EXPERIMENTS
3. Experiments

General. The melting points are uncorrected. IR spectra were recorded on a Shimadzu IR-435, Perkin-Elmer 595 & Shimadzu-FT Infrared Spectrophotometers using KBr pellets. The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker WH-270 MHz, Bruker 200 MHz, Bruker AMX-400 MHz and Jeol GSX-400 MHz spectrometers in CDCl$_3$ solution using TMS as internal reference. Dynamic $^1$H NMR spectra were recorded in CDCl$_3$ for the compounds 28, 45 & 46 and acetone-$d_6$ solutions for the compounds 31 & 49 and DMSO-$d_6$ for the compound 56 using Jeol GSX-400 MHz NMR Spectrometer. The other low temperature studies were carried out in CDCl$_3$ solution using Jeol GSX-400 MHz NMR Spectrometer. Mass spectra were recorded on a Jeol JMS-D 300 spectrometer operating at 70 eV.

The $\tau$-2,$\sigma$-6-diphenylpiperidin-4-ones 5a-d,27,5e,$^3$$^8$c,$^5$$^8$,41, $\tau$-2,$\sigma$-6-diphenylpiperidines 7a-b,34,7c,35,7d,$^5$$^6$,58, $\tau$-2,$\sigma$-7-diphenylhexahydro-1,4-diazepin-5-ones 11a,b,d,$^5$$^9$,60 were prepared according to the reported procedures. The azabicyclic compounds 16b & 17b were prepared by following the literature methods.$^6$$^7$a,$^7$$^8$. The Wolf-Kishner reduction of the 3-azabicyclic ketone 16a$^6$$^7$a and 3,7-diazabicyclic ketone 17a$^6$$^7$c yielded the reduced 3-azabicyclic compound 16b$^6$$^7$a and 3,7-diazabicyclic compound 17b$^6$$^7$a, respectively.

N-Ethoxycarbonyl-$\tau$-2,$\sigma$-6-diphenylpiperidin-4-one (28). To a solution of $\tau$-2,$\sigma$-6-diphenylpiperidin-4-one 5a (0.63 g, 2.5 mmol) in anhydrous benzene (50 mL) was added Et$_3$N (2.8 mL, 20 mmol). The solution was cooled at 0-5 °C and ethyl chloroformate (0.7
mL, 7.3 mmol) was added and the reaction mixture was allowed to reflux on a water bath. Additional quantities of ethyl chloroformate were added with the time interval of 4 h till the total amounted to about 2.9 mL (30 mmol). The course of the reaction was monitored by TLC (silica, CHCl₃ : C₆H₆ (4:1) as eluent). The precipitated ammonium salt was filtered off and the filtrate was washed with H₂O (4 X 25 mL). The organic layer was dried (Na₂SO₄), passed through a short column of silica (eluent: CHCl₃) and evaporated. The oily mass, crystallised twice from petroleum ether (60-80°C), afforded crystals of 28, yield 0.66 g, (82%), mp 61-63°C. Anal. calcd for C₂₀H₂₁NO₃: C, 74.30; H, 6.50; N, 4.33. Found: C, 74.58; H, 6.81; N, 4.60%.

N-Ethoxycarbonyl-t-3-methyl-r-2,c-6-diphenylpiperidin-4-one (29). The procedure described for the compound 28 was followed for the ethoxycarbonylation of 3-methylpiperidin-4-one 5b (0.66 g, 2.5 mmol). Crystallisation of the oily mass twice from petroleum ether (60-80°C) yielded colorless crystals of 29, yield 0.72 g (85.5%), mp 79-81°C. Anal. calcd for C₂₁H₂₃NO₃: C, 74.78; H, 6.83; N, 4.15. Found: C, 75.06; H, 7.22; N, 4.40%.

N-Ethoxycarbonyl-t-3-ethyl-r-2,c-6-diphenylpiperidin-4-one (30). The procedure described for the preparation of 28 was followed for the ethoxycarbonylation of 3-ethylpiperidin-4-one 5c (0.70 g, 2.5 mmol). Crystallisation of the oily mass twice from petroleum ether (60-80°C) afforded colorless crystals of 30, yield 0.70 g (80.0 %), mp 54-56°C. Anal. cald for C₂₂H₂₅NO₃: C, 75.21; H, 7.21; N, 3.99%). Found: C, 75.41; H, 7.32; N, 4.11%.
**N-Ethoxycarbonyl-t-3-isopropyl-r-2,c-6-diphenylpiperidin-4-one** (31). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3-isopropylpiperidin-4-one 5d (0.73 g, 2.5 mmol). The compound 31 was separated as a viscous mass, which decomposed on distillation, yield 0.65 g (71.2%). Hence the spectral data were obtained after careful purification by passing through a long column of silica gel, evaporation of the solvent at low temperature, followed by drying in vacuum at room temperature before measurements.

**N-Ethoxycarbonyl-c-3,t-3-dimethyl-r-2,c-6-diphenylpiperidin-4-one** (32). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3,3-dimethylpiperidin-4-one 27 (0.70 g, 2.5 mmol). The oily mass was crystallised twice from petroleum ether (60-80°C) afforded colorless needles of 32, yield 0.77 g (87.8%), mp 76-78°C Anal. calcd. for C_{22}H_{25}NO_{3}: C, 75.21; H, 7.21; N, 3.99. Found: C, 75.51; H, 7.34; N, 4.20%.

**N-Ethoxycarbonyl-t-3,t-5-dimethyl-r-2,c-6-diphenylpiperidin-4-one** (33). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3,5-dimethylpiperidin-4-one 5e (0.70 g, 2.5 mmol). The oily mass was crystallised twice from petroleum ether (60-80°C) yielded colorless crystals of 33, yield 0.72 g (82.1%), mp 101-103°C. Anal. calcd for C_{22}H_{25}NO_{3}: C, 75.21; H, 7.21; N, 3.99. Found: C, 75.40; H, 7.41; N, 4.27%.
N-Ethoxycarbonyl-γ-2,γ-6-diphenylpiperidine (36). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of piperidine 7a (0.59 g, 2.5 mmol). Crystallisation of the oily mass twice from petroleum ether (60-80°C) afforded colorless crystals of 36, yield 0.66 g (85.4%), mp 55-57°C. Anal. calcd for C_{20}H_{23}NO_{2}: C, 77.67; H, 7.44; N, 4.53. Found: C, 77.95; H, 7.66; N, 4.69%.

N-Ethoxycarbonyl-γ-3-methyl-γ-2,γ-6-diphenylpiperidine (37). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3-methylpiperidine 7b (0.63 g, 2.5 mmol). The oily mass was crystallised twice from petroleum ether (60-80°C) yielded crystals 37, yield 0.67 g (83%), mp 70-71°C. Anal. calcd for C_{21}H_{25}NO_{2}: C, 78.02; H, 7.74; N, 4.33. Found: C, 78.30; H, 7.98; N, 4.70%.

N-Ethoxycarbonyl-γ-3-ethyl-γ-2,γ-6-diphenylpiperidine (38). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3-ethylpiperidine 34 (0.66 g, 2.5 mmol). The compound 38 was separated as a viscous mass and purified as described for the compound 31, yield 0.62 g (73.6%).

N-Ethoxycarbonyl-γ-3-isopropyl-γ-2,γ-6-diphenylpiperidine (39). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3-isopropylpiperidine 7c (0.70 g, 2.5 mmol). The compound was separated as a viscous mass and purified as described for the compound 31, yield 0.63 g (71.8%).
N-Ethoxycarbonyl-3,3-dimethyl-2,6-diphenylpiperidine (40). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3,3-dimethylpiperidine 35 (0.66 g, 2.5 mmol). The compound 40 was separated as viscous mass and purified as described for the compound 31. yield 0.61 g (72.4%).

N-Ethoxycarbonyl-3,5-dimethyl-2,6-diphenylpiperidine (41). The procedure described for the preparation of compound 28 was followed for the ethoxycarbonylation of 3,5-dimethylpiperidine (0.66 g, 2.5 mmol). Crystallisation of the oily mass twice from petroleum ether (60-80°C) yielded colorless crystals of 41, yield 0.69 g (81.9%), mp 68-70 °C. Anal. calcd for C_{22}H_{27}NO_2: C, 78.34; H, 8.01; N, 4.15. Found: C, 78.40; H, 8.36; N, 4.51%.

N^1,N^4-Diethoxycarbonylhexahydro-2,7-diphenyl-5H-1,4-diazepin-5-one (45). To a ice-cold solution of hexahydro-2,7-diphenyl-1,4-diazepin-5-one 11a (0.67 g, 2.5 mmol) in anhydrous benzene (60 mL), triethylamine (4.2 mL, 30 mmol) and ethyl chloroformate (4.0 mL, 41.6 mmol) were added. The reaction mixture was allowed to reflux on a water bath for 5 h and the course of the reaction was monitored by TLC [silica, CHCl_3: CH_3COOEt (9:1) as eluent]. The precipitated ammonium salt was filtered off and the filtrate was washed with water (4x25 mL). The organic layer was dried (anhydrous Na_2SO_4), passed through a short column of silica (eluent: CH_2Cl_2) and evaporated. The oily mass was crystallised from petroleum ether (60-80°C) at 0°C,
yield 0.65 g (63.4 %), mp 85-86°C. Anal. Calcd for C_{23}H_{26}N_{2}O_{5}: C, 67.30; H, 6.39; N, 6.83. Found: C, 67.52; H, 6.53; N, 6.85%.

\( N^1,N^4 \)-Diethoxycarbonylhexahydror-t-3-methyl-\( \tau \)-2,\( \zeta \)-7-diphenyl-5H-1,4-diazepin-5-one (46). The procedure described for the compound 45 was followed for the ethoxycarbonylation of hexahydro-t-3-methyl-\( \tau \)-2,\( \zeta \)-7-diphenyl-5H-1,4-diazepin-5-one 11b (0.7 g, 2.5 mmol). The oily mass was crystallised from petroleum ether (60-80°C), yield 0.64 g (60.4 %), mp 113-115°C.

Anal. Calcd for C_{24}H_{28}N_{2}O_{5}: C, 67.91; H, 6.65; N, 6.60. Found: C, 67.60; H, 6.43; N, 6.28%.

4-Ethoxycarbonylhexahydror-t-3-isopropyl-\( \tau \)-2,\( \zeta \)-7-diphenyl-5H-1,4-diazepin-5-one (47). To a ice-cold solution of hexahydro-3-isopropyl-\( \tau \)-2,\( \zeta \)-7-diphenyl-1,4-diazepin-5-one 11d (0.308 g, 1 mmol) in anhydrous benzene (40 mL), triethylamine (0.7 mL, 5 mmol) and ethylchloroformate (0.5 mL, 5mmol) were added. The reaction mixture was allowed to reflux on a water bath for 2 h and the reaction was monitored by TLC (silica, CHCl_3 as eluent). The precipitated ammonium salt was filtered off and the filtrate was washed with water (4 x 25 mL). The organic layer was dried with anhydrous sodium sulfate, filtered, passed through a short column of silica (eluent: CH_2Cl_2) and evaporated. The oily mass was crystallised from petroleum ether (60-80°C) at 0°C, yield 0.24 g (63.2 %), mp 79-81 °C. Anal. Calcd for C_{23}H_{28}N_{2}O_{3}: C, 72.60; H, 7.42; N, 7.36. Found: C, 72.82; H, 7.51; N, 7.21%.
N-Acetyl-\(\tau\)-2,\(4\)-diphenyl-3-azabicyclo[3.3.1]nonane (48). A mixture of azabicyclic compound 16b (0.69 g, 2.5 mmol), acetic anhydride (0.7 mL, 7.5 mmol) and triethylamine (1.0 mL, 7.5 mmol), in anhydrous benzene (50 mL) was kept under reflux on a water bath and the progress of the reaction was monitored by TLC (silica, CHCl\(_3\) as eluent). After 8 h the reaction mixture was washed with 10% sodium bicarbonate solution (2 X 25 mL) and with water (4 X 25 mL). The organic layer was dried (Na\(_2\)SO\(_4\)), passed through a short column of silica (eluent: CHCl\(_3\)) and evaporated. Recrystallisation from petroleum ether (60-80°C) yielded colorless crystals of 48, yield 0.63 g (79.0%), mp 160-161°C. Anal. calcd for C\(_{22}\)H\(_{25}\)NO: C, 82.72; H, 7.89; N, 4.39. Found: C, 82.41; H, 7.80; N, 4.53 %.

3-Ethoxycarbonyl-\(\tau\)-2,\(4\),\(\tau\)-6,\(\tau\)-8-tetraphenyldiazabicyclo[3.3.1]nonane (49). To an ice-cold solution of diazabicyclic compound 17b (1.08 g, 2.5 mmol) in anhydrous benzene (75 mL) was added triethylamine (2.8 mL, 20 mmol) and ethyl chloroformate (2.9 mL, 30 mmol). The reaction mixture was allowed to reflux on a water bath for 6 hr and monitored by TLC (silica, CHCl\(_3\) as eluent). The precipitated ammonium salt was filtered off and the filtrate was washed with water (4 X 25mL). The organic layer was dried (anhydrous Na\(_2\)SO\(_4\)), passed through a short column of silica (eluent: CHCl\(_3\)) and concentrated. Crystallisation from the benzene:petroleum ether (60-80°C) mixture (1:2) at 0°C afforded colorless crystals of 49, yield 0.83 g (66.1%), mp 181-183°C. Anal. calcd for C\(_{34}\)H\(_{34}\)N\(_2\)O\(_2\): C, 81.24; H, 6.82; N, 5.57. Found: C, 81.02; H, 6.61; N, 5.82.
3-Acetyl-r-2,c-4,t-6,t-8-tetraphenyl-3,7-
diazabicyclo[3.3.1]nonane (50). The procedure described for the
preparation of 48 was followed for the acetylation of
diazabicyclic compound 17b (1.075 g, 2.5 mmol) and the reaction
mixture was allowed to reflux for 3 h. Crystallisation from
benzene:petroleum ether (60-80°C) mixture (1:2) at 0°C yielded
colorless crystals of 50, yield 0.86 g (72.9 %), mp 223-224°C.
Anal. calcd C_{33}H_{32}N_{2}O: C, 83.86; H, 6.83; N, 5.93.
Found: C,83.51; H, 6.92; N, 5.62.

N-Acetyl-r-2,c-6-diphenylpiperidine (52). The procedure
described for the preparation of compound 48 was followed for the
acetylation of piperidine 7a (0.59 g, 2.5 mmol).
Crystallisation of the oily mass twice from petroleum ether (60-
80°C) afforded colorless crystals of 52, yield 0.60 g (86.3%),
mp 58-60°C.

2,3-dihydro-2,2,4-trimethyl-1H-1,5-benzodiazepine(62).
To a ice cold solution of 1,2-diaminobenzene (10.80 g, 100 mmol)
in glacial acetic acid (30 mL), acetone (16 mL, 218 mmol) was
added while shaking and kept at 25 °C for 16 h crushed ice was
added to the reaction mixture and neutralised with ammonia. The
precipitated solid was separated, washed thoroughly with water
and dried. The solid was dissolved in ethanol, allowed reflux
with charcoal and filtered. Recrystallisation from ethanol twice
after treatment with charcoal afforded yellow crystals of 62,
yield 9.9 g (53%), mp 123-124°C [lit. mp 125-128°C\textsuperscript{31b}].
Tetrahydro-2,2,4-trimethyl-1H-1,5-benzodiazepine (20b).
Benzodiazepine 62 (3.42 g, 18.2 mmol) was dissolved in methanol (75 mL) and stirred with magnetic stirrer. Sodium borohydride (0.62 g, 16.76 mmol) was added in five portions for a period of 1 h while maintaining the temperature at 45-50°C. After the addition was over, the solution was stirred for another 2 h. Methanol was evaporated partially and poured into water. The mixture was extracted with dichloromethane several times. The organic extractions were combined, dried with anhydrous sodium sulfate and evaporated. The yellow oil obtained was recrystallised from petroleum ether (60-80)/aqueous ethanol to afford colorless crystals of 20b, Yield 3.04 g (88%), mp 56-57°C [lit. mp 56-58°C].

5-Benzoyltetrahydro-2,2,4-trimethyl-1H-1,5-benzodiazepine (53).
To an ice-cold solution of tetrahydrobenzodiazepine 20b (0.95 g, 5 mmol) in anhydrous benzene (25 mL) was added triethylamine (2 mL, 14.4 mmol) and benzoyl chloride (2.5 mL, 18 mmol). The reaction mixture was stirred at room temperature for 1 h. The precipitated ammonium salt was filtered off and the filtrate was washed with water (4x10 mL). The benzene solution was dried (anhydrous Na₂SO₄), passed through a short column of silica and concentrated. The resulting solid was recrystallised from benzene: petroleum ether (60-80) mixture (10:1) yielded colorless crystals of 53, yield 0.89 g (60.5%), mp 128-130°C.
Anal. Calcd. C_{19}H_{22}N_{2}O: C, 77.52; H, 7.53; N, 9.52.
Found: C, 77.38; H, 7.64; N, 9.31.
5-Phenylcarbamoyltetrahydro-2,2,4-trimethyl-1H-1,5-benzodiazepine (54). To a solution of tetrahydrobenzodiazepine 20b (0.95 g, 5 mmol) in anhydrous benzene (25 mL) was added catalytic amount of triethylamine and phenyl isocyanate (0.6 mL, 5 mmol). The reaction mixture was stirred at room temperature for 6 h. The benzene solution was washed with water (4 x 20 mL) and dried (anhydrous Na₂SO₄). The solution was passed through a short column of silica and concentrated. The resulting solid was recrystallised from benzene afforded colorless crystals of 54, yield 1.41 g (91.3%), mp 167-168°C. Anal. Calcd. for C₁₉H₂₃N₃O: C, 73.75; H, 7.49; N, 13.58. Found: C, 73.47; H, 7.62; N, 13.32.

1,5-Diacetyltetrahydro-2,2,4-trimethyl-1H-1,5-benzodiazepine (55). To a ice-cold solution of tetrahydrobenzodiazepine 20b (0.95 g, 5 mmol) in anhydrous benzene (25 mL) was added triethylamine (3 equivalents) and acetyl chloride (3 equivalents). The reaction mixture was stirred at room temperature for 2 h. The precipitated ammonium salt was filtered off and the filtrate was washed with water (4 x 20 mL). The benzene solution was dried (anhydrous Na₂SO₄), passed through a short column of silica and concentrated. The resulting solid was crystallised from benzene yielded pale yellowish brown crystals of 55, yield 1.06 g (77.4%), mp 199-200°C. Anal. Calcd. C₁₆H₂₂N₂O₂: C, 70.04; H, 8.09; N, 10.21. Found: C, 70.26; H, 8.41; 10.02.
1,5-Diformyltetrahydro-2,2,4-trimethyl-1H-1,5-benzodiazepine (56). To a ice-cold acetic anhydride (10 mL) was added slowly 85% formic acid (5 mL) while shaking and the resulting solution was heated to 60°C. Immediately the temperature of the solution was raised steeply to about 90-100°C and the solution was externally cooled and then maintained at 50-60°C for 1.5 h. The resulting acetic formic anhydride was cooled to 5°C and added slowly to a cold solution tetrahydrobenzodiazepine 20b (0.95, 5 mmol) in anhydrous benzene (30 mL). The reaction mixture was stirred at room temperature for 5 h and the solution was poured into water (250 mL). The benzene layer was separated and the aqueous layer was extracted with chloroform (4x25 mL). The organic extracts were combined, dried (anhydrous Na₂SO₄), passed through a short column of silica and concentrated. Crystallisation from benzene:petroleum ether (60-80°C) mixture (1:1) yielded colorless crystals of 56, Yield 1.12 g (91.1%), mp 111-113°C. Anal. Calcd. C₁₄H₁₈N₂O₂ : C, 68.27; H, 7.37; N, 11.37. Found: C, 68.51; H, 7.15; N, 11.42.

t-4-Cyano-t-2,c-6-diphenyl-c-4-N-phenylaminopiperidine (57).
To a solution of t-2,c-6-diphenylpiperidin-4-one 5a (3.14 g, 12.5 mmol) in glacial acetic acid (30 mL), aniline (1.2 mL, 12.5 mmol) and potassium cyanide (40.0 mmol) were added. The mixture was stirred in an ice-bath for 24 h with excess addition of cyanide for three times. It was then poured into crushed ice containing excess ammonia solution. The light yellow colored precipitate formed was filtered, washed thoroughly with water and
fractionally recrystallised from benzene:petroleum ether 60-80°C (1:4) mixture. The crude yellow product contains the reactant also which was separated by the above said fractional recrystallisation. The compound 57 was isolated as colorless solid, yield 1.5 g (34%), mp 175-77°C. The remaining solid was isolated as reactant. Anal. calcd for $\text{C}_{24}\text{H}_{23}\text{N}_3$: C, 81.55; H, 6.56; N, 11.89. Found: C, 81.66; H, 6.75; N, 12.02%.

$t$-4-Cyano-$t$-3-methyl-$t$-2,c-6-diphenyl-$c$-4-N-phenylaminopiperidine (58). Strecker reaction of 5b (3.31 g, 12.5 mmol) was carried out by following the procedure as described for the compound 57. The crude product contains the reactant and the product was recrystallised fractionally from benzene:petroleum-ether 60-80°C (4:1) mixture, yield 1.39 g (30.3 %), mp 174-76°C. Anal. calcd for $\text{C}_{25}\text{H}_{25}\text{N}_3$: C, 81.71; H, 6.86; N, 11.43. Found: C, 81.74; H, 7.14; N, 11.66%.

$t$-4-Cyano-$t$-3-ethyl-$t$-2,c-6-diphenyl-$c$-4-N-phenylaminopiperidine (59). Strecker reaction of 5c (3.49 g, 12.5 mmol) was carried out by following the procedure as described for the compound 57. The crude product contains the reactant and the product was recrystallised fractionally from benzene:petroleum-ether 60-80°C (4:1) mixture, yield 1.4 g (29.4 %), mp 180-81°C. Anal. calcd for $\text{C}_{26}\text{H}_{27}\text{N}_3$: C, 81.85; H, 7.13; N, 11.01. Found: C, 81.70; H, 7.56; N, 10.80%.

$t$-4-Cyano-$t$-3-isopropyl-$t$-2,c-6-diphenyl-$c$-4-N-phenylaminopiperidine (60). Strecker reaction of 5d (3.66 g, 12.5 mmol) was carried out by following the procedure as
described for the compound 57. The crude product contains the reactant and the product was recrystallised fractionally from benzene:petroleum-ether 60-80° C (4:1) mixture, yield 0.75 g (15.2 %), mp 150-51° C. Anal. calcd for $C_{27}H_{29}N_3$: C, 81.99; H, 7.39; N, 10.62. Found: C, 82.19; H, 7.21; N, 10.60.