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Homogeneous catalysis, heterogeneous recycling: a new family of branched molecules with hydrocarbon or fluorocarbon chains for the Friedländer synthesis of quinoline under solvent-free conditions

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ABSTRACT

A new family of branched catalysts with hydrocarbon or fluorocarbon chains was used to catalyze Friedländer reaction between 2-aminoarylketones and α-methylene ketones under solvent-free conditions in good to excellent yields. The catalysts exhibit temperature-dependent solubility and such a thermomorphic character allows them to be recovered by filtration conveniently at room temperature and reused at least five times. To some extent, the branched catalysts with hydrocarbon chains are superior to those with fluorocarbon chains, as they are cheaper and more biodegradable.

1. Introduction

Many new tools with the potential for green chemistry applications have been introduced during the development of combinatorial chemistry.[1] Among them, the fluorous chemistry has demonstrated good potential to become a new platform technology for green chemistry applications. A molecule tagged with fluorous ponytails has been successfully recycled from the reaction mixture mainly through three methods: (1) liquid–liquid extraction by partition between fluorous and organic solvent,[2] (2) solid phase extraction by using fluorous silica gel and PTFE as the non-covalent support[3] or by F-SPE[4] and (3) liquid–solid phase separation by exploiting its own solubility in common organic solvents.[5,6] Appropriately designed fluorous organocatalysts can be applied under homogeneous condition at elevated temperature to realize fluorous catalysis without fluorous solvents and also efficiently recovered by simple filtration at lower temperature. However, to our knowledge, only a few examples of this kind of catalysts have been reported.[6,7]

Quinolines and their derivatives are very important biological compounds that occur widely in natural products, such as antimalarial, antiasthmatic, antihypertensive, antibacterial, and tyrosine kinase inhibiting agents.[8] A straightforward synthesis of quinolines is Friedländer reaction. This reaction is generally carried out either by refluxing an aqueous or alcoholic solution of reactants in the presence of base or by heating a mixture of reactants at 150–220 °C in the absence of catalyst.[9] In order to improve the generality of Friedländer method, some Brønsted acids, such as hydrochloric acid,[10] *p*-toluenesulfonic acid,[11] dodecylphosphonic acid,[12] sulfuric acid-modified PEG-6000[13] have been employed. Also, modified methods, using Lewis acids,[14] inorganic salts,[15] ionic liquids,[16] have been reported for this reaction. However, most of reported procedures have significant drawbacks, such as long reaction time, harsh reaction conditions, or the use of volatile, and hazardous organic solvents. Therefore, the new efficient and environmentally friendly methods for the Friedländer reaction are still in demand.

Given the challenges mentioned above and also inspired by our recent work,[17,18] we hypothesized that the introduction of branched structure may change the solubility of catalysts, due to the fragments are highly branched, well-defined, and can be easily separated from reaction mixture for their large sizes. Herein we report a new family of branched compounds with hydrocarbon or fluorocarbon chains as catalysts (Fig. 1). Since there are six carboxyl groups on the periphery of these catalysts, which act as the acidic groups, this kind of molecules was used to catalyze Friedländer reactions of 2-aminoarylketones with various α-methylene

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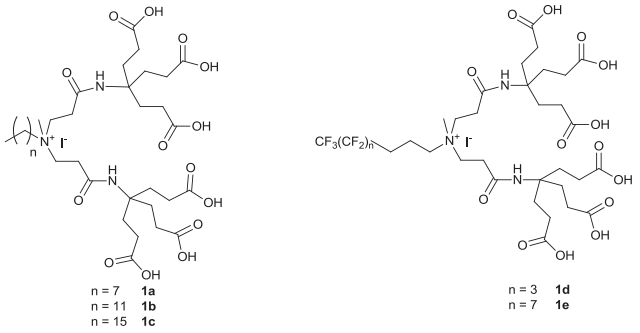


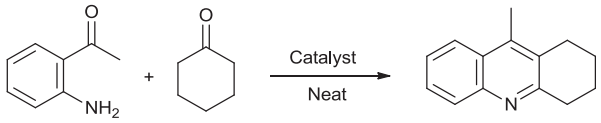
Fig. 1. Branched molecules.

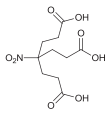
ketones. The branched catalysts with fluorocarbon chains showed the temperature-dependent solubility as designed. For comparison, some similar structures with hydrocarbon chains were also synthesized. To our surprise, they have similar solubility and catalytic activity, however, they are cheaper and more biodegradable.

2. Results and discussion

In order to optimize the reaction conditions, the condensation of *o*-aminoacetophenone (1.0 mmol) with cyclohexanone (1.2 mmol) was examined in the presence of different amounts of branched catalysts ranging from room temperature to 100 °C under solvent-free conditions (Table 1). The best result was obtained in the presence of 5 mol % of **1e** at 80 °C with 94% yield (Table 1, entry 2). However, it was noted that only 2 mol % of catalyst (**1e**) could work well to afford the product with excellent yield (Table 1, entries 2–5). The reaction was also tested without any catalyst and the desired product was not detected (Table 1, entry 1). Other branched molecules (**1a**–**d**) have similar catalytic effect (Table 1, entries 10–13).

Table 1
The model Friedländer reaction between *o*-aminoacetophenone and cyclohexanone[a]



Entry	Catalyst	Amount/mol %	Temperature/°C	Time/h	Yield[b] (%)
1	—	—	80	10	—
2	**1e**	5	80	3	94
3	**1e**	3	80	3	93
4	**1e**	2	80	3	93
5	**1e**	1	80	3	52
6	**1e**	2	rt	10	—
7	**1e**	2	40	6	29
8	**1e**	2	60	6	33
9	**1e**	2	100	3	87
10	**1a**	2	80	3	87
11	**1b**	2	80	3	90
12	**1c**	2	80	3	91
13	**1d**	2	80	3	85
14		6	80	3	15
15		6	80	3	12

[a] Reaction conditions: *o*-aminoacetophenone (1.0 mmol), cyclohexanone (1.2 mmol).
[b] Isolated yield.

On the other hand, to assess the capability and superiority of our branched catalysts, some similar fragments including 4-(2-carboxyethyl)-4-nitroheptanedioic acid (Table 1, entry 14) and octadecyl trimethyl ammonium chloride (Table 1, entry 15) were used to catalyze this reaction, which resulted in 15% and 12% yield, respectively.

With the photographs given in Fig. 2, the phenomenon of this reaction could be represented more clearly. The catalyst **1e** (2 mol %) was added to a mixture of *o*-aminoacetophenone and cyclohexanone (1.0:1.2 mol ratio) at room temperature (Table 1, entry 4). As expected, there was no visually detectable dissolution of **1e**. When the mixture was warmed to 80 °C, homogeneous solution formed. After 3 h, the sample was cooled to room temperature. The catalyst **1e** precipitated from the solution and could be recovered easily by filtration.

Fig. 2. Photographs of recycling sequences (Table 1, entry 4): (A) room temperature; (B) 80 °C; (C) room temperature after heated.

To better gauge the extent of catalyst recovery, the rate of the reaction of *o*-aminoacetophenone and cyclohexanone was monitored as a function of cycle. The recovered catalyst (**1c** or **1e**) could be reused at least five times without obviously loss of catalytic activity (Fig. 3).

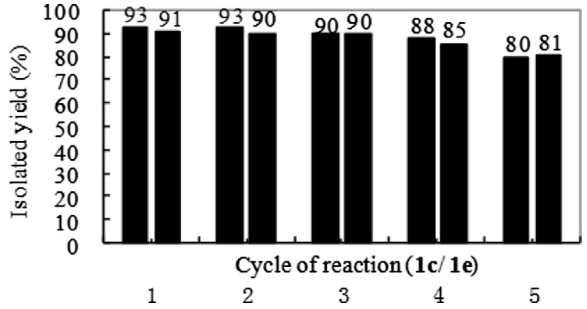
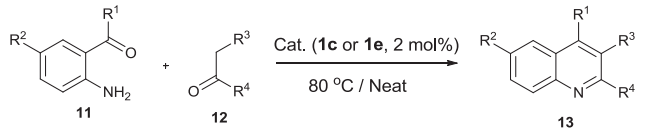


Fig. 3. The catalytic activity of **1c**/**1e** in five cycles for the reaction of *o*-aminoacetophenone and cyclohexanone.

To realize the efficiency and the scope of the branched catalysts for the synthesis of quinolines, 2-aminoarylketones were reacted with various α-methylene ketones including cyclic 1,3-diketones, aliphatic ketones, and cyclic ketones under the optimized reaction conditions. The results are displayed in Table 2. As shown, cyclic mono-functionalized ketones were efficiently condensed with 2-aminoarylketones, and the corresponding quinolines were obtained in good to excellent yields in short reaction time (Table 2, entries 1, 3, 6, 8, 11, 13). Interestingly, 1,3-cyclohexanedione was successfully reacted with 2-aminoarylketones to afford the tricyclic quinolines in reasonable yields (Table 2, entries 4, 9, 14) while 1,3-cyclopentanedione could only give much lower yields (Table 2, entries 5, 10, 15) probably because of steric effects. Moreover, owing to the low boiling point of 2-butanone (79.6 °C), the corresponding quinoline **13b** was formed with a moderate yield at 60 °C (Table 2, entry 2). Furthermore, the catalysts with hydrocarbon chains have similar activity to those with fluorocarbon chains.

Table 2
The Friedländer reaction between 2-aminoarylketones and various α-methylene ketones[a]



11a: R^1 = H, R^2 = H
11b: R^1 = Ph, R^2 = H
11c: R^1 = Ph, R^2 = Cl

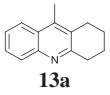
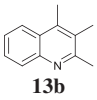
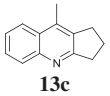
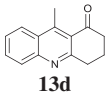
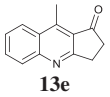
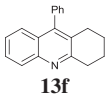
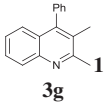
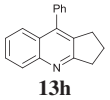
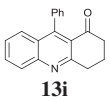
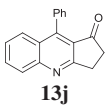
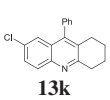
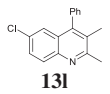
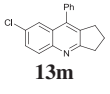
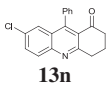
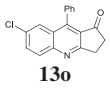
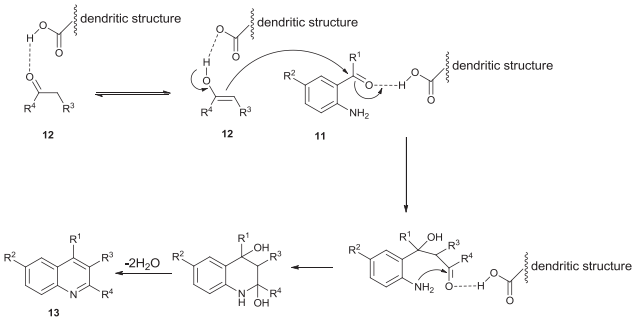
Entry	2-Aminoketone (**11**)	Ketone (**12**)	Product (**13a–p**)	Temperature (°C)	Yield[b] (%) (**1c**/**1e**)
1	**11a**		 **13a**	80	91/93
2	**11a**		 **13b**	60	57/55
3	**11a**		 **13c**	80	80/83
4	**11a**		 **13d**	80	89/89
5	**11a**		 **13e**	80	43/50
6	**11b**		 **13f**	80	82/80
7	**11b**		 **3g**	60	41/40
8	**11b**		 **13h**	80	78/82
9	**11b**		 **13i**	80	89/90
10	**11b**		 **13j**	80	40/45
11	**11c**		 **13k**	80	79/80
12	**11c**		 **13l**	60	33/35
13	**11c**		 **13m**	80	84/82

Table 2 (*continued*)

Entry	2-Aminoketone (**11**)	Ketone (**12**)	Product (**13a–p**)	Temperature (°C)	Yield[b] (%) (**1c**/**1e**)
14	**11c**		 **13n**	80	79/78
15	**11c**		 **13o**	80	28/32

[a] Reaction conditions: 2-aminoaryl ketone (1 mmol), α-methylene ketone (1.2 mmol).
[b] Isolated yield, the reactions were catalyzed with **1c** and **1e**, respectively.

Due to the weak acidity of the catalysts, the mechanism of the reaction was proposed. The catalysts help in enolization of **12** by forming hydrogen bonds and, thus, they increase the nucleophilic character of the methylene carbon of **12**. Meanwhile, it also increases the electrophilic character of carbonyl **11** by forming hydrogen bonds with the carbonyl oxygen. After elimination of 2 equiv H_2O, compound **13** is formed (Scheme 1).



Scheme 1. Plausible mechanism for the Friedländer condensation.

3. Conclusions

In summary, we have developed a series of branched catalysts with hydrocarbon or fluorocarbon chains for Friedländer synthesis of 2-aminoarylketones and various ketones. They have temperature-dependent solubility and therefore they could be applied under homogeneous conditions at elevated temperature and efficiently recovered by simple liquid/solid phase separations at room temperature. Moreover, the reaction was conducted under solvent-free condition to avoid the use of hazardous solvents.

4. Experimental

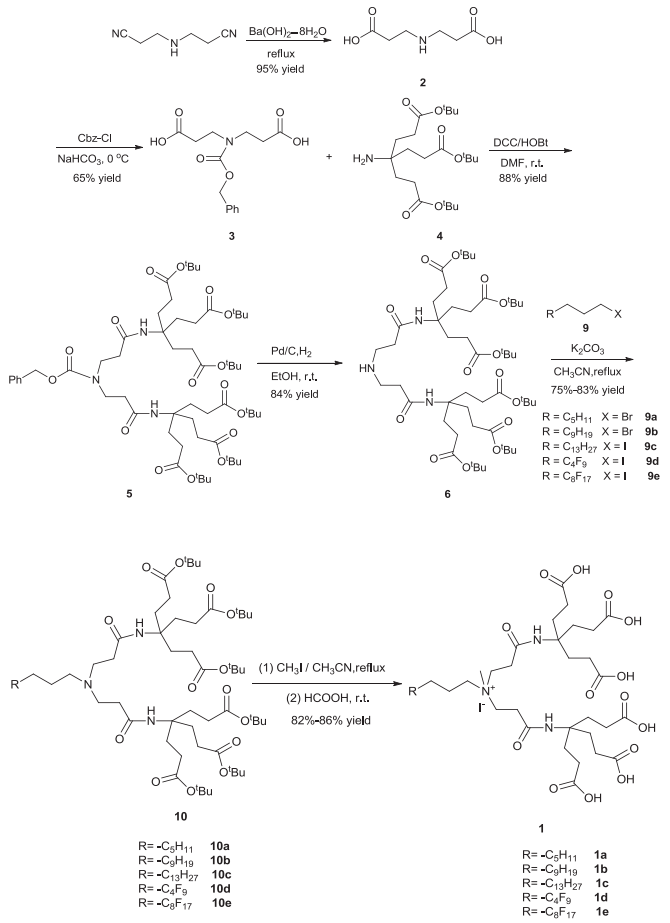
4.1. General

Melting points were determined with an X-4 apparatus and ^1H (400 MHz) NMR and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker Avance 400 spectrometer using TMS as internal reference. Mass spectra were recorded on a Micromass GCTTM mass spectrometer.

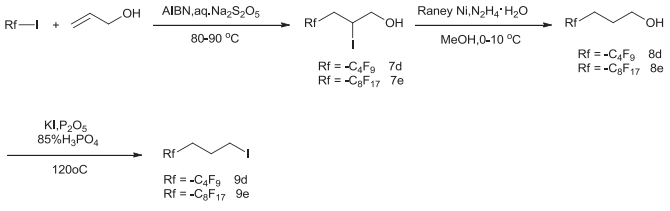
Behera's amine (**4**), 3-(perfluoroalkyl)propyl iodides (**9d**, **9e**), and compound **3** were synthesized by a method according to literature procedures (Schemes 2 and 3).[19–21]

4.2. The synthetic route to branched amphiphilic molecules

*4.2.1. 3,3′-Iminodipropionic acid (**2**).* A mixture of 3,3′-azanediyldipropanenitrile (5.0 g, 40.7 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (27.0 g, 86.0 mmol) in 60 mL H_2O was refluxed with stirring for 8 h. Equivalent



Scheme 2. The synthetic route to branched molecules.



Scheme 3. The synthesis of perfluoroalkyl propyl iodide.

sulfuric acid was added and the formed precipitate was removed by centrifugation. The filtrate was then evaporated off and washed with methanol to afford a white solid (6.3 g, yield: 95%). Mp 149–151 °C; ^{1}H NMR (D_2O, 400 MHz): δ 2.71 (t, J=6.40 Hz, 4H); 3.32 (t, J=6.4 Hz, 4H).

*4.2.2. N-(Benzyloxycarbonyl)-imino-3,3′-bis(propionic acid) (**3**).* Benzyloxycarbonyl chloride (5.7 mL, 40.0 mmol) was added dropwise to a stirred aqueous solution of **2** (6.0 g, 37.2 mmol) in saturated aqueous $NaHCO_3$ solution (75 mL) at 0 °C. The pH of the reaction mixture was kept alkaline by adding the required amount of $NaHCO_3$ solution. It was left to stir for 6 h before being refrigerated for 12 h. The reaction mixture was warmed up to room temperature, washed with Et_2O (2×60 mL), neutralized with diluted HCl, and extracted with EtOAc (3×60 mL). The organic portion was dried and evaporated in vacuum to give a white solid (7.1 g, yield: 65%). Mp 112–115 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50–2.70 (m, 4H), 3.57 (t, J=6.4 Hz, 4H), 5.11 (s, 2H), 7.22–7.39 (m, 5H), 9.66 (br, 2H).

*4.2.3. Compound **5**.* A mixture of **3** (2.60 g, 8.8 mmol), DCC (3.63 g, 17.6 mmol), and HOBt (2.38 g, 17.6 mmol) in 60 mL DMF was stirred for 1 h. After the addition of **4** (7.31 g, 17.6 mmol), the mixture kept stirring for 48 h. Then the solvent was removed in vacuo and the residue was dissolved in CH_2Cl_2, washed with water (3×20 mL), and dried. Evaporation of the solvent gave a crude product, which was purified by silica gel column chromatography with petroleum ether and ethyl acetate (4:1) to give the pure product as a yellow oil (8.44 g, yield: 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 54H), 1.93 (t, J=8.0 Hz, 12H), 2.16 (t, J=8.0 Hz, 12H), 2.44 (s, 4H), 3.53 (t, J=7.2 Hz, 4H), 5.14 (s, 2H), 6.24 (br, 2H), 7.31–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.1, 29.8, 36.3, 57.5, 67.3, 80.6, 128.1, 128.2, 128.6, 136.6, 156.3, 170.1, 172.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{58}H_{96}N_3O_{16}$: 1090.6791; found: 1090.6798.

*4.2.4. Compound **6**.* A mixture of **5** (4.52 g, 4.14 mmol) in EtOH (60 mL) with Pd/C (1 g) was hydrogenated at 50 psi and at room temperature for 24 h. The catalyst was cautiously filtered. The solvent was removed in vacuo, affording a yellow oil, which was purified by silica gel column chromatography with EtOAc to give a white solid (3.33 g, yield: 84%). Mp 138–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 54H), 1.95 (t, J=8.0 Hz, 12H), 2.20 (t, J=8.0 Hz, 12H), 2.30 (t, J=5.6 Hz, 4H), 2.85 (t, J=5.6 Hz, 4H), 7.20 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.2, 30.1, 36.8, 45.9, 57.3, 80.7, 171.9, 172.9. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{50}H_{90}N_3O_{14}$: 956.6423; found: 956.6417.

*4.2.5. Typical procedure for the preparation of compound **10e**.* A mixture of **7** (3.00 g, 3.14 mmol), **10e** (1.91 g, 3.25 mmol), K_2CO_3 (0.45 g, 3.25 mmol) in CH_3CN (60 mL) was refluxed for 30 h. After completion of reaction (monitored by TLC), the precipitate was removed by centrifugation and the filtrate was then evaporated off. The resulting residue was purified by silica gel column chromatography using petroleum ether and ethyl acetate (1:1) to give the pure product as a yellow oil (3.7 g, yield: 83%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.25 (m, 2H), 1.42 (s, 54H), 1.77 (m, 2H), 1.95 (t, J=8.0 Hz, 12H), 2.20 (t, J=8.0 Hz, 12H), 2.30 (t, J=6.8 Hz, 4H), 2.54 (t, J=7.6 Hz, 2H), 2.75 (t, J=6.8 Hz, 4H), 6.76 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3, 17.8, 21.2, 28.2, 30.0, 30.1, 34.7, 49.8, 52.7, 57.5, 60.5, 80.7, 171.3, 172.9. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{61}H_{95}F_{17}N_3O_{14}$: 1416.6543; found: 1416.6536. This procedure was followed for the preparation of the compound **10a**–**d**.

*4.2.5.1. Compound **10a**.* A yellow oil. Yield: 75%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, J=6.4 Hz, 3H), 1.25 (s, 12H), 1.43 (s, 54H), 1.95 (t, J=8.0 Hz, 12H), 2.20 (t, J=8.0 Hz, 12H), 2.31 (t, J=6.8 Hz, 4H), 2.46 (t, J=8.0 Hz, 2H), 2.73 (t, J=6.8 Hz, 4H), 7.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 22.7, 26.4, 27.8, 28.2, 29.4, 29.6, 30.0, 30.0, 31.9, 34.1, 49.9, 53.1, 57.3, 80.6, 171.4, 172.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{58}H_{106}N_3O_{14}$: 1068.7675; found: 1068.7673.

*4.2.5.2. Compound **10b**.* A yellow oil. Yield: 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (t, J=6.8 Hz, 3H), 1.27 (s, 20H), 1.42 (s, 54H), 1.93 (t, J=8.0 Hz, 12H), 2.18 (t, J=8.0 Hz, 12H), 2.29 (t, J=6.4 Hz, 4H), 2.44 (t, J=7.6 Hz, 2H), 2.73 (t, J=6.4 Hz, 4H), 7.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 22.7, 26.3, 27.8, 28.2, 28.2, 28.8, 29.4, 29.5, 29.6, 29.7, 29.7, 29.8, 30.0, 30.0, 32.0, 32.9, 34.1, 49.9, 53.2, 57.3, 80.6, 171.4, 172.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{62}H_{114}N_3O_{14}$: 1124.8301; found: 1124.8307.

*4.2.5.3. Compound **10c**.* A yellow oil. Yield: 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, J=6.8 Hz, 3H), 1.24 (s, 26H), 1.42 (s, 54H), 1.94 (t, J=8.0 Hz, 12H), 2.19 (t, J=8.0 Hz, 12H), 2.31 (t, J=6.8 Hz, 4H), 2.45 (t, J=8.0 Hz, 2H), 2.73 (t, J=6.8 Hz, 4H), 7.16 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 22.8, 27.8, 28.2, 29.5, 29.8, 29.8, 30.0, 30.0, 32.0, 34.2, 49.9, 53.3, 57.3, 80.7, 171.5, 172.9. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{66}H_{122}N_3O_{14}$: 1180.8927; found: 1180.8926.

*4.2.5.4. Compound **10d**.* A yellow oil. Yield: 78%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.19 (m, 2H), 1.39 (s, 54H), 1.75 (m, 2H), 1.91 (t, J=8.0 Hz, 12H), 2.17 (t, J=8.0 Hz, 12H), 2.27 (t, J=6.8 Hz, 4H), 2.51 (t, J=7.6 Hz, 2H), 2.72 (t, J=6.8 Hz, 4H), 6.76 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3, 28.2, 30.0, 30.2, 34.7, 49.9, 52.7, 57.5, 60.5, 80.8, 171.3, 172.9. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{57}H_{95}F_9N_3O_{14}$: 1216.6670; found: 1216.6666.

*4.2.6. Typical procedure for the preparation of compound **1e**.* A mixture of **10e** (3.70 g, 2.61 mmol), CH_3I (1.6 mL, 10 equiv) in CH_3CN was refluxed for 12 h under N_2. After the evaporation of the solvent, the residue was stirred in HCOOH (20 mL) for 24 h. The solvent was removed in vacuo, affording a yellow oil, which was washed with acetone (3×20 mL) to give a yellow solid (1.97 g, yield: 85%). Mp 165–168 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.83 (t, J=7.6 Hz, 12H), 1.98 (br, 2H), 2.12 (t, J=7.6 Hz, 12H), 2.30 (m, 2H), 2.63 (s, 4H), 2.99 (s, 3H), 3.34 (m, 2H), 3.48 (s, 4H), 7.96 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 13.7, 28.6, 28.8, 29.1, 29.3, 47.6, 57.1, 57.8, 167.6, 175.1. HRMS (ESI): m/z $[M-I]^+$ calcd for $C_{38}H_{49}F_{17}N_3O_{14}$: 1094.2943; found: 1094.2930. This procedure was followed for the preparation of the compound **1a**–**d**.

*4.2.6.1. Compound **1a**.* A yellow solid. Yield: 83%. Mp 175–177 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.82 (s, 3H), 1.23 (s, 10H), 1.61 (s, 2H), 1.81 (s, 12H), 2.10 (s, 12H), 2.61 (s, 4H), 2.91 (s, 3H), 3.16 (s, 2H), 3.42 (s, 4H), 7.47 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 14.2, 15.4, 21.8, 22.3, 26.0, 28.3, 28.7, 29.1, 29.3, 31.4, 47.8, 57.2, 57.7, 168.0, 174.8. HRMS (ESI): m/z $[M-I]^+$ calcd for $C_{35}H_{60}N_3O_{14}$: 746.4075; found: 746.4077.

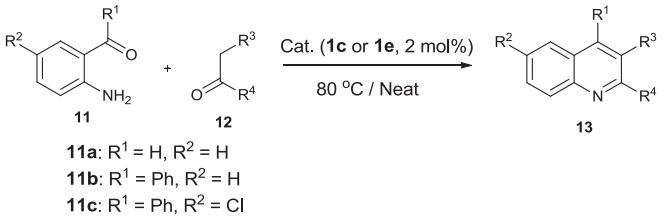
*4.2.6.2. Compound **1b**.* A yellow solid. Yield: 85%. Mp 161–163 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.85 (t, J=6.8 Hz, 3H), 1.24 (s, 18H), 1.63 (s, 2H), 1.85 (t, J=8.0 Hz, 12H), 2.12 (t, J=8.0 Hz, 12H), 2.62 (s, 3H), 2.93 (s, 3H), 3.17–3.19 (m, 2H), 3.44 (s, 4H), 7.61 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 14.0, 21.6, 22.2, 25.9, 28.3, 28.6, 28.8, 28.9, 29.0, 29.1, 29.2, 30.8, 31.4, 47.5, 57.0, 57.4, 61.0, 167.6, 174.7. HRMS (ESI): m/z $[M-I]^+$ calcd for $C_{39}H_{68}N_3O_{14}$: 802.4701; found: 802.4692.

*4.2.6.3. Compound **1c**.* A yellow solid. Yield: 86%. Mp 129–131 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.85 (t, J=6.8 Hz, 3H), 1.23 (s, 26H), 1.63 (s, 2H), 1.85 (t, J=7.6 Hz, 12H), 2.12 (t, J=7.6 Hz, 12H), 2.61 (s, 4H), 2.94 (s, 3H), 3.18 (m, 2H), 3.44 (s, 4H), 7.75 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 14.1, 22.2, 25.9, 28.5, 28.7, 28.8, 29.0, 29.1, 29.2, 29.3, 30.8, 31.4, 47.6, 57.1, 57.5, 167.7, 174.8. HRMS (ESI): m/z $[M-I]^+$ calcd for $C_{43}H_{76}N_3O_{14}$: 858.5327; found: 858.5330.

*4.2.6.4. Compound **1d**.* A yellow solid. Yield: 82%. Mp 155–157 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.84 (s, 12H), 1.98 (s, 2H), 2.12 (s, 12H), 2.33 (m, 2H), 2.63 (s, 4H), 3.00 (s, 3H), 3.33 (m, 2H), 3.48 (s, 4H), 7.98 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 13.8, 26.9, 28.8, 29.0, 29.5, 30.8, 47.7, 57.2, 57.8, 167.6, 175.2. HRMS (ESI): m/z $[M-I]^+$ calcd for $C_{34}H_{49}F_{17}N_3O_{14}$: 894.3071; found: 894.3063.

4.3. Preparation of quinolines under solvent-free conditions

A mixture of 2-aminoaryl ketone (**11**a–**c**, 1 mmol) and α-methylene ketone (**12**, 1.2 mmol) was added to 2 mol % of compound **1c** or **1e** (Scheme 4). The reaction mixture was heated at the appropriate temperature with stirring for about 3 h (Table 2). The extent of reaction was monitored by TLC. After completion of the reaction, the mixture was added ethyl acetate (5 mL) when the mixture was solid at room temperature. The catalyst was essentially insoluble in ethyl acetate when the product could be easily dissolved. Then after filtration, the catalyst could be recovered. The crude mixture was purified by silica gel column chromatography with petroleum ether and ethyl acetate (4:1) to give the pure product (**13a**–**o**).



Scheme 4. The Friedländer reaction between 2-aminoarylketones and various α-methylene ketones.

*4.3.1. 9-Methyl-1,2,3,4-tetrahydroacridine (**13a**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.94 (m, 4H), 2.56 (s, 3H), 2.90 (t, J=7.6 Hz, 2H), 3.12 (t, J=7.6 Hz, 2H), 7.46 (t, J=7.6 Hz, 1H), 7.60 (t, J=7.6 Hz, 1H), 7.95–7.99 (m, 2H).

*4.3.2. 2,3,4-Trimethylquinoline (**13b**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (s, 3H), 2.63 (s, 3H), 2.73 (s, 3H), 7.49 (t, J=7.6 Hz, 1H), 7.62 (t, J=7.6 Hz, 1H), 7.96–8.04 (m, 2H).

*4.3.3. 9-Methyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**13c**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.17–2.25 (m, 2H), 2.60 (s, 3H), 3.07 (t, J=7.6 Hz, 2H), 3.17 (t, J=7.6 Hz, 2H), 7.48 (t, J=7.6 Hz, 1H), 7.61 (t, J=7.6 Hz, 1H), 7.93–8.02 (m, 2H).

*4.3.4. 9-Methyl-3,4-dihydroacridin-1(2H)-one (**13d**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.17–2.24 (m, 2H), 2.81 (t, J=6.4 Hz, 2H), 3.05 (s, 3H), 3.28 (t, J=6.4 Hz, 2H), 7.56 (t, J=7.6 Hz, 1H), 7.65 (t, J=7.6 Hz, 1H), 7.99–8.22 (m, 2H).

*4.3.5. 9-Methyl-2,3-dihydro-1H-cyclopenta[b]quinolin-1-one (**13e**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.86 (t, J=6.8 Hz, 2H), 3.01 (s, 3H), 3.36 (t, J=6.8 Hz, 2H), 7.60 (t, J=7.6 Hz, 1H), 7.83 (t, J=7.6 Hz, 1H), 8.07–8.22 (m, 2H).

*4.3.6. 9-Phenyl-1,2,3,4-tetrahydroacridine (**13f**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.75–1.82 (m, 2H), 1.93–1.98 (m, 2H), 2.60 (t, J=6.8 Hz, 2H), 3.20 (t, J=6.8 Hz, 2H), 7.22–7.60 (m, 8H), 8.01 (d, J=8.4 Hz, 1H).

*4.3.7. 2,3-Dimethyl-4-phenylquinoline (**13g**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.18 (s, 3H), 2.76 (s, 3H), 7.23–7.64 (m, 8H), 8.03 (d, J=8.4 Hz, 1H).

*4.3.8. 9-Phenyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**13h**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14–2.21 (m, 2H), 2.91 (t, J=7.2 Hz, 2H), 3.23 (t, J=7.2 Hz, 2H), 7.26–8.08 (m, 8H), 8.06 (d, J=8.8 Hz, 1H).

*4.3.9. 9-Phenyl-3,4-dihydroacridin-1(2H)-one (**13i**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.22–2.28 (m, 2H), 2.71 (t, J=6.4 Hz, 2H), 3.38 (t, J=6.4 Hz, 2H), 7.16–7.78 (m, 8H), 8.06 (d, J=8.4 Hz, 1H).

*4.3.10. 9-Phenyl-2,3-dihydro-1H-cyclopenta[b]quinolin-1-one (**13j**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.84 (t, J=7.2 Hz, 2H), 3.45 (t, J=7.2 Hz, 2H), 7.34–7.85 (m, 8H), 8.15 (d, J=8.4 Hz, 1H).

*4.3.11. 7-Chloro-9-phenyl-1,2,3,4-tetrahydroacridine (**13k**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.76–1.80 (m, 2H), 1.94–1.98 (m, 2H), 2.59 (t,

J=6.4 Hz, 2H), 3.18 (t, *J*=6.4 Hz, 2H), 7.19–7.55 (m, 7H), 7.94 (d, *J*=9.2 Hz, 1H).

*4.3.12. 6-Chloro-2,3-dimethyl-4-phenylquinoline (**13l**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.18 (s, 3H), 2.75 (s, 3H), 7.21–7.56 (m, 7H), 7.95 (d, *J*=8.8 Hz, 1H).

*4.3.13. 7-Chloro-9-phenyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**13m**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14–2.19 (m, 2H), 2.90 (t, *J*=7.6 Hz, 2H), 3.22 (t, *J*=7.6 Hz, 2H), 7.26–7.98 (m, 7H), 7.99 (d, *J*=8.8 Hz, 1H).

*4.3.14. 7-Chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one (**13n**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.21–2.28 (m, 2H), 2.71 (t, *J*=6.4 Hz, 2H), 3.35 (t, *J*=6.4 Hz, 2H), 7.14–8.01 (m, 8H).

*4.3.15. 7-Chloro-9-phenyl-2,3-dihydro-1H-cyclopenta[b]quinolin-1-one (**13o**).* ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.84 (t, *J*=7.2 Hz, 2H), 3.43 (t, *J*=7.2 Hz, 2H), 7.32–8.09 (m, 8H).

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Supplementary data

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