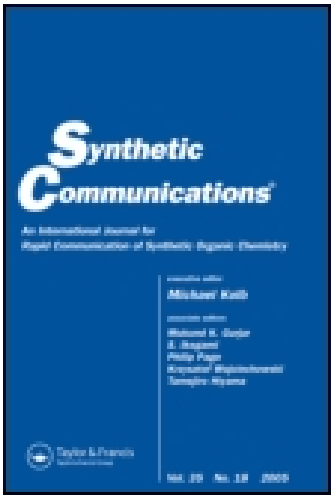

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SOLVENT-FREE, MICROWAVE-ASSISTED, ONE-POT SYNTHESIS OF 2-ACETYL-*N*,3-DIARYL-4-NITRO-BUTANAMIDES

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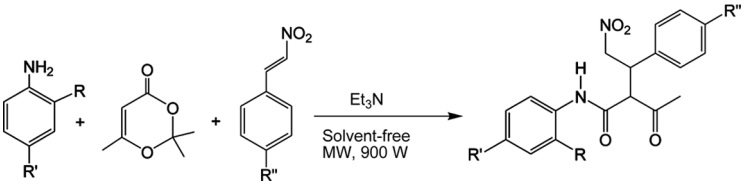
GRAPHICAL ABSTRACT



Abstract *A microwave-assisted diastereoselective synthesis of 2-acetyl-*N*,3-diaryl-4-nitro-butanamides* via *reaction of anilines, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one, and* **β***-nitrostyrenes in the presence of catalytic amounts of triethylamine under solvent-free conditions is described.*

Keywords Aniline; butanamide; Michael addition; microwave irradiation; β-nitrostyrene

INTRODUCTION

Michael addition of carbon nucleophiles to electron-deficient olefins is a classical and fundamental carbon–carbon bond-forming reaction. Michael adducts are versatile building blocks for agricultural and pharmaceutical compounds.[1] This reaction and its close variants have been extensively used in organic synthesis.[2] Generally, Michael additions are conducted in a suitable solvent in the presence of a strong base, either at room temperature or at elevated temperatures.[3] Because of the presence of the strong base, side reactions such as multiple condensations, polymerizations, rearrangements, and retro-Michael additions are common. These undesirable side reactions decrease the yield of the target adduct and render its purification difficult.

β-Nitrostyrenes, because of their strongly electron-withdrawing group,[4] can be easily transformed into a variety of valuable functionalities such as amines,

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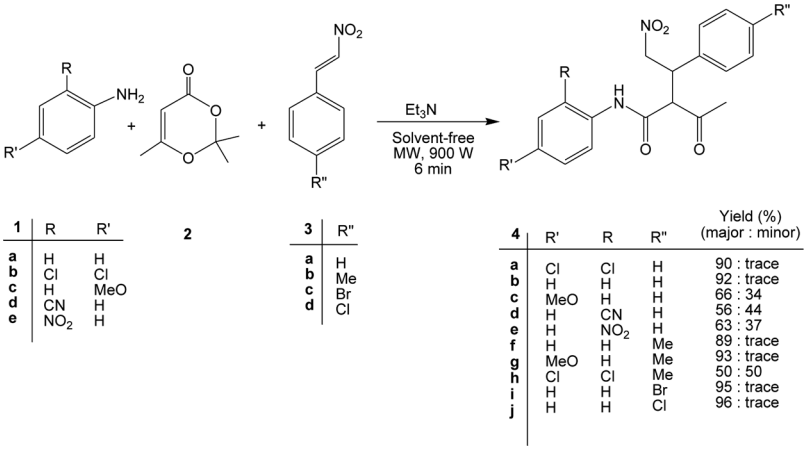


1	R	R'
a	H	H
b	Cl	Cl
c	H	MeO
d	CN	H
e	NO_2	H

2

3	R"
a	H
b	Me
c	Br
d	Cl

4	R'	R	R"	Yield (%) (major : minor)
a	Cl	Cl	H	90 : trace
b	H	H	H	92 : trace
c	MeO	H	H	66 : 34
d	H	CN	H	56 : 44
e	H	NO_2	H	63 : 37
f	H	H	Me	89 : trace
g	MeO	H	Me	93 : trace
h	Cl	Cl	Me	50 : 50
i	H	H	Br	95 : trace
j	H	H	Cl	96 : trace

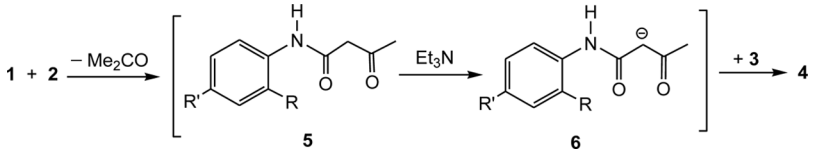
Scheme 1. Synthesis of 2-acetyl-*N*,3-diaryl-4-nitro-butanamides.

ketoximes, hydroxylamines, and nitroalkanes.[5–8] Therefore, conjugate addition to β-nitrostyrenes has received much attention in recent years. There have been many reports on the conjugate addition of β-nitrostyrenes mediated by organometallics including Grignard reagents,[9,10] alkyllithiums, and organoaluminums. However, most of these reagents were not satisfactory because of undesirable side reactions and poor conversion. For the purposes of ecofriendly "green chemistry," a reaction should ideally be conducted under solvent-free conditions with minimal or no side-product formation and utmost atom economy.[11]

In this context, we planned to conduct the Michael addition reaction under environmentally benign solvent-free conditions, wherein several disadvantages such as long reaction time and tedious workup can be overcome. As part of our current studies on the development of new routes in organic synthesis,[12–15] we report an efficient synthesis of functionalized 2-acetyl-*N*,3-diaryl-4-nitro-butanamides (Scheme 1).

RESULTS AND DISCUSSION

The reaction of anilines (**1**) and 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**2**) with β-nitrostyrenes (**3**) in the presence of catalytic amounts of Et_3N with microwave irradiation under solvent-free conditions led to 2-acetyl-*N*,3-diaryl-4-nitro-butanamides (**4**) in good yields (Scheme 1). Structures of compounds **4a–j** were assigned by infrared (IR), ^{1}H NMR, and ^{13}C NMR spectra. For example, the ^{1}H NMR spectrum of **4a** exhibited characteristic signals for the methyl and aryl protons at appropriate reagions of the spectrum. Because of the presence of a stereogenic center in these products, protons of the CH_2 group are diasterotopic and exhibit (AB)X systems. The adjacent methine groups in **4a** appear as a multiplet (4.31–4.42 ppm) and doublet (4.65 ppm). The ^{13}C NMR spectrum of **4a** showed the carbonyl groups at 166.0 and 201.9 ppm. The mass spectrum of **4a** displayed a molecular ion peak at $m/z = 395$. Compounds **4a-j** possess two stereogenic centers, and they can exist as



Scheme 2. Rationalization for the formation of 2-acetyl-*N*,3-diaryl-4-nitro-butanamides.

two diastereoisomers. The ^{1}H and ^{13}C NMR spectra of these compounds confirm the presence of these diastereoisomers.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation. Presumably, the intermediate **5** formed from the reaction of **1** and **2** is converted to **6** in the presence of Et_3N. Finally, Michael addition of **6** to β-nitrostyrene **3** leads to the desired products **4** (Scheme 2).

In conclusion, microwave irradiation of anilines, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one, and β-nitrostyrenes in the presence of a catalytic amount of Et_3N, under solvent-free conditions, led to 2-acetyl-*N*,3-diaryl-4-nitro-butanamides in good yields. The present procedure has the advantages that the Michael addition reaction is carried out under environmentally benign solvent-free conditions and the starting materials can be used without prior activation or modification.

EXPERIMENTAL

Anilines (**1**), 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**2**), and Et_3N were obtained from Fluka and were used without further purification. β-Nitrostyrenes (**3**) were prepared according to the literature procedure.[16] Melting points were determined on an Electrothermal-9100 apparatus. IR spectra were measured with a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were found with a Bruker DRX-500 Avance instrument in acetone-d_6 at 500 and 125.7 MHz, respectively (δ in parts per million, *J* in hertz). Electron-impact mass spectrometry (70 eV) was conducted on Finnigan-MAT-8430 mass spectrometer, in m/z. Elemental analyses (C, H, N) were performed with a Vario EL III CHNOS elemental analyzer. The reactions were carried out in a domestic microwave oven, MW 3070 GS, (Feller, Germany).

General Procedure

Anilines (**1**, 2 mmol) and 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**2**, 0.28 g, 2 mmol) were mixed in an agate mortar for 2 min and then irradiated in the microwave oven at 900 W for 3 min. A mixture of Et_3N (0.08 g) and β-nitrostyrene (**3**, 2 mmol) was added to the reaction mixture and irradiated in the microwave oven. After completion of the reaction (6 min), as indicated by thin-layer chromatography (TLC, hexane/AcOEt 4:1), the workup of the reaction is simply done by extraction with acetone and evaporating the solvent under reduced pressure to leave a residue, which was purified by column chromatography (SiO_2; hexane/AcOEt 5:1) to afford the pure desired products.

Selected Data

***2-Acetyl-N-(2,4-dichlorophenyl)-4-nitro-3-phenyl-butanamide* (4a).** Yellow oil, yield: 0.71 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 3450, 3265, 1719, 1655, 1551, 1513, 1473, 1377, 1293, 1117, 816, 695. ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 2.08$ (3 H, s, Me), 4.31–4.42 (1 H, m, CH), 4.65–4.82 (1 H, d, ^2J 10.8 Hz, CH), 4.88–5.11 (2 H, m, CH_2), 7.22–7.55 (8 H, m, CH), 9.21 (1 H, s, NH). ^{13}C NMR (125.7 MHz, acetone-d_6): $\delta = 29.6$ (Me), 47.6 (CH), 63.9 (CH), 78.7 (CH_2), 126.8 (CH), 127.9 (CH), 128.7 (CH), 129.4 (CH), 129.6 (CH), 129.8 (CH), 129.9 (C), 131.2 (C), 134.1 (C), 138.0 (C), 166.0 (C=O), 201.9 (C=O). EI-MS: 395 (M+, 2), 246 (16), 162 (100), 77 (62), 43 (49). Anal. calcd. (%) for $C_{18}H_{16}Cl_2N_2O_4$ (395.23): C, 54.70; H, 4.08; N, 7.09. Found: C, 54.65; H, 3.98; N, 7.00.

***2-Acetyl-4-nitro-N,3-diphenyl-butanamide* (4b).** White powder, yield: 0.60 g (92%), mp 168–170 °C. IR (KBr) (ν_{max}/cm^{-1}): 3275, 1715, 1651, 1552, 1440, 1377, 1354, 1152, 751, 694. ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 2.34$ (3 H, s, Me), 4.33–4.35 (2 H, m, CH), 4.83–4.94 (2 H, m, CH), 7.03 (1 H, t, ^3J 7.3 Hz, CH), 7.18 (1 H, t, ^3J 7.3 Hz, CH), 7.20 (2 H, t, ^3J 7.5 Hz, CH), 7.26 (2 H, t, ^3J 7.4 Hz, CH), 7.35 (2 H, d, ^3J 7.5 Hz, CH), 7.38 (2 H, d, ^3J 7.1 Hz, CH), 9.35 (1 H, s, NH). ^{13}C NMR (125.7 MHz, acetone-d_6): $\delta = 29.8$ (CH), 43.9 (Me), 64.9 (CH), 79.1 (CH_2), 120.8 (CH), 125.0 (CH), 128.5 (CH), 129.3 (CH), 129.3 (CH), 129.4 (CH), 138.4 (C), 139.1 (C), 165.3 ($CONH_2$), 202.2 (C=O). EI-MS: 326 (M+, 1), 238 (4), 177 (15), 93 (100), 77 (60), 43 (50). Anal. calcd. (%) for $C_{18}H_{18}N_2O_4$ (326.34): C, 66.25; H, 5.56; N, 8.58. Found: C, 66.10; H, 5.54; N, 8.35.

***2-Acetyl-N-(4-methoxyphenyl)-4-nitro-3-phenyl-butanamide* (4c).** Yellow powder, mp 170–172 °C. IR (KBr) (ν_{max}/cm^{-1}): 3280, 1711, 1642, 1551, 1508, 1413, 1375, 1249, 1028, 824, 697. EI-MS: 356 (M^+, 1), 207 (17), 123 (100), 77 (59), 43 (52). Anal. calcd. (%) for $C_{19}H_{20}N_2O_6$ (356.37): C, 64.04; H, 5.66: N, 7.86. Found: C, 63.95; H, 5.60; N, 7.94. NMR data for the major isomer (0.47 g, 66%); ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 2.12$ (3 H, s, Me), 3.71 (3 H, s, MeO), 4.19 (1 H, d, ^3J 8.9 Hz, CH), 4.28–4.36 (1 H, m, CH), 4.83–5.01 (2 H, m, CH_2), 6.76 (2 H, d, ^3J 9.0 Hz, CH), 7.21 (2 H, d, ^3J 7.0 Hz, CH), 7.26 (2 H, t, ^3J 7.7 Hz, CH), 7.34–7.38 (1 H, m, CH), 7.35 (2 H, d, ^3J 9.1 Hz, CH), 9.28 (1 H, s, NH). ^{13}C NMR (125.7 MHz, acetone-d_6): $\delta = 29.7$ (Me), 43.9 (CH), 55.6 (MeO), 64.7 (CH), 79.2 (CH_2), 114.5 (CH), 122.5 (CH), 128.4 (CH), 129.2 (C), 129.3 (CH), 132.1 (C), 138.5 (C), 157.4 (C), 165.0 ($CONH_2$), 202.3 (C=O). NMR data for the minor isomer (0.24 g, 34%): ^{1}H-NMR (500 MHz, acetone-d_6): $\delta = 2.06$ (1 H, s, Me), 3.78 (1 H, s, MeO), 4.28–4.36 (2 H, m, CH), 4.83–5.01 (2 H, m, CH_2), 6.90 (2 H, d, ^3J 9.0 Hz, CH), 7.18 (2 H, d, ^3J 7.4 Hz, CH), 7.25–7.28 (1 H, m, CH), 7.32 (2 H, t, ^3J 7.6 Hz, CH), 7.54 (1 H, d, ^3J 9.0 Hz, CH), 9.50 (1 H, s, NH). ^{13}C NMR (125.7 MHz, acetone-d_6): $\delta = 29.9$ (Me), 43.9 (CH), 55.7 (MeO), 64.8 (CH), 78.8 (CH_2), 114.7 (CH), 122.4 (CH), 128.6 (CH), 129.1 (C), 129.5 (CH), 132.4 (C), 138.8 (C), 157.6 (C), 165.5 ($CONH_2$), 201.6 (C=O).

***2-Acetyl-N-(2-cyanophenyl)-4-nitro-3-phenyl-butanamide* (4d).** White powder, mp 159–161 °C. IR (KBr) (ν_{max}/cm^{-1}): 3410, 2250, 1717, 1694, 1577, 1543, 1518, 1442, 1373, 762. EI-MS: 351 (M^+, 1), 202 (18), 118 (100), 77 (64), 43 (55). Anal. calcd. (%) for $C_{19}H_{17}N_3O_4$(351.35): C, 64.95; H, 4.88; N, 11.96.

Found: C, 64.82; H, 4.80; N, 12.07. NMR data for the major isomer (0.39 g, 56%): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.99$ (3 H, s, Me), 4.13 (1 H, d, ^3J 10.9 Hz, CH), 4.27–4.31 (1 H, m, CH), 4.82–5.32 (2 H, m, CH_2), 7.19 (1 H, t, ^3J 7.6 Hz, CH), 7.22 (1 H, d, ^3J 7.0 Hz, CH), 7.28–7.33 (4 H, m, CH), 7.51 (1 H, t, ^3J 8.3 Hz), 7.52–7.87 (1 H, m, CH), 7.86 (1 H, d, ^3J 8.4 Hz, CH), 8.61 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 30.2$ (Me), 43.9 (CH), 62.8 (CH), 78.0 (CH_2), 115.7 (CN), 124.6 (C), 127.8 (CH), 128.5 (CH), 128.8 (CH), 129.1 (CH), 129.3 (CH), 132.4 (CH), 133.6 (C), 133.9 (CH), 135.0 (C), 164.6 ($CONH_2$), 203.9 (C=O). NMR data for the minor isomer (0.31 g, 44%): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.47$ (3 H, s, Me), 4.21 (1 H, d, ^3J 8.4 Hz, CH), 4.27–4.31 (1 H, m, CH), 4.82–5.32 (2 H, m, CH_2), 7.21 (1 H, d, ^3J 7.0 Hz, CH), 7.28–7.39 (5 H, m, CH), 7.55 (1 H, d, ^3J 7.7 Hz), 7.52–7.87 (1 H, m, CH), 8.15 (1 H, d,^3J 8.2 Hz, CH), 8.93 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 31.0$ (Me), 45.3 (CH), 64.4 (CH), 78.6 (CH_2), 115.9 (CN), 124.7 (C), 127.9 (CH), 128.5 (CH), 128.9 (CH), 129.2 (CH), 129.5 (CH), 132.7 (CH), 133.8 (C), 134.0 (CH), 135.6 (C), 164.9 ($CONH_2$), 204.7 (C=O).

2-Acetyl-4-nitro-N-(2-nitrophenyl)-3-phenyl-butanamide **(4e).** Yellow powder, mp 90–92 °C. IR (KBr) (ν_{max}/cm^{-1}): 3345, 1723, 1653, 1665, 1550, 1498, 1451, 1340, 1274, 1150, 734, 698. EI-MS: 571 (M^+, 2), 222 (14), 138 (100), 77 (60), 43 (55). Anal. calcd. (%) for $C_{18}H_{17}N_3O_6$ (571.34): C, 58.22; H, 4.61; N, 11.32. Found: C, 58.12; H, 4.52; N, 11.13. NMR data for the major isomer (0.47 g, 63%): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.45$ (3 H, s, Me), 4.19 (1 H, d, ^2J 9.9 Hz, CH), 4.30 (1 H, m, CH), 4.83 (2 H, m, CH_2), 7.18–7.38 (6 H, m, CH), 7.58 (1 H, t, ^3J 7.6 Hz, CH), 8.13 (1 H, d, ^3J 8.4 Hz, CH), 8.32 (1 H, d, ^3J 8.4 Hz, CH), 10.41 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 29.6$ (Me), 43.6 (CH), 65.1 (CH), 77.7 (CH_2), 122.5 (CH), 124.5 (CH), 125.9 (CH), 128.7 (CH), 129.4 (CH), 133.3 (C), 135.6 (C), 135.8 (C), 164.8 ($CONH_2$), 202.2 (C=O). NMR data for the minor isomer (0.28 g, 37%); ^{1}H NMR (500 MHz, $CDCl_3$: $\delta = 2.059$ (3 H, s, Me), 4.11 (1 H, d, ^2J 10.4 Hz, CH), 4.30 (1 H, m, CH), 4.83 (2 H, m, CH_2), 7.18–7.38 (6 H, m, CH), 7.7 (1 H, t, ^3J 7.6 Hz, CH), 8.25 (1 H, d, ^3J 8.4 Hz, CH), 8.67 (1 H, d, ^3J 8.4 Hz, CH), 10.82 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 30.2$ (Me), 44.2 (CH), 65.7 (CH), 77.0 (CH_2), 122.4 (CH), 124.2 (CH), 125.6 (CH), 128.5 (CH), 129.2 (CH), 133.1 (C), 135.4 (C), 135.8 (C), 165.2 ($CONH_2$), 202.2 (C=O).

2-Acetyl-4-nitro-N-phenyl-3-p-tolyl-butanamide **(4f).** White powder, yield: 0.61 g (89%), mp 193–195 °C. IR (KBr) (ν_{max}/cm^{-1}): 3270, 1712, 1649, 1555, 1440, 1354, 1153, 804, 750. ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 2.21$ (3 H, s, Me), $\delta = 2.35$ (3 H, s, Me), 4.29–4.35 (2 H, m, CH), 4.81–4.92 (2 H, m, CH), 7.03–7.09 (3 H, m, CH), 7.21–7.27 (4 H, m, CH), 7.39–7.40 (2 H, m, CH), 9.45 (1 H, s, NH). ^{13}C NMR (125.7 MHz, acetone-d_6): $\delta = 20.9$ (Me), 29.7 (Me), 43.5 (CH), 64.9 (CH), 79.3 (CH_2), 120.6 (CH), 120.7 (CH), 124.9 (CH), 129.1 (CH), 129.4 (CH), 129.9 (CH), 135.3 (C), 138.0 (C), 128.7 (CH), 139.2 (C), 165.3 ($CONH_2$), 202.3 (C=O). EI-MS: 340 (M^+, 2), 177 (18), 93 (100), 91 (63), 43 (52). Anal. calcd. (%) for $C_{19}H_{20}N_2O_4$ (340.37): C, 67.05; H, 5.92; N, 8.23. Found: C, 67.00; H, 5.80; N, 8.32.

2-Acetyl-N-(4-methoxyphenyl)-4-nitro-3-p-tolyl-butanamide **(4g).** White powder, yield: 0.69 g (93%), mp 176–178 °C. IR (KBr) (ν_{max}/cm^{-1}): 3275, 1715, 1649, 1554, 1511, 1433, 1377, 1354, 1251, 1038, 845. ^{1}H NMR (500 MHz,

acetone-d_6): δ = 2.21 (3 H, s, Me), 2.34 (3 H, s, Me), 3.78 (3 H, s, MeO), 4.27–4.29 (2 H, m, CH), 4.80–4.90 (2 H, m, CH_2), 6.77 (2 H, d, ^3J 7.1 Hz, CH), 7.07 (2 H, d, ^3J 7.9 Hz, CH), 7.23–7.26 (4 H, m, CH), 9.29 (1 H, s, NH). ^{13}C NMR (125.7 MHz, acetone-d_6): δ = 20.9 (Me), 29.9 (CH), 43.5 (Me), 55.6 (MeO), 64.8 (CH), 79.3 (CH_2), 114.5 (CH), 122.4 (CH), 129.0 (CH), 129.9 (CH), 132.3 (C), 135.4 (C), 138.0 (C), 157.4 (C), 165.0 ($CONH_2$), 202.4 (C=O). EI-MS: 370 (M^+, 1), 207 (15), 123 (100), 91 (66), 43 (54). Anal. calcd. (%) for $C_{20}H_{22}N_2O_5$ (370.39): C, 64.85; H, 5.99; N, 7.56. Found: C, 64.51; H, 5.78; N, 7.67.

***2-Acetyl-N-(2,4-dichlorophenyl)-4-nitro-3-p-tolyl-butanamide* (4h).** Yellow powder, mp 146–148 °C. IR (KBr) (ν_{max}/cm^{-1}): 3240, 3095, 1722, 1651, 1554, 1526, 1472, 1377, 1297, 1149, 821, 545. EI-MS: 409 (M^+, 1), 246 (18), 163 (100), 91 (62), 43 (53). Anal. calcd. (%) for $C_{19}H_{18}Cl_2N_2O_4$(409.26): C, 55.76; H, 4.43; N, 6.84. Found: C, 55.84; H, 4.49; N, 6.95. NMR data for the major isomer (0.72 g, 88%): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (3 H, s, Me), 2.33 (3 H, s, Me), 4.02 (1 H, d, ^3J 11.1 Hz, CH), 4.16–4.20 (1 H, m, CH), 4.76–4.93 (2 H, m, CH_2), 7.06 (2 H, d, ^3J 7.9 Hz, CH), 7.12–7.16 (3 H, m, CH), 7.31 (1 H, d, ^4J 2.25 Hz, CH), 7.94 (1 H, d, ^3J 8.8 Hz, CH), 8.50 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.03 (Me), 29.3 (Me), 43.8 (CH), 63.1 (CH), 77.4 (CH_2), 122.8 (CH), 124.4 (C), 127.6 (CH), 127.8 (CH), 128.8 (CH), 129.8 (CH), 130.0 (C), 131.7 (C), 132.4 (C), 138.6 (C), 164.1 ($CONH_2$), 204.8 (C=O). NMR data for the minor isomer (0.72 g, 88%); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.27 (3 H, s, Me), 2.41 (3 H, s, Me), 4.08 (1 H, d, ^3J 8.0 Hz, CH), 4.16–4.20 (1 H, m, CH), 4.75–4.93 (2 H, m, CH_2), 7.07 (2 H, d, ^3J 7.9 Hz, CH), 7.12–7.16 (2 H, m, CH), 7.25–7.27 (1 H, m, CH), 7.41 (1 H, d, ^4J 2.25 Hz, CH), 8.19 (1 H, d, ^3J 8.8 Hz, CH), 8.82 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 22.6 (Me), 29.7 (Me), 45.1 (CH), 64.7 (CH), 78.0 (CH_2), 122.9 (CH), 124.7 (C), 127.7 (CH), 127.8 (CH), 129.1 (CH), 130.1 (CH), 130.4 (C), 132.4 (C), 132.5 (C), 138.7 (C), 164.4 ($CONH_2$), 205.2 (C=O).

***2-Acetyl-3-(4-bromophenyl)-4-nitro-n-phenylbutanamide* (4i).** White powder, yield: 0.77 g (95%), mp 195–197 °C. IR (KBr) (ν_{max}/cm^{-1}): 3261, 3014, 1734, 1653, 1601, 1541, 1436, 1364, 1217, 1006, 752. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.03 (3 H, s, Me), 3.93–3.99 (1 H, m, CH), 4.18–4.23 (1 H, m, CH), 4.75–4.82 (2 H, m, CH_2), 7.03–7.52 (9 H, m, CH), 8.07 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 30.7 (Me), 44.3 (CH), 64.7 (CH), 78.0 (CH_2), 120.16 (C), 122.9 (CH), 125.4 (CH), 129.1 (CH), 129.5 (CH), 132.3 (CH), 134.9 (C), 137.0 (C), 163.6 ($CONH_2$), 202.6 (C=O). EI-MS: 405 (M^+, 1), 177 (16), 93 (100), 77 (65), 43 (56). Anal. calcd. (%) for $C_{18}H_{17}BrN_2O_4$ (405.24): C, 53.35; H, 4.23; N, 6.91. Found: C, 53.29; H, 4.28; N, 6.88.

***2-Acetyl-3-(4-chlorophenyl)-4-nitro-n-phenylbutanamide* (4j).** White powder, yield: 0.69 g (96%), mp 189–191 °C. IR (KBr) (ν_{max}/cm^{-1}): 3263, 3014, 2356, 1734, 1604, 1547, 1437, 1364, 1216, 1094, 824. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.43 (3 H, s, Me), 3.95–4.01 (1 H, m, CH), 4.22 (1 H, d, ^3J 7.4 Hz, CH), 4.78–4.92 (2 H, m, CH_2), 7.13–7.53 (9 H, m, CH), 7.94 (1 H, s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.5 (Me), 30.3 (CH), 43.4 (CH), 63.1 (CH_2), 120.1 (CH), 120.4 (CH), 125.3 (CH), 125.5 (CH), 129.1 (C), 129.2 (C), 129.4 (C), 129.7 (C), 172.0 ($CONH_2$), 203.2 (C=O). EI-MS: 360 (M^+, 1), 177 (15), 93 (100), 77

(66), 43 (54). Anal. calcd. (%) for $C_{18}H_{17}ClN_2O_4$ (360.79): C, 59.92; H, 4.75; N, 7.76. Found: C, 59.78; H, 4.64; N, 7.70.

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