*Continued*)

Table 1. (Continued)

Entry	R	R[1]	Ketone **2**	Product **3**	Time [h]	Yield [%][A]	mp [°C]
10	Ph	H		 **3j**	80	90	160–161 162–163[19b]
11	Ph	H		 **3k**	50	91	164–165 168–169[43]
12	Ph	H		 **3l**	20	93	158–159 156–158[12]
13	Ph	H		 **3m**	30	82	189–190 187[27]
14	Ph	H		 **3n**	40	91	131–132 131–133[12]
15	Ph	H		 **3o**	45	91	98–99 99–102[19]
16	Ph	H		 **3p**	45	92	63–64 64[27]
17	Ph	H		 **3q**	50	88	116–117 117–120[23]
18	Ph	H		 **3r**	40	90	79–80

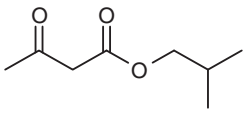
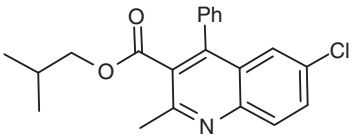
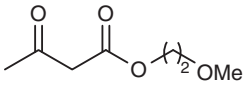
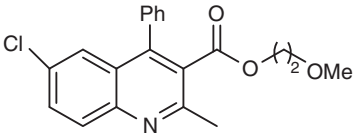
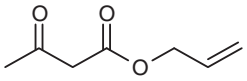
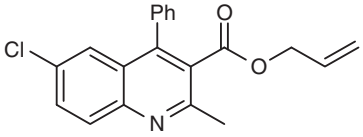
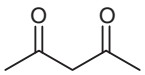
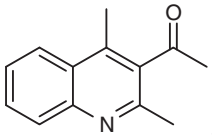
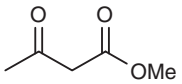
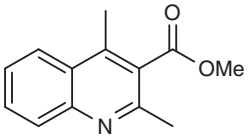
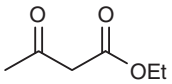
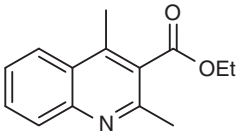
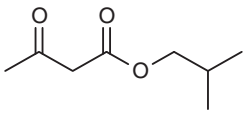
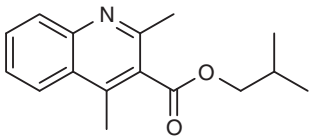
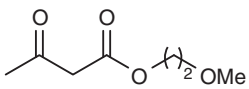
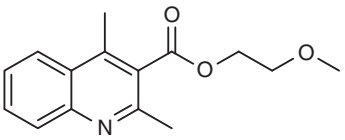
(*Continued*)

Table 1. (Continued)

Entry	R	R^1	Ketone **2**	Product **3**	Time [h]	Yield [%][A]	mp [°C]
19	Ph	H		 **3s**	60	90	85–86
20	Ph	H		 **3t**	40	94	93–94
21	Ph	Cl		 **3u**	40	85	154–155 157–158[17]
22	Ph	Cl		 **3v**	70	85	216–217 214–216[17]
23	Ph	Cl		 **3w**	20	88	130–131 129[21]
24	Ph	Cl		 **3x**	50	75	164–165 160–162[12]
25	Ph	Cl		 **3y**	65	95	165–166
26	Ph	Cl		 **3z**	25	80	218–219 219–220[19]
27	Ph	Cl		 **3aa**	35	88	134–135 136–137[17]
28	Ph	Cl		 **3ab**	40	86	104–105 105–107[12]

(*Continued*)

Table 1. (Continued)

Entry	R	R^1	Ketone **2**	Product **3**	Time [h]	Yield [%][A]	mp [°C]
29	Ph	Cl		 **3ac**	40	90	118–119
30	Ph	Cl		 **3ad**	40	92	86–87
31	Ph	Cl		 **3ae**	75	94	124–125
32	Me	H		 **3af**	120	85	oil oil[15]
33	Me	H		 **3ag**	90	91	oil oil[12]
34	Me	H		 **3ah**	110	89	oil oil[12]
35	Me	H		 **3ai**	120	90	oil
36	Me	H		 **3aj**	90	92	oil

[A]Isolated yield.

*2-(*tert*-Pentyl)-9-phenyl-1,2,3,4-tetrahydroacridine (**3g**)*

ν_{max} (KBr)/cm^{-1} 2964, 2875, 1605, 1487, 1400, 1388, 763. δ_H (500 MHz, $CDCl_3$) 0.76 (s, 3H), 0.77 (t, *J* 7.5, 3H), 0.81 (s, 3H), 2.28–2.28 (m, 2H), 1.52–1.58 (m, 2H), 2.07–2.10 (m, 1H), 2.29–2.35 (m, 1H), 2.61–2.65 (m, 1H), 3.09–3.16 (m, 1H), 3.30–3.35 (m, 1H), 7.22–7.24 (m, 2H), 7.29–7.33 (m, 2H), 7.47 (t, *J* 7.5, 1H), 7.52 (t, *J* 8.0, 1H), 7.58–7.61 (m, 1H), 8.01 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 8.1, 23.7, 23.8, 23.9, 28.9, 32.4, 34.9, 42.2, 125.3, 125.8, 126.7, 127.8, 128.3, 128.6, 128.7, 128.9, 129.2, 137.1, 146.3, 146.6, 159.4. Anal. Calc. for $C_{24}H_{27}N$: C 87.49, H 8.26, N 4.25. Found: C 87.68, H 8.09, N 4.42.

*9-Phenyl-3,4-dihydro-1*H*-spiro[acridine-2,2′-[1,3] di-oxolane] (**3h**)*

ν_{max} (KBr)/cm^{-1} 2935, 2879, 1614, 1658, 1558, 1417, 1377, 1257, 1155, 1120, 1060, 947, 763. δ_H (500 MHz, $CDCl_3$) 2.18 (t, *J* 7.0, 2H), 2.87 (s, 2H), 3.428 (t, *J* 7.0, 2H), 3.92–4.03 (m, 4H), 7.26 (d, *J* 7.0, 2H), 7.33–7.36 (m, 2H), 7.50 (t, *J* 7.5, 1H),

7.55 (t, *J* 7.5, 1H), 7.63–7.66 (m, 1H), 8.05 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) δ: 31.7, 32.2, 37.8, 64.5, 108.0, 125.6, 125.7, 125.8, 126.5, 127.9, 128.5, 128.8, 129.1, 136.6, 146.5, 147.3. Anal. Calc. for $C_{21}H_{19}NO_2$: C 79.47, H 6.03, N 4.41. Found: C 79.62, H 5.85, N 4.23 %.

*11-Phenyl-7,8,9,10-tetrahydro-6*H*-cyclohepta[*b*]quinoline (**3i**)*

ν_{max} (KBr)/cm^{-1} 2927, 2850, 1579, 1571, 1485, 1398, 1350, 1197, 962, 763. δ_H (500 MHz, $CDCl_3$) 1.85–1.87 (m, 4H), 2.71 (t, *J* 5.5, 2H), 3.29 (t, *J* 5.5, 2H), 3.48–3.50 (m, 2H), 7.23–7.25 (m, 2H), 7.27–7.29 (m, 1H), 7.33 (t, *J* 7.5, 1H), 7.59 (t, *J* 7.5, 1H), 8.02 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 27.1, 28.5, 30.7, 31.9, 40.2, 125.6, 126.4, 126.9, 127.6, 128.2, 128.4, 128.6, 129.5, 133.8, 137.7, 145.5, 145.9, 164.8. Anal. Calc. for $C_{20}H_{19}N$: C 87.87, H 7.01, N 5.12. Found: C 87.68, H 6.92, N 4.95 %.

iso-*Butyl 2-Methyl-4-phenylquinoline-3-carboxylate (**3r**)*

ν_{max} (KBr)/cm^{-1} 2974, 1712, 1614, 1581, 1488, 1467, 1407, 1390, 1301, 1238, 1217, 1128, 1068, 974, 767. δ_H (500 MHz, $CDCl_3$) 0.75 (s, 3H), 0.76 (s, 3H), 1.63–1.71 (m, 1H), 2.79 (s, 3H), 3.78 (d, *J* 6.5, 2H), 7.42–7.44 (m, 1H), 7.45–7.49 (m, 3H), 7.59 (d, *J* 8.5, 1H), 8.07 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 19.0, 23.9, 27.4, 71.7, 125.1, 126.4, 126.5, 127.7, 128.3, 128.5, 128.9, 129.4, 130.2, 135.7, 145.9, 147.8, 154.5, 168.8. Anal. Calc. for $C_{21}H_{21}NO_2$: C 78.97, H 6.63, N 4.39. Found: C 79.16, H 6.80, N 4.58 %.

*2-Methoxyethyl 2-Methyl-4-phenylquinoline-3-carboxylate (**3s**)*

ν_{max} (KBr)/cm^{-1} 2929, 1716, 1612, 1564, 1485, 1415, 1294, 1244, 1217, 1130, 1095, 1070, 958, 771. δ_H (500 MHz, $CDCl_3$) 2.79 (s, 3H), 3.26–3.29 (m, 5H), 4.15 (t, *J* 5.0, 2H), 7.37–7.39 (m, 2H), 7.42 (t, *J* 7.5, 1H), 7.47–7.49 (m, 3H), 7.57 (d, *J* 7.5, 2H), 8.07 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 23.8, 58.8, 64.1, 69.9, 125.1, 126.4, 126.5, 127.1, 128.3, 128.5, 128.9, 129.4, 130.3, 135.8, 146.4, 147.8, 154.7, 168.5. Anal. Calc. for $C_{20}H_{19}NO_3$: C 74.75, H 5.96, N 4.36. Found: C 74.93, H 6.15, N 4.20 %.

*Allyl 2-Methyl-4-phenylquinoline-3-carboxylate (**3t**)*

ν_{max} (KBr)/cm^{-1} 3066, 2993, 1712, 1577, 1560, 1485, 1400, 1296, 1232, 1180, 1130, 1066, 931, 767. δ_H (500 MHz, $CDCl_3$) 3.06 (s, 3H), 4.48 (d, *J* 7.0, 2H), 5.11–5.16 (m, 2H), 5.52–5.59 (m, 1H), 7.35–7.37 (m, 2H), 7.43 (t, *J* 7.5, 1H), 7.47–7.50 (m, 3H), 7.58 (d, *J* 7.5, 2H), 7.72 (td, *J* 7.5, 2.0, 1H), 8.07 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 23.9, 66.1, 119.1, 125.1, 126.4, 126.5, 127.2, 128.3, 128.5, 128.9, 129.4, 130.3, 131.2, 135.7, 146.4, 147.8, 154.6, 168.2. Anal. Calc. for $C_{20}H_{17}NO_2$: C 79.19, H 5.65, N 4.62. Found: C 79.01, H 5.48, N 4.80 %.

*7-Chloro-9-phenyl-3,4-dihydro-1*H*-spiro[acridine-2,2′-[1,3]dioxolane] (**3y**)*

ν_{max} (KBr)/cm^{-1} 2916, 2877, 1579, 1479, 1446, 1375, 1145, 1103, 1060, 947, 827, 717. δ_H (500 MHz, $CDCl_3$) 2.14 (t, *J* 7.0, 2H), 2.82 (s, 2H), 3.37 (t, *J* 7.0, 2H), 3.90–4.00 (m, 4H), 7.21 (d, *J* 7.5, 2H), 7.29 (d, *J* 7.5, 1H), 7.47–7.50 (m, 1H), 7.52–7.56 (m, 3H), 7.98 (d, *J* 8.0, 1H). δ_C (125 MHz, $CDCl_3$) 31.6, 32.2, 37.9, 64.6, 107.8, 124.6, 126.8, 127.2, 128.3, 129.0, 129.6, 130.2, 131.4, 135.9, 144.9, 146.5, 157.8. Anal. Calc. for $C_{21}H_{18}ClNO_2$: C 71.69, H 5.16, N 3.98. Found: C 71.88, H 4.98, N 4.16 %.

iso-*Butyl 6-Chloro-2-methyl-4-phenylquinoline-3-carboxylate (**3ac**)*

ν_{max} (KBr)/cm^{-1} 2920, 1728, 1601, 1218, 1064, 940, 764. δ_H (500 MHz, $CDCl_3$) 0.77 (s, 3H), 0.79 (s, 3H), 1.66–1.74 (m, 1H), 2.80 (s, 3H), 3.81 (d, *J* 6.5, 2H), 7.38–7.40 (m, 2H), 7.51–7.53 (m, 3H), 7.58 (d, *J* 2.0, 1H), 7.68 (dd, *J* 7.5, 2.0, 1H), 8.04 (d, *J* 8.0, 1H). δ_C (125 MHz, $CDCl_3$) 18.9, 23.8, 27.4, 71.9, 125.2, 125.9, 128.4, 128.8, 129.3, 130.6, 131.1, 132.4, 134.9, 145.1, 146.1, 154.9, 168.4. Anal. Calc. for $C_{21}H_{20}ClNO_2$: C 71.28, H 5.70, N 3.96. Found: C 71.10, H 5.52, N 4.15 %.

*2-Methoxyethyl 6-Chloro-2-methyl-4-phenylquinoline-3-carboxylate (**3ad**)*

ν_{max} (KBr)/cm^{-1} 2922, 1716, 1579, 1560, 1481, 1404, 1309, 1230, 1132, 1070, 840, 767. δ_H (500 MHz, $CDCl_3$) 2.81 (s, 3H), 3.30 (s, 3H), 3.32 (t, *J* 5.0, 2H), 4.19 (t, *J* 5.0, 2H), 7.38–7.40 (m, 2H), 7.53–7.55 (m, 3H), 7.57 (d, *J* 2.0, 1H), 7.68 (dd, *J* 7.5, 2.0, 1H), 8.04 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 23.8, 58.8, 64.2, 69.9, 125.2, 125.9, 127.9, 128.5, 128.8, 129.3, 130.6, 131.2, 132.4, 135.0, 145.5, 146.2, 155.1, 168.1. Anal. Calc. for $C_{20}H1_8ClNO_3$: C 67.51, H 5.10, N 3.94. Found: C 67.33, H 4.95, N 4.12 %.

*Allyl 6-Chloro-2-methyl-4-phenylquinoline-3-carboxylate (**3ae**)*

ν_{max} (KBr)/cm^{-1} 3076, 2925, 1720, 1600, 1581, 1481, 1394, 1307, 1218, 1068, 935, 765. δ_H (500 MHz, $CDCl_3$) 2.79 (s, 3H), 4.50 (d, *J* 6.5, 2H), 5.13–5.18 (m, 2H), 5.53–5.61 (m, 1H), 7.35–7.37 (m, 2H), 7.52–7.54 (m, 3H), 7.56 (d, *J* 2.0, 1H), 7.68 (dd, *J* 7.5, 2.0, 1H), 8.03 (d, *J* 8.5, 1H). δ_C (125 MHz, $CDCl_3$) 23.8, 66.2, 119.3, 125.3, 125.9, 127.9, 128.5, 129.3, 130.6, 131.1, 131.2, 132.4, 134.9, 145.5, 146.2, 154.9, 167.9. Anal. Calc. for $C_{20}H_{16}ClNO_2$: C 71.11, H 4.77, N 4.15. Found: C 70.93, H 4.96, N 3.98 %.

iso-*Butyl 2,4-Dimethylquinoline-3-carboxylate (**3ai**)*

ν_{max} (KBr)/cm^{-1} 2962, 1728, 1589, 1498, 1404, 1373, 1392, 1286, 1232, 1215, 1161, 1055, 758, 648. δ_H (500 MHz, $CDCl_3$) 1.04 (s, 3H), 1.06 (s, 3H), 2.07–2.15 (m, 1H), 2.68 (s, 3H), 2.73 (s, 3H), 4.22 (d, *J* 6.5, 2H), 7.56 (t, *J* 7.5, 1H), 7.73 (t, *J* 7.5, 1H), 8.01 (d, *J* 7.5, 1H), 8.03 (d, *J* 7.5, 1H). δ_C (125 MHz, $CDCl_3$) 15.8, 19.2, 23.8, 27.8, 71.9, 124.0, 125.8, 126.3, 128.1, 129.3, 130.1, 141.4, 147.1, 154.3, 169.4. Anal. Calc. for $C_{16}H_{19}NO_2$: C 74.68, H 7.44, N 5.44. Found: C 74.86, H 7.28, N 5.62 %.

*2-Methoxyethyl 2,4-Dimethylquinoline-3-carboxylate (**3aj**)*

ν_{max} (KBr)/cm^{-1} 2927, 1728, 1614, 1589, 1568, 1450, 1404, 1288, 1163, 1082, 983, 759. δ_H (500 MHz, $CDCl_3$) 2.69 (s, 3H), 2.73 (s, 3H), 3.44 (s, 3H), 3.76 (t, *J* 5.0, 2H), 4.30 (t, *J* 5.0, 2H), 7.56 (t, *J* 7.5, 1H), 7.73 (t, *J* 7.5, 1H), 8.01 (d, *J* 7.5, 1H), 8.03 (d, *J* 7.5, 1H). δ_C (125 MHz, $CDCl_3$) 15.7, 23.8, 58.9, 64.3, 70.2, 70.3, 124.0, 125.7, 126.3, 127.7, 129.3, 130.1, 141.7, 147.2, 154.4, 169.1. Anal. Calc. for $C_{15}H_{17}NO_3$: C 69.48, H 6.61, N 5.40. Found: C 69.66, H 6.80, N 5.23 %.

Supplementary Material

Copies of ^{1}H NMR and ^{13}C NMR spectra of all new compounds are available on the Journal's website.

Acknowledgements

We are grateful for financial support from the National Natural Science Foundation of China (21072042), the Nature Science Foundation of Hebei

Province (B2011205031) and the Undergraduate Scientific and Technological Innovation Project of Hebei Normal University.

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