Gold(III)/Sodium Diphenylphosphinobenzene-3-sulfonate (TPPMS) Catalyzed Dehydrative N-Benzyla tion of Electron-Deficient Anilines in Water

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Abstract A strategy for the dehydrative N-benzylation of electron-deficient anilines in water has been developed. The gold(III)/sodium diphenylphosphinobenzene-3-sulfonate (TPPMS) catalyst is highly effective as a Lewis acid for the activation of alcohols and tolerates aerobic conditions. A Hammett study in the reaction of para-substituted benzhydryl alcohols shows negative $\sigma$ values, indicating a build-up of cationic charge during the rate-determining $sp^2$ C–O bond-cleavage step. The inverse kinetic solvent isotope effect (KSIE = 0.6) is consistent with a specific acid catalysis mechanism. This simple protocol can be performed under mild conditions in an atom-economic process without the need for base or other additives, furnishing the electron-deficient N-benzylic anilines in moderate to excellent yields along with water as a sole coproduct.

Key words gold, water, benzyl alcohol, aniline, N-benzylation

The gold-catalyzed dehydrative substitution reaction of alcohols with amines affords the desired products along with water as the sole coproduct. This reaction has emerged as a powerful methodology for the formation of C–N bonds due to the advantages of being a salt-free and atom-economical process that does not transform the hydroxyl into a good leaving group.1,2 In 2005, the pioneering work of Campagne demonstrated the nucleophilic substitution of propargylic alcohols using the NaAuCl4·2H2O catalyst, which activated the alcohols through coordination with the $sp^3$ bond.3 Campagne and Prim et al. developed the direct catalytic amination of benzyl alcohols with poor amine nucleophiles.4 Such efficiency is mainly due to the Lewis acidic character of the gold(III) catalyst for the activation of several $sp^3$ C–O bonds, thus promoting unique chemical transformations.5 While these are green and sustainable strategies for direct functionalization of organic molecules due to their advantages in atom economy, the use of hazardous organic solvents such as CH2Cl2 or CICH2CH2Cl under extrusion of moisture conditions is generally required. Recently, the Wang group developed a gold-catalyzed borrowing-hydrogen reaction in good yields with high chemoselectivity under wet conditions.6c Therefore, developing more efficient and environmentally friendly protocols is highly desirable due to the scope of applications and industrial utility.6,7

Water is widely recognized as a greener solvent alternative for organic synthesis because of its universal abundance, nontoxicity and environmental compatibility.8,9 We have been developing a strategy for dehydrative substitution of alcohols catalyzed by NaAuCl4·2H2O and sodium diphenylphosphinobenzene-3-sulfonate (TPPMS) in water.10 Recently, we described the first example of a selective N-benzylation of water-soluble substrates such as unprotected anthranilic acids.10c As an extension of our investigation, we herein report a strategy for the catalytic dehydrative N-benzylation of electron-deficient anilines. To our knowledge, this is the first report of a gold-catalyzed direct modification of nitroanilines under mild reaction conditions in water without the need for base or other additives (Scheme 1). Notably, the gold(III)/TPPMS catalyst is highly effective as a Lewis acid for the activation of alcohols, while common Lewis or Brønsted acid such as Cu(II),11 Co(II),12 or Fe(III) were ineffective for dehydrative N-benzylation of 4-nitroaniline (1a) (see Table 1).

**Scheme 1** Catalytic dehydrative N-benzylation of 4-nitroaniline (1a)
Initially, 4-nitroaniline (1a) and benzhydrol (2a) were chosen as model compounds to optimize the dehydrative amination. The desired product 3a was obtained in 63% yield when using NaAuCl₄·2H₂O (2 mol%) and TPPMS L₁ (2 mol%) in water at 40 °C for 16 hours (Table 1, entry 1). A control experiment using HCl indicated that the gold(III) catalyst played a crucial role in the catalytic system (entry 2). Furthermore, no reaction occurred when using only NaAuCl₄·2H₂O catalyst (entry 3). The yield of 3a was increased to 90% in a shorter reaction time when using NaAuCl₄·2H₂O (5 mol%) and TPPMS (5 mol%) at 70 °C (entry 4). Increasing the amount of the TPPMS ligand resulted in a slightly lower yield (entry 5). With regard to the gold catalysts, NaAuCl₄·2H₂O gave the best result (entry 4 vs. entries 6–9). Other water-soluble phosphine ligands L₂–7 resulted in no reaction or lower yields (entries 10–15).¹³ Other chloride salts such as Cu(II), Co(II) or Fe(III) were less effective than NaAuCl₄·2H₂O (entries 16–18). Organic solvents such as EtOH, DMF, 1,4-dioxane or CH₂Cl₂ were not suitable compared with water in our catalytic system (entries 19–22).

With the optimized conditions in hand, we examined the substrate scope of the dehydrative amination (Scheme 2). First, the scope of benzylic alcohols 2 with 4-nitroaniline (1a) as the coupling partner was examined. As expected, both electron-donating (OMe and Me) and electron-withdrawing (Cl and F) groups on the benzene ring of substituted benzhydrols 2 were well tolerated, and the corresponding N-benzylated products 3b–f were formed in moderate to excellent yields (72–89%). In contrast, decafluorobenzhydrol failed to react under the same conditions, suggesting that stability of the diarylcation was critical to the success of the reaction. We explored the direct amination of the hydroxyl group of n-activated alcohols such as trans-1,3-diphenyl-2-propan-1-ol, which afforded the corresponding product 3g in 86% yield. Furthermore, a simple benzylic alcohol such as 4-methoxybenzalcohol could be transformed into 3h in 70% yield.

Encouraged by these results, we next examined the scope of electron-deficient anilines 1 with benzhydrol (2a) as the coupling partner. Various nitroanilines 1 showed good reactivities, regardless of whether they had electron-donating or withdrawing substitutents (72–98%, 3i–q). The carbon–bromine moiety in 3n was left intact, which could be employed for further cross-coupling. Furthermore, replacement of the NO₂ group with several electron-withdrawing groups (CN, CF₃, Ac and CO₂Et) was also tolerated to produce the corresponding N-benzylated products 3r–u (55–83%). In contrast, electron-sufficient 4-anisidine did not react due to poisoning of the Lewis acidic gold(III) catalyst. A sterically demanding 4-nitro-1-naphthylamine (1b) led to the corresponding N-benzylated 3v along with C-benzylated 4 in 67% and 20% yields, respectively (Scheme 3). Ghorai et al. reported the dehydrative Friedel–Crafts benzylaion of 4-nitroaniline via Hofmann–Martius rearrangement catalyzed by Re₂O₇. Therefore, the benzyl cation species would be generated from 3v followed by the formation of ortho-benzylated aniline 4 in our catalytic system.¹⁴

To demonstrate the electronic effect of the substituents on the rates of the sp³ C–O bond cleavage of alcohols and the C–N bond-formation reaction, Hammett studies were conducted on the gold-catalyzed dehydrative amination.¹⁵ First, the relative rates of coupling of 4-substituted 2-nitroanilines 1 (X = OMe, Me, H, F, and Br groups) with benzhydrol (2a) were examined. Scheme 4A shows no correla-

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**Table 1** Optimization of Reaction Conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. (mol%)</th>
<th>Ligand (mol%)</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Solv.</th>
<th>Yield (%)</th>
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<td>16</td>
<td>H₂O</td>
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<td>L₁ (5)</td>
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<td>16</td>
<td>CH₂Cl₂</td>
<td>48</td>
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</table>

*反应条件：4-硝基苯胺(1a) (1 mmol), 催化剂 (2 or 5 mol%), 溶剂 (4 mL), 在含3,5-三甲基环己烯的密闭管中，微波照射.*

*b* 测定数据使用的是1H NMR分析，化合物在1,3,5-三甲基环己烯中作为内部参照。

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and relative rates of the reaction between 4-nitroaniline (1a) and para-substituted benzhydryl alcohols 2 (Y = OMe, Me, H, F, and Br groups) were examined. Scheme 4B shows excellent correlation ($R^2 = 0.99$) between the log ($k_2/k_1$) and the $\rho$ value of the respective substituents that resulted in a negative $\rho$ value of 2.8. This result indicates a build-up of positive charge in the transition state.

To gain insight into the catalytic sp$^3$ C–O bond-activation step, we carried out kinetic isotope effect (KIE) experiments. The reactions of 4-nitroaniline (1a) with benzhydryl (2a) were monitored by $^1$H NMR spectroscopy to determine the zero-order kinetics for construction of 3a (Scheme 5). The rate of reaction was 1.8 times greater in D$_2$O than in H$_2$O with an inverse kinetic solvent isotope effect (KSIE: $k_{D_2O}/k_{H_2O}$) of 0.6, indicating a specific acid catalysis mechanism as follows. Aqua complex A with alcohol 2a is in a fast equilibrium with its Lewis acid adduct (conjugate acid) B. The rate-determining step involving the sp$^3$ C–O bond cleavage occurs via B to form the benzyl cation species C. Since the overall rate of the reaction depends only on the activation of alcohol 2a catalyzed by complex A, species B should form more slowly in H$_2$O than in D$_2$O. This is explained by the fact that hydrogen bonds of H$_2$O would be less effective at solvating gold cation A, which makes it less able to activate alcohol 2a in H$_2$O than in D$_2$O. Soper et al. investigated the structures of light and heavy water with X-ray diffraction and found that the OH bond length in H$_2$O is 3% longer than the OD bond length in D$_2$O. Harada et al. reported that the vibration profile of pre-edge excited HDO...
water has a greater OH-stretch contribution compared with OD, which supports the preference for OH being the weakened or broken hydrogen bond.19

Based on these results and on previous reports, the following mechanism can be suggested (Scheme 6). Initially, the treatment of NaAuCl4·2H2O with water-soluble phosphine ligand TPPMS generates an aqua complex A. Subsequently, the Lewis acidic gold(III) cation A coordinates with the oxygen atom of alcohol 2a to form intermediate B (Step 1: ligand exchange), and sp3 C–O bond activation occurs to generate the benzylic cation C (Step 2: C–O bond cleavage). The observed negative Hammett ρ value of 2.8 in the reaction of para-substituted benzhydryl alcohols 2 clearly shows cationic charge build-up during the rate-determining sp3 C–O bond-cleavage step (see Scheme 4B). Furthermore, the inverse kinetic solvent isotope effect (KSIE) of 0.6 is consistent with the specific acid catalysis mechanism (see Scheme 5). Next, the hydroxyl anion of gold species D acts as a base to remove the acidic proton of substrate 1a, which attacks the electrophilically active benzyl cation C to afford the corresponding N-benzylated product 3a (Step 3: N-benzylation).

Several control experiments were performed to examine the possibility of a radical pathway based on a single-electron transfer (SET). First, radical clock experiments using α-cyclopropylbenzyl alcohol (2b) were conducted to observe the rapid isomerization of the cyclopropylmethyl radical to the allylmethyl radical, which is well known in free-radical chemistry (Scheme 7A). As expected, corresponding 3w was obtained in 68% isolated yield via the cyclopropylmethyl cation and not the ring-opened product. Next, in the presence of a radical scavenger (BHA: 3-tert-butyl-4-hydroxyanisole, 1 equiv) or under an Ar atmosphere, the yield of the desired product 3a remained unchanged (Scheme 7B). These results suggest that a radical pathway based on a SET is not involved in this catalytic system.

Finally, to demonstrate the synthetic utility of our catalytic system, a gram-scale reaction of substrate 1a with alcohol 2a in the presence of gold(III)/TPPMS catalyst in water was carried out (Scheme 8). After 16 h, the reaction mixture was extracted with EtOAc, then crude product 3a was purified simply by recrystallization from n-hexane and EtOAc to give desired 3a in 77% isolated yield. The developed process avoids the use of column chromatography.

In summary, we have reported an environmentally benign protocol for the direct dehydrative amination of benzylc alcohols using a water-soluble gold(III)/TPPMS catalyst in water. This catalytic system is applicable for the direct modification of electron-deficient anilines and proceeds in moderate to excellent yields. This greener method has reduced waste generation, uses safer solvents and reaction
conditions, and increases energy efficiency, all of which contribute to the efficiency of a chemical transformation. Moreover, this reaction can be easily amplified to a gram level without the use of column chromatography for purification. Therefore, this strategy has emerged as an attractive alternative to traditional synthetic methods.

All of the starting materials and solvents were purchased from Sigma–Aldrich Japan (Tokyo, Japan), FUJIFILM Wako Pure Chemical Co. (Osaka, Japan), and TCI Co., Ltd. (Tokyo, Japan). All commercially available reagents and solvents were used without further purification. CHROMATOREX Q-PACK SI50 (Fuji Silysia Chemical Ltd, Japan) was used for flash column chromatography. All melting points were determined using a Yanako micro melting point apparatus without correction. IR (KBr) spectra were recorded with a JASCO FT/IR-4100 spectrometer. Mass spectra were obtained using a JEOL the JMS-700 MStation Mass Spectrometer.

**General Procedure**

A mixture of aniline (1 mmol), NaAuCl₄·2H₂O (20 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS) (18 mg, 0.05 mmol) and benzylic alcohol (1.2 mmol) in H₂O (4 mL) was heated at 80 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc) to give desired product 3.

**N-Benzhydryl-4-nitroaniline (3a)**

By following the scale-up experiment procedure (Scheme S5), 3a was obtained.

Yield: 2.34 g (77%); pale-yellow solid; mp 178–181 °C.

IR (KBr): 3408, 1600, 1513 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 2.34 (s, 3 H), 4.97 (br d, J = 4.8 Hz, 1 H), 5.59 (d, J = 4.8 Hz, 1 H), 6.50 (d, J = 9.2 Hz, 2 H), 7.15–7.20 (m, 4 H), 7.27–7.38 (m, 5 H), 8.03 (d, J = 9.4 Hz, 2 H).

13C NMR (100 MHz, DMSO-d₆): δ = 20.6, 60.0, 111.9, 125.9, 127.2, 127.4, 128.6, 129.2, 136.2, 138.1, 142.1, 153.6.

MS (FAB): m/z = 319 [M + H]⁺.

**N-[4-(4-Chlorophenyl)(phenyl)methyl]-4-nitroaniline (3d)**

By following the general procedure, 3d was obtained.

Yield: 258 mg (76%); yellow solid; mp 138–140 °C.

IR (KBr): 3371, 1599, 1531 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 5.61 (s, 1 H), 6.50 (d, J = 9.2 Hz, 2 H), 7.06 (dd, J = 8.5, 8.5 Hz, 4 H), 7.26 (dd, J = 7.1, 7.1 Hz, 4 H), 8.05 (d, J = 9.1 Hz, 2 H).

13C NMR (100 MHz, DMSO-d₆): δ = 60.2, 111.9, 125.9, 127.3, 127.4, 128.6, 136.3, 141.9, 153.6.

MS (FAB): m/z = 339 [M + H]⁺.

**N-[4-(4-Methoxyphenyl)(phenyl)methyl]-4-nitroaniline (3b)**

By following the general procedure, 3b was obtained.

Yield: 291 mg (85%); yellow powder; mp 123–125 °C.

IR (KBr): 3408, 1600, 1513 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 3.80 (s, 3 H), 4.97 (br d, J = 4.6 Hz, 1 H), 5.59 (d, J = 4.8 Hz, 1 H), 6.50 (d, J = 9.2 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 8.5 Hz, 2 H), 7.27–7.83 (m, 5 H), 8.02 (d, J = 9.2 Hz, 2 H).

13C NMR (100 MHz, DMSO-d₆): δ = 55.1, 59.6, 111.9, 114.0, 125.9, 127.2, 127.3, 128.6, 133.9, 136.2, 142.3, 153.6, 158.5.

MS (FAB): m/z = 335 [M + H]⁺.

**N-[4-Methoxyphenyl](phenyl)methyl]-4-nitroaniline (3e)**

By following the general procedure, 3e was obtained.

Yield: 28 mg (82%); yellow solid; mp 120–123 °C.

IR (KBr): 3408, 1602, 1515 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 3.80 (s, 3 H), 4.97 (br d, J = 4.6 Hz, 1 H), 5.59 (d, J = 4.8 Hz, 1 H), 6.50 (d, J = 9.2 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 8.5 Hz, 2 H), 7.27–7.83 (m, 5 H), 8.02 (d, J = 9.2 Hz, 2 H).

13C NMR (100 MHz, DMSO-d₆): δ = 55.1, 59.6, 111.9, 114.0, 125.9, 127.2, 127.3, 128.6, 133.9, 136.2, 142.3, 153.6, 158.5.

MS (FAB): m/z = 335 [M + H]⁺.

**N-[4-(4-Methoxyphenyl)](phenyl)methyl]-4-nitroaniline (3f)**

By following the general procedure, 3f was obtained.

Yield: 28 mg (82%); yellow solid; mp 120–123 °C.

IR (KBr): 3408, 1602, 1515 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 3.80 (s, 3 H), 4.97 (br d, J = 4.6 Hz, 1 H), 5.59 (d, J = 4.8 Hz, 1 H), 6.50 (d, J = 9.2 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 8.5 Hz, 2 H), 7.27–7.83 (m, 5 H), 8.02 (d, J = 9.2 Hz, 2 H).

13C NMR (100 MHz, DMSO-d₆): δ = 55.1, 59.6, 111.9, 114.0, 125.9, 127.2, 127.3, 128.6, 133.9, 136.2, 142.3, 153.6, 158.5.

MS (FAB): m/z = 335 [M + H]⁺.
N-(4-Methoxybenzyl)-4-nitroaniline (3h)\textsuperscript{21}

By following the general procedure, 3h was obtained.
Yield: 181 mg (70%); yellow solid; mp 135–137 °C.

IR (KBr): 3357, 1598, 1511 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}); \(\delta = 3.81\ (s, 3\ H), 4.35\ (s, 2\ H), 6.57\ (d, J = 9.2\ Hz, 2\ H), 6.90\ (d, J = 8.7\ Hz, 2\ H), 7.26\ (d, J = 8.7\ Hz, 2\ H), 8.09\ (d, J = 9.1\ Hz, 2\ H).

\textsuperscript{13}C NMR (100 MHz, DMSO-\textsubscript{d}\textsubscript{6}); \(\delta = 45.4, 55.1, 111.3, 113.9, 126.2, 128.6, 130.3, 135.8, 154.4, 158.4.

MS (FAB): \(m/z = 259\ [M + H]^+\).

N-Benzhydryl-2-nitroaniline (3i)\textsuperscript{24}

By following the general procedure, 3i was obtained.
Yield: 219 mg (72%); brown solid; mp 98–100 °C.

IR (KBr): 3382 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}); \(\delta = 4.60\ (d, J = 3.7\ Hz, 1\ H), 5.57\ (d, J = 4.5\ Hz, 1\ H), 6.80\ (dd, J = 8.1, 2.4\ Hz, 1\ H), 7.50\ (ddd, J = 8.1, 1.7, 0.8\ Hz, 1\ H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}); \(\delta = 62.0, 115.2, 116.0, 126.8, 127.2, 127.9, 129.1, 132.5, 136.1, 141.3, 144.2.

MS (EI): \(m/z = 304\ [M + H]^+\).

N-Benzhydryl-4-methoxy-2-nitroaniline (3j)\textsuperscript{24}

By following the general procedure, 3j was obtained.
Yield: 264 mg (79%); brown solid; mp 144–146 °C.

IR (KBr): 3372, 1541, 1518 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}); \(\delta = 3.77\ (s, 3\ H), 5.71\ (d, J = 5.5\ Hz, 1\ H), 6.69\ (d, J = 9.4\ Hz, 1\ H), 7.01\ (dd, J = 9.3, 3.2\ Hz, 1\ H), 7.26–7.36\ (m, 10\ H), 7.65\ (d, J = 3.0\ Hz, 1\ H), 8.51\ (br d, J = 5.0\ Hz, 1\ H).

\textsuperscript{13}C NMR (100 MHz, DMSO-\textsubscript{d}\textsubscript{6}); \(\delta = 55.6, 60.4, 106.8, 117.1, 126.8, 126.9, 127.6, 129.0, 130.9, 139.5, 142.0, 149.6.

MS (FAB): \(m/z = 335\ [M + H]^+\).

Anal. Calc'd for C\textsubscript{20}H\textsubscript{18}N\textsubscript{2}O\textsubscript{2}: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.87; H, 5.46; N, 8.32.

N-Benzhydryl-4-methyl-2-nitroaniline (3k)\textsuperscript{24}

By following the general procedure, 3k was obtained.
Yield: 252 mg (79%); pale-yellow solid; mp 123–126 °C.

IR (KBr): 3382, 1631, 1567, 1525 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}); \(\delta = 2.24\ (s, 3\ H), 5.72\ (d, J = 5.5\ Hz, 1\ H), 6.63\ (d, J = 8.7\ Hz, 1\ H), 7.01\ (dd, J = 9.3, 3.2\ Hz, 1\ H), 7.26–7.39\ (m, 10\ H), 7.65\ (d, J = 3.0\ Hz, 1\ H), 8.51\ (br d, J = 5.0\ Hz, 1\ H).

\textsuperscript{13}C NMR (100 MHz, DMSO-\textsubscript{d}\textsubscript{6}); \(\delta = 19.4, 60.3, 115.6, 125.2, 125.5, 126.6, 126.8, 127.5, 128.5, 129.0, 131.4, 137.9, 141.9, 142.0.

HRMS (FAB): \(m/z = 323\ [M + H]^+\) calcd for C\textsubscript{19}H\textsubscript{16}N\textsubscript{2}O\textsubscript{2}: 323.1196; found: 323.1196.

N-Benzhydryl-3-nitroaniline (3p)\textsuperscript{2}2

By following the general procedure, 3p was obtained.
Yield: 229 mg (75%); yellow solid; mp 111–113 °C.

IR (KBr): 3386 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}); \(\delta = 5.74\ (d, J = 5.5\ Hz, 1\ H), 6.66\ (ddd, J = 9.1, 7.2, 1.3\ Hz, 1\ H), 6.72\ (d, J = 8.6\ Hz, 1\ H), 8.20\ (dd, J = 8.6, 1.6\ Hz, 1\ H), 8.61\ (d, J = 5.4\ Hz, 1\ H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}); \(\delta = 62.8, 107.6, 112.3, 119.0, 127.2, 127.9, 129.1, 132.5, 136.5, 141.3, 144.2.

MS (EI): \(m/z = 304\ [M + H]^+\).

N-Benzhydryl-2-methyl-3-nitroaniline (3q)\textsuperscript{2}

By following the general procedure, 3q was obtained.
Yield: 228 mg (72%); brown solid; mp 95–97 °C.

IR (KBr): 3383 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}); \(\delta = 5.54\ (d, J = 4.5\ Hz, 1\ H), 5.64\ (d, J = 5.2\ Hz, 1\ H), 6.32\ (d, J = 8.8\ Hz, 1\ H), 7.65\ (d, J = 2.2\ Hz, 1\ H), 7.75\ (dd, J = 8.8, 2.3\ Hz, 1\ H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}); \(\delta = 12.6, 63.0, 112.5, 114.7, 115.5, 126.9, 127.4, 127.8, 129.0, 141.9, 146.2, 151.5.

MS (EI): \(m/z = 318\ [M + H]^+\).
N-Benzhydryl-2-methoxy-4-nitroaniline (3q)
By following the general procedure, 3q was obtained.
Yield: 329 mg (98%); yellow solid; mp 159–161 °C.
IR (KBr): 3418, 1594, 1498, 1329 cm⁻¹.
1H NMR (400 MHz, CDCl₃): δ = 5.30 (br d, J = 4.6 Hz, 1 H), 5.64 (d, J = 5.0 Hz, 1 H), 6.73 (s, 1 H), 6.92 (d, J = 8.0 Hz, 1 H), 7.29–7.39 (m, 10 H), 7.81 (d, J = 8.9 Hz, 1 H), 7.92 (d, J = 7.8, 15.1 Hz, 1 H).
13C NMR (100 MHz, CDCl₃): δ = 53.3 (br d, J = 4.6 Hz, 1 H), 5.64 (d, J = 5.0 Hz, 1 H), 6.73 (s, 1 H), 6.92 (d, J = 8.0 Hz, 1 H), 7.29–7.39 (m, 10 H), 7.81 (d, J = 8.9 Hz, 1 H), 7.92 (d, J = 7.8, 15.1 Hz, 1 H).
MS (FAB): m/z (%) = 354 (100) [M⁺].

Synthesis of 3v and 4-
A mixture of 4-nitronaphthalen-1-amine 1b (188 mg, 1 mmol), NaAuCl₄·2H₂O (20 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS) (18 mg, 0.05 mmol) and benzhydryl 2a (1.2 mmol) in H₂O (4 ml) was heated at 120 °C for 16 h under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was washed with hexanes, then purified by flash column chromatography (silica gel, hexanes/EtOAc) to give N-benzylated product 3v (237 mg, 0.67 mmol) and C-benzylated product 4 (71 mg, 0.20 mmol).

N-Benzhydryl-4-nitronaphthalen-1-amine (3v)
Mp 198–200 °C; brown solid.
IR (KBr): 3437 cm⁻¹.
1H NMR (400 MHz, CDCl₃): δ = 5.69 (br d, J = 4.4 Hz, 1 H), 5.83 (d, J = 4.7 Hz, 1 H), 6.39 (d, J = 8.9 Hz, 1 H), 7.55 (ddd, J = 9.2, 6.2, 1.3 Hz, 1 H), 7.72 (ddd, J = 8.8, 5.7, 1.3 Hz, 1 H), 7.88 (d, J = 8.5 Hz, 1 H), 8.31 (d, J = 8.8 Hz, 1 H), 9.00 (dd, J = 8.8, 0.6 Hz, 1 H).
13C NMR (100 MHz, CDCl₃): δ = 62.7, 103.6, 102.1, 122.0, 125.0, 126.0, 126.5, 127.4, 128.2, 128.5, 128.9, 129.2, 129.6, 135.8, 140.9, 148.0.
MS (EI); m/z (%) = 354 [M⁺].

2-Benzhydryl-4-nitronaphthalen-1-amine (4)
Brown solid; mp 198–201 °C.
IR (KBr): 3377, 1641, 1558 cm⁻¹.
1H NMR (400 MHz, CDCl₃): δ = 4.89 (br s, 2 H), 5.59 (s, 1 H), 7.16 (dd, J = 6.9, 1.6 Hz, 4 H), 7.54 (t, J = 7.4 Hz, 1 H), 7.70 (t, J = 7.7 Hz, 1 H), 7.80 (d, J = 8.5 Hz, 1 H), 7.96 (s, 1 H), 8.91 (d, J = 8.8 Hz, 1 H).
13C NMR (100 MHz, DMSO-d₆): δ = 49.7, 119.2, 121.9, 124.0, 124.1, 125.9, 127.1, 127.2, 129.1, 129.7, 130.6, 130.9, 132.2, 142.6, 150.5.
MS (EI): m/z (%) = 354 (100) [M⁺].


N-[Cyclopropyl(phenyl)methyl]-4-nitronaphthalene-3-carboxylic acid (3w)
By following the general procedure, 3w was obtained.
Yield: 181 mg (68%); yellow solid; mp 60–62 °C.
IR (KBr): 3415, 1598, 1513 cm⁻¹.
1H NMR (400 MHz, CDCl₃): δ = 0.39 (ddd, J = 9.6, 9.6, 5.3 Hz, 1 H), 0.48 (ddd, J = 9.4, 4.8 Hz, 1 H), 0.57–0.71 (m, 2 H), 1.19–1.28 (m, 12 H), 3.84 (br, d, J = 8.0 Hz, 1 H), 5.17 (br, s, 1 H), 6.41 (d, J = 9.2 Hz, 2 H), 7.26–7.37 (m, 5 H), 7.97 (d, J = 9.4 Hz, 2 H).
13C NMR (100 MHz, DMSO-d₆): δ = 3.4, 4.8, 18.4, 60.7, 111.4, 126.0, 126.4, 127.0, 128.4, 135.7, 142.8, 153.7.
MS (FAB): m/z (%) = 269 [M⁺].
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References


