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Synthesis and Reactions of 11-Substituted 3,3-Dimethyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones

KEIZO MATSUO,* MITSUHIRO YOSHIDA, MASANOBU OHTA, and KUNIYOSHI TANAKA

Faculty of Pharmaceutical Sciences, Kinki University, 3-4-1 Kowakae, Higashiosaka, Osaka 577, Japan

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11-Substituted 3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones were synthesized by dehydrative cyclization of 3-(2-acylaminoanilino)-5,5-dimethyl-2-cyclohexen-1-ones with polyphosphoric acid. The 11-phenyl derivative showed moderate analgesic activity.

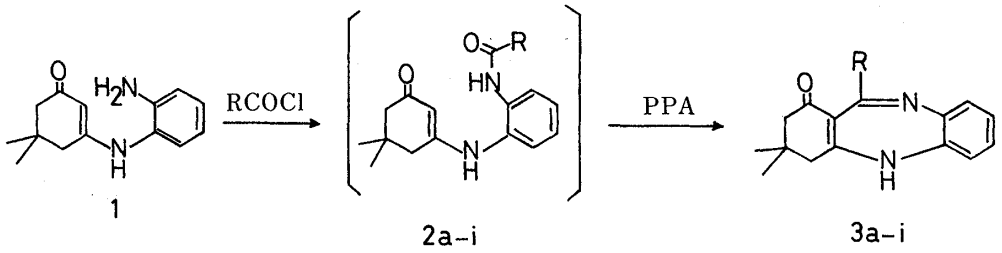
Keywords——11-substituted 3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one; polyphosphoric acid; dimedone; dehydrative cyclization; Mannich reaction; analgesic activity

Miyano and Abe synthesized 3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**6**) by Mannich-type cyclization of 3-(2-aminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (**1**) and benzaldehyde in the presence of a catalytic amount of acetic acid in good yield.[1] They also found that it had narcotic and analgesic activities.[2]

In the course of our synthetic studies on biologically active compounds using dimedone, tetronic acids, and tetramic acids,[3] we planned to synthesize 11-substituted 3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones (**3**), because Sternbach *et al.* had reported that 5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-ones were usually superior to the corresponding tetrahydro derivatives in muscle relaxant and taming, and anticonvulsant activities.[4]

For the preparation of 3,3-dimethyl-11-phenyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*]-[1,4]diazepin-1-one (**3a**), dehydrogenation of **6** was expected to be a convenient method; however, an attempt failed.[5] As the next approach, dehydrative cyclization of 3-(2-acylaminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (**2**) with polyphosphoric acid (PPA) was tried, because the α-position of the enaminone system is particularly reactive to electrophilic reagents.[1] Thus, 3-(2-benzoylaminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (**2a**) was prepared from 3-(2-aminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (**1**)[1] and benzoyl chloride in pyridine in 86% yield. The resulting enaminone **2a** was then treated with excess PPA at 120—130 °C for 1 h, and dehydrative cyclization took place. After the addition of water to the cooled reaction mixture, the precipitates formed were collected and recrystallized from dimethyl sulfoxide (DMSO) and water. The desired compound, 3,3-dimethyl-11-phenyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**3a**) was obtained in 86% yield.

In order to examine the generality of this reaction, electron-withdrawing and electron-releasing substituents were introduced on the phenyl ring of **2a**, and further, the phenyl ring was replaced by a heteroaromatic ring or an alkyl group. The reaction occurred smoothly in all cases. However, in the cases of **3d**, **3e**, and **3f**, the usual work-up mentioned above gave phosphoric acid salts. Therefore, the crude products were treated with dil. NaOH solution before recrystallization to obtain the free bases. The yields were fair to moderate, except in the case of **3d** and **3i**. In the latter case, 3-(2-aminoanilino)-2-isobutyryl-5,5-dimethyl-2-cyclohexen-1-one (**5**) was obtained in 53% yield along with **3i**. The by-product **5** was



a : R=phenyl
b : R=2-fluorophenyl
c : R=4-chlorophenyl
d : R=2-tolyl
e : R=4-tolyl
f : R=4-methoxyphenyl
g : R=4-nitrophenyl
h : R=2-thienyl
i : R=isopropyl

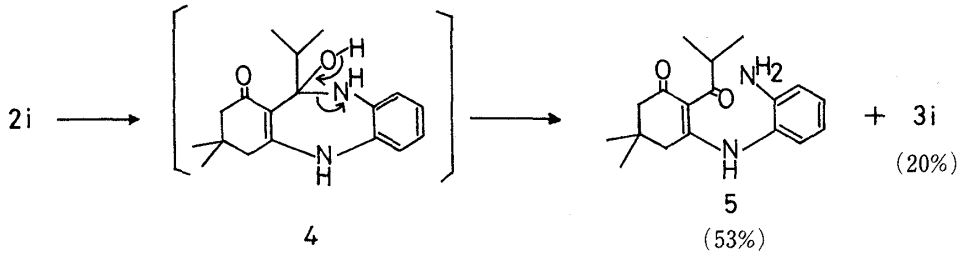
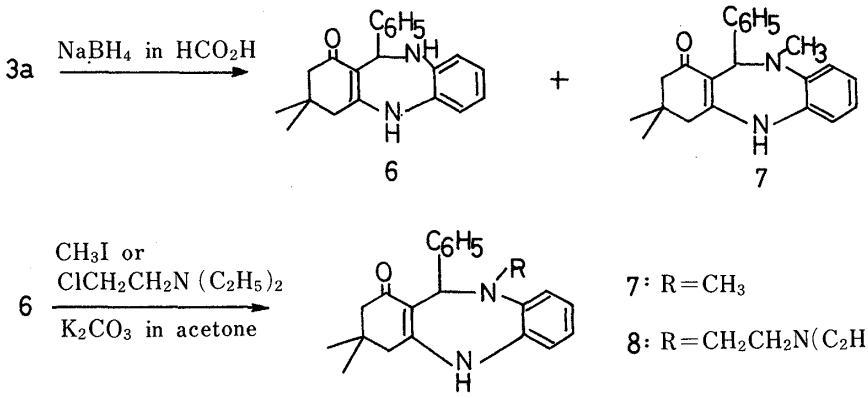


Chart 1



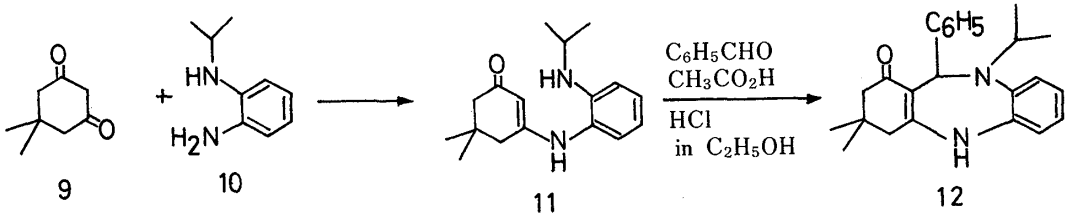


Chart 2

presumably derived through isomerization of the initially formed intermediate **4** as shown in Chart 1.

Next, we examined some reactions of **3a** and related compounds. When **3a** was treated with sodium borohydride in 90% formic acid at 10—18 °C.[6] **6** and 3,3,10-trimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**7**) were obtained in 76 and 14% yields, respectively. Because of our interest in biological activities, alkylation of the N-10 position of **6** was tried. When compound **6** was treated with methyl iodide or 2-chlorotriethylamine in acetone in the presence of potassium carbonate, and sodium iodide in

TABLE I. Melting Points, Yields, and Elemental Analyses or MS of **3a—i**

Compound	R	mp (°C) (Recryst. solvent)[a]	Yield (%)[b]	Formula	Analysis (%) or MS (M^+: m/z) Calcd (Found)		
					C	H	N
a	Phenyl	>300 (i)	86	$C_{21}H_{20}N_2O$	79.72 (79.73)	6.37 6.42	8.85 8.76)
b	2-Fluorophenyl	187—190 (i)	46	$C_{21}H_{19}FN_2O$	75.43 (75.34)	5.73 5.59	8.38 8.39)
c	4-Chlorophenyl	290—293 (i)	72	$C_{21}H_{19}ClN_2O \cdot 1/2H_2O$	70.09 (69.79	5.60 5.34	7.79 7.81)
d	2-Tolyl	262—264 (ii)	35	$C_{22}H_{22}N_2O$	79.97 (80.12	6.71 6.61	8.48 8.57)
e	4-Tolyl	291—293 (i)	50	$C_{22}H_{22}N_2O$	79.97 (80.18	6.71 6.67	8.48 8.50)
f	4-Methoxyphenyl	244—248 (i)	64	$C_{22}H_{22}N_2O_2$	76.28 (76.49	6.40 6.39	8.09 8.21)
g	4-Nitrophenyl	281—284 (i)	60	$C_{21}H_{19}N_3O_3$	69.79 (69.62	5.30 5.26	11.63 11.44)
h	2-Thienyl	291—294 (i)	45	$C_{19}H_{18}N_2OS$	70.78 (70.85	5.63 5.71	8.69 8.59)
i	Isopropyl	207—208 (ii)	20	$C_{18}H_{22}N_2O$	282.1732[c] (282.1714)		

a) Recrystallized from i) DMSO–H_2O, and ii) iso-PrOH–hexane. *b*) Based on **2**. *c*) Satisfactory microanalysis was not obtained, because of the instability of this product.

the latter case, the *N*-alkylation product **7** or 10-(2-diethylaminoethyl)-3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**8**) was obtained in 92 or 32% yield. An attempt to introduce an isopropyl group at the N-10 position using the same reaction conditions as above failed and resulted in the recovery of the starting material, possibly because of steric hindrance. Therefore, an alternative route was applied, namely Miyano's procedure.[1] Thus, 3-(2-isopropylaminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (**11**), which was derived from dimedone (**9**) and 2-isopropylaminoaniline (**10**)[7] by *p*-toluenesulfonic acid (*p*-TsOH)-catalyzed dehydration, was treated with benzaldehyde in ethanol in the presence of acetic acid and conc. HCl at room temperature. The desired Mannich-type cyclization product, 10-isopropyl-3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**12**) was isolated in 73% yield.

Finally, when compounds **3a** and **3c** were tested for analgesic activity using the phenylquinone writhing method, **3a** showed moderate activity (45.9% inhibition) in the dose of 50 mg/kg (using mice as the test animal), but **3c** was inactive. Pharmacological testing of the other compounds and further chemical modifications of **3** are now under way.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus, model MP-S3, and are uncorrected. Infrared (IR) and proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured in Nujol mulls with a Hitachi 260-30 infrared spectrometer, and a JEOL JNM-FX 200 (200 MHz) spectrometer using tetramethylsilane (TMS) as an internal standard, respectively. Mass spectra (MS) were measured with a JEOL JMS-HX 100 spectrometer.

3-(2-Benzoylaminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (2a)——A solution of benzoyl chloride (0.31 g, 2.2 mmol) in dry benzene (2 ml) was added to a solution of 3-(2-aminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (**1**) (0.46 g, 2 mmol) in dry pyridine (5 ml) with stirring and ice-cooling. The reaction mixture was stirred at room

TABLE II. IR and NMR Spectral Data for **3a—i**

Compound	IR ν_{max}^{Nujol} cm^{-1} [a]	^{1}H-NMR δ (J in Hz) [b]
a	3250, 1610, 1590, 1510, 1225, 1160, 1055, 910	(DMSO-d_6) 1.10 (6H, s, 2×CH_3), 2.13 and 2.47 (each 2H, s, 2×CH_2), 6.74—7.50 (9H, m, ArH), 8.01 (1H, s, NH)
b	3260, 1630, 1610, 1585, 1510, 1270, 1225, 1155, 1060, 940, 760	(DMSO-d_6) 1.00 (6H, s, 2×CH_3), 2.02 and 2.39 (each 2H, s, 2×CH_2), 6.68—7.44 (8H, m, ArH), 8.01 (1H, s, NH)
c	3275, 1630(sh), 1610, 1590, 1330, 1220, 1160, 1095, 1020, 910, 840	(DMSO-d_6) 1.06 (6H, s, 2×CH_3), 2.12 and 2.46 (each 2H, s, 2×CH_2), 6.70—7.46 (8H, m, ArH), 8.09 (1H, s, NH)
d	3250, 1630, 1600, 1575, 1500, 1210, 1160, 1050, 910, 780, 760, 750	($CDCl_3$) 1.05 (6H, s, 2×CH_3), 2.08 and 2.19 (each 2H, s, 2×CH_2), 2.50 (3H, s, $ArCH_3$), 5.55 (1H, br s, NH), 6.86—7.22 (8H, m, ArH)
e	3280, 1610, 1590(sh), 1605, 1330, 1220, 1180, 1160, 1055, 910, 825, 755	(DMSO-d_6) 1.09 (6H, s, 2×CH_3), 2.12 and 2.46 (each 2H, s, 2×CH_2), 2.30 (3H, s, $ArCH_3$), 6.70—7.38 (8H, m, ArH), 7.95 (1H, s, NH)
f	3270, 1610(sh), 1595, 1605, 1255, 1170, 840, 760	(DMSO-d_6) 1.10 (6H, s, 2×CH_3), 2.14 and 2.46 (each 2H, s, 2×CH_2), 3.78 (3H, s, OCH_3), 6.70—8.46 (8H, m, ArH), 7.93 (1H, s, NH)
g	3250, 1630, 1600, 1580, 1520, 1500, 1345, 1215, 1155, 865, 850, 755	(DMSO-d_6) 1.08 (6H, s, 2×CH_3), 2.12 and 2.46 (each 2H, s, 2×CH_2), 6.72—8.20 (8H, m, ArH), 8.23 (1H, s, NH)
h	3260, 1610, 1590, 1505, 1220, 1055, 970, 760, 715	(DMSO-d_6) 1.09 (6H, s, 2×CH_3), 2.20 and 2.43 (each 2H, s, 2×CH_2), 6.72—7.56 (7H, m, ArH), 8.05 (1H, s, NH)
i	3275, 1650, 1610, 1590, 1510, 1270, 1160, 1095, 950, 820, 780	($CDCl_3$) 1.08 (6H, s, 2×CH_3), 1.24 (6H, d, J=7, $CH(C\underline{H}_3)_2$), 2.22 and 2.30 (each 2H, s, 2×CH_2), 3.02 (1H, sep, J=7, $=CC\underline{H}(CH_3)_2$), 5.14 (1H, br s, NH), 6.40—7.20 (4H, m, ArH)

a) sh, shoulder. b) br s, broad singlet; d, doublet; m, multiplet; s, singlet; sep, septet.

temperature overnight. Water was added, and the mixture was extracted with chloroform three times. The combined extract was washed with water and brine, dried over Na_2SO_4 and then evaporated under reduced pressure to give an oil, which was crystallized from benzene to furnish 0.577 g (86%) of **2a** as colorless prisms; mp 189—191 °C. IR ν_{max}^{Nujol} cm^{-1}: 3225, 1645, 1610, 1510 (br), 1330, 1290, 1255, 1155, 910. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (6H, s, 2×CH_3), 2.12 (2H, s, CH_2), 2.24 (2H, s, CH_2), 5.08 (1H, s, COCH=C), 7.12—7.96 (10H, m, Ar-H and NH), 9.13 (1H, s, NH). MS m/z: 334.1693 (M^+). *Anal.* Calcd for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.60; H, 6.43; N, 8.54.

Other amides (**2b—i**) were synthesized similarly and used for the next reaction after confirmation of their homogeneity on an SiO_2 thin layer chromatogram.

General Method for Synthesis of 11-Substituted 3,3-Dimethyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (3)——A mixture of **2** (3.7 mmol) and PPA (26.4 g) was stirred at 120—130 °C for 1 h, then allowed to cool to room temperature. Water was added under cooling to form precipitates, which were collected by filtration and crystallized from the appropriate solvent to give **3a**, **3b**, **3c**, **3g**, **3h**, or **3i**. In the cases of **3d**, **3e**, and **3f**, phosphoric acid salts were obtained. Free bases were prepared by treatment of the salts with dil. NaOH solution, filtration of the resulting precipitates, and recrystallization from the appropriate solvent. Yields, melting points, microanalyses or exact masses, IR, and ^{1}H-NMR spectra data are listed in Tables I and II.

5,5-Dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (6) and 3,3,10-trimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (7)——5,5-Dimethyl-11-phenyl-2,3,4,5-tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**3a**) (0.5 g, 1.58 mmol) was dissolved in 90% formic acid (5 ml) with stirring. The temperature was maintained at 10 °C and one pellet of sodium borohydride was added. The temperature rose to 18 °C, which dropped to 10 °C on cooling. Another pellet was then added. A similar rise in temperature was noted. This procedure was repeated until 0.514 g (13.6 mmol) of sodium borohydride had been added. The mixture was stirred for 1 h at room temperature, then water was added under cooling, and the whole was made basic with 10 N NaOH solution. The precipitates formed were filtered off, washed with water, and crystallized from iso-PrOH–hexane to give 0.18 g of **6**; mp 264—267 °C (lit.,[1] mp 258.5—259.5 °C). IR and ^{1}H-NMR spectral data were identical with

those of an authentic sample. *Anal.* Calcd for $C_{21}H_{22}N_2O$: C, 79.21; H, 6.96; N, 8.80. Found: C, 79.36; H, 6.73; N, 8.79. The filtrate was concentrated and separated into two compounds on SiO_2 preparative thin layer plates using a mixture of chloroform and methanol (60 : 1) as a developing solvent. The more polar band gave 0.201 g of **6**, and the total yield was 76%. The less polar band furnished 76 mg (14%) of **7**; mp 237—237.5 °C (iso-PrOH–hexane). **7**: IR ν_{max}^{Nujol} cm^{-1}: 3330, 1610, 1580, 1535, 1505, 1330, 755, 700. ^{1}H-NMR ($CDCl_3$) δ: 1.06 (3H, s, CH_3), 1.15 (3H, s, CH_3), 2.18 (1H, d, J=16 Hz, CH_2), 2.31 (1H, d, J=16 Hz, CH_2), 2.41 (1H, d, J=15.5 Hz, CH_2), 2.62 (1H, d, J=15.5 Hz, CH_2), 3.00 (3H, s, NCH_3), 5.68 (1H, s, NCHAr), 6.40—7.12 (10H, m, Ar-H and NH). MS *m/z*: 332.1898 (M^+). *Anal.* Calcd for $C_{22}H_{24}N_2O$: C, 79.48; H, 7.28; N, 8.43. Found: C, 79.42; H, 7.22; N, 8.22.

The same compound **7** was also obtained by the following procedures; methyl iodide (0.178 g, 1.256 mmol) and K_2CO_3 (0.13 g, 0.942 mmol) were added to a solution of the amide **4** (0.2 g, 0.628 mmol) in dry acetone (10 ml) and the whole was stirred at reflux temperature for 2 h. After the solvent had been removed under reduced pressure, water was added and the whole was extracted with chloroform three times. The combined extract was washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure to give a residue, which was crystallized from iso-PrOH–hexane to give 0.383 g (92%) of **7**.

10-(2-Diethylaminoethyl)-3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (8)——2-Chlorotriethylamine (0.256 g, 1.884 mmol), K_2CO_3 (0.26 g, 1.884 mmol), and sodium iodide (0.282 g, 1.884 mmol) were added to a solution of **6** (0.4 g, 1.256 mmol) in dry acetone (10 ml) and the whole was stirred and refluxed for 3 h. The solvent was evaporated off under reduced pressure, then water was added and the mixture was extracted three times with chloroform. The combined extract was washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure to give a foamy residue, which was dissolved into iso-PrOH. Dry HCl gas was introduced into this solution under ice-water cooling. When the solution was saturated with HCl gas, excess ether was added, and the precipitates formed were collected by filtration. The free base **8**, 0.167 g (32%), was obtained by treatment of the precipitates with Na_2CO_3 solution and recrystallization of the crude product from iso-PrOH–hexane as pale yellow needles; mp 166—167 °C. IR ν_{max}^{Nujol} cm^{-1}: 3290, 1575, 1540, 1500, 1320, 1160, 1070, 755, 700. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (6H, t, J=7 Hz, 2 × $CH_2C\underline{H}_3$), 1.12 (3H, s, CH_3), 1.16 (3H, s, CH_3), 2.22 (1H, d, J=16 Hz, CCH_2C), 2.34 (1H, d, J=16 Hz, CCH_2C), 2.43 (1H, d, J=16 Hz, CCH_2C), 2.54 (1H, d, J=16 Hz, CCH_2C), 2.55 (4H, q, J=7 Hz, 2 × $NC\underline{H}_2CH_3$), 2.67 (2H, t, J=7 Hz, $NC\underline{H}_2CH_2NAr$), 3.24 (1H, dt, J=13, 7 Hz, $NCH_2C\underline{H}_2NAr$), 3.42 (1H, dt, J=13, 7 Hz, $NCH_2C\underline{H}_2NAr$), 5.82 (1H, s, NCHAr), 6.25 (1H, br s, NH), 6.6—7.1 (9H, m, Ar-H). MS *m/z*: 417.2816 (M^+). *Anal.* Calcd for $C_{27}H_{35}N_3O$: C, 77.66; H, 8.45; N, 10.06. Found: C, 77.71; H, 8.35; N, 10.06.

3-(2-Isopropylaminoanilino)-5,5-dimethyl-2-cyclohexen-1-one (11)——A solution of dimedone (**9**) (2.268 g, 16.18 mmol), 2-isopropylaminoaniline (**10**) (2.431 g, 16.18 mmol), and a catalytic amount of *p*-TsOH · H_2O in benzene (50 ml) was stirred at reflux temperature, while water was removed as an azeotropic mixture. When no more water appeared, the reaction mixture was extracted three times with dil. HCl solution. The combined extract was made basic with Na_2CO_3 solution, and then extracted with chloroform three times. The combined extract was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give an oil, which was crystallized from iso-PrOH–hexane to furnish 1.786 g (41%) of **11** as colorless plates; mp 180.5—182 °C. IR ν_{max}^{Nujol} cm^{-1}: 3355, 3250, 1595, 1570, 1545, 1510, 1280, 1245, 1150, 750. ^{1}H-NMR ($CDCl_3$) δ: 1.50 (6H, s, 2 × CH_3), 1.18 (6H, d, J=5 Hz, 2 × $CHC\underline{H}_3$), 2.19 (2H, s, CH_2), 2.32 (2H, s, CH_2), 3.60 (2H, br s, NH and $NC\underline{H}(CH_3)_2$), 5.05 (1H, s, C=CH), 5.90 (1H, s, NH). 6.60—7.20 (4H, m, Ar-H). MS *m/z*: 272.1880 (M^+). *Anal.* Calcd for $C_{17}H_{24}N_2O$: C, 74.96; H, 8.88; N, 10.28. Found: C, 74.79; H, 8.75; N, 10.02.

10-Isopropyl-3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (12)——An enaminone **11** (0.3 g, 1.1 mmol) was dissolved in ethanol (6 ml). Benzaldehyde (0.117 g, 1.1 mmol), acetic acid (6 drops), and conc. HCl (5 drops) were added to the above solution, and the whole was stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure, treated with dil. NaOH solution, and extracted with chloroform twice. The combined extract was washed with $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated under reduced pressure to give a solid, which was recrystallized from iso-PrOH to furnish 0.288 g (73%) of **12** as yellow needles; mp 247—248.5 °C. IR ν_{max}^{Nujol} cm^{-1}: 3280, 1570, 1530, 1500, 1320, 1275, 1190, 1160, 755. ^{1}H-NMR ($CDCl_3$) δ: 1.10 (3H, d, J=6.5 Hz, $CHC\underline{H}_3$), 1.16 (6H, s, 2 × CH_3), 1.23 (3H, d, J=6.5 Hz, $CHC\underline{H}_3$), 2.33 (2H, s, CH_2), 2.38 (1H, d, J=15.5 Hz, CH_2), 2.52 (1H, d, J=15.5 Hz, CH_2), 3.53 (1H, sep, J=6.5 Hz, $NC\underline{H}(CH_3)_2$), 5.95 (1H, s, NCHAr), 6.38 (1H, s, NH), 6.50—7.12 (9H, m, ArH). MS *m/z*: 360.2229 (M^+). *Anal.* Calcd for $C_{24}H_{28}N_2O$: C, 79.96; H, 7.83; N, 7.77. Found: C, 79.88; H, 7.78; N, 7.54.

3-(2-Aminoanilino)-2-isobutyryl-5,5-dimethyl-2-cyclohexen-1-one (5)——A mixture of **2i** (0.738 g, 2.46 mmol) and PPA (17 g) was treated according to the general procedure mentioned above (basic work-up) to give 0.136 g (20%) of **3i**, and 0.389 g (53%) of **5** (recrystallized from iso-PrOH–hexane) as colorless prisms; mp 139—140 °C. IR ν_{max}^{Nujol} cm^{-1}: 3420, 3340, 3240, 1630 (sh), 1610 (sh), 1595, 1545, 1285, 1155, 1135, 1095, 920, 755. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (6H, s, 2 × CH_3), 1.12 (6H, d, J=6.5 Hz, $COCH(C\underline{H}_3)_2$), 2.34 (2H, s, CH_2), 2.36 (2H, s, CH_2), 3.78 (2H, s, NH_2), 4.04 (1H, sep, J=6.5 Hz, $COC\underline{H}(CH_3)_2$), 6.72—7.24 (4H, m, ArH), 13.62 (1H, br s, NH). MS *m/z*: 300.1829 (M^+). *Anal.* Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 72.22; H, 8.12; N, 9.33.

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