Preparation of Cyclohepta and Benzo[*ef*]cycl[3.2.2]azines

Michihiko Noguchi*, Noriyuki Tanigawa and Shoji Kajigaeshi

Department of Industrial Chemistry, Faculty of Engineering,
Yamaguchi University, Tokiwadai, Ube 755, Japan

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Some cyclohepta[*ef*]cycl[3.2.2]azines were prepared from cyclohepta[*hi*]indolizines and electron deficient acetylenes in the presence of appropriate oxidants. Also, benzo[*ef*]cycl[3.2.2]azines were obtained similarly in good yields.

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Much attention has been paid for the synthesis of the heterocyclic compounds with new ring systems because of the interest concerning their chemical and physicochemical properties as well as biological activities.

Now, in the continuation of our studies on the heterocyclic compounds with bridgehead nitrogen atom [1], our research interest has been focused on the [*ef*]condensed cycl[3.2.2]azine [2] derivatives and attempts have been made to prepare such heterocycles.

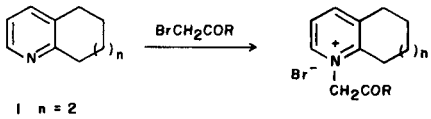
In this paper, we wish to describe the preparations of some 4,5,6,7-tetrahydrocyclohepta[*ef*]cycl[3.2.2]azine and 5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine derivatives in the reaction of the [*hi*]condensed indolizines with electron deficient acetylenes.

Preparation of [*hi*]Condensed Indolizine Derivatives.

The reactions of 2,3-cycloalkenopyridines **1**, **2** and **3** with bromoacetone (**4a**) or phenacyl bromide (**4b**) in dry acetone gave the corresponding pyridinium salts **5-7** in good yields (Table 1).

Table 1

Preparation of Pyridinium Salts **5-7**



1 n = 2
2 n = 1
3 n = 0

4a R = Me
4b R = Ph

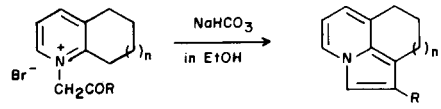
Compound	n	R	Yield (%)
5a	2	Me	93
5b	2	Ph	96
6a	1	Me	93
6b	1	Ph	95
7	0	Ph	62

The treatment of *N*-acetonyl-2,3-cycloheptenopyridinium bromide (**5a**) with sodium hydrogencarbonate in ethanol afforded an oily product **8a** in 78% yield. Similarly, the alkaline treatment of the pyridinium salt **5b**, **6a** and **6b** gave the corresponding products **8b**, **9a** and **9b** in 74-88% yields (Table 2).

From their analytical and spectral data, the products **8** and **9** were assigned to the 1-substituted cyclohepta[*hi*]indolizine and the 1-substituted pyrrolo[3,2,1-*ij*]quinoline derivatives, respectively.

Table 2

Preparation of [*hi*]Condensed Indolizines **8** and **9**

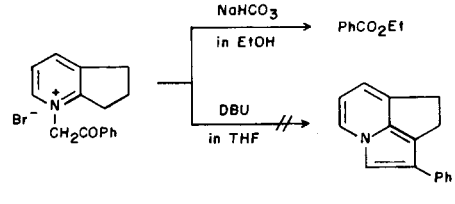


Compound	n	R	Yield (%)
8a	2	Me	78
8b	2	Ph	74
9a	1	Me	76
9b	1	Ph	88

On the other hand, under the similar conditions the alkaline treatment of **7** in ethanol gave ethyl benzoate quantitatively.

Unfortunately, some efforts to obtain the desired cyclopenta[*hi*]indolizine, *eg.*, the treatment with DBU in THF, were made without success. The mixture of many troublesome products were mainly obtained in every case. Probably, the condensation between ketone and methylene moieties in pyridinium salt would be inhibited owing to the geometrical factors.

Scheme I

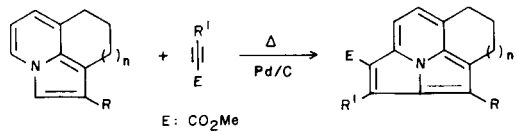


Preparation of [*ef*]Condensed Cycl[3.2.2]azine Derivatives.

The next conversions of the [*hi*]condensed indolizines to the [*ef*]condensed cycl[3.2.2]azines were carried with the modification of Boekelheid's method [3]. The reaction of the indolizine **8a** with dimethyl acetylenedicarboxylate (DMAD) in refluxing toluene in the presence of palladium-charcoal gave 1,2-dimethoxycarbonyl-3-methyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl[3.2.2]azine (**10a**) in 85%

Table 3

Preparation of [*ef*]Condensed Cycl[3.2.2]azine Derivatives **10**, **11**, **12** and **13**

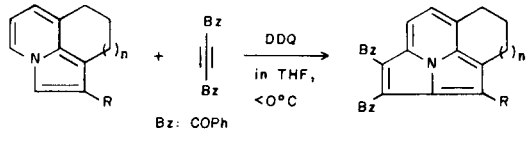


Cyclazines	n	R	R'	Reaction solvent	Conditions (hours)	Yield (%)
10a	2	Me	E	toluene	(70)	85
10b	2	Ph	E	toluene	(50)	33
				xylene	(50)	61
11a	1	Me	E	toluene	(50)	77
11b	1	Ph	E	toluene	(65)	58
12	2	Me	H	toluene	(70)	75
13	1	Me	H	toluene	(70)	75

yield. Similarly, dimethoxycarbonyl substituted [*ef*]condensed cycl[3.2.2]azine derivatives **10b**, **11a** and **11b** were obtained by the reaction of the corresponding indolizines with DMAD in good yields. Also, 1-methoxycarbonyl-3-methyl-4,5,6,7-tetrahydrocyclohepta- (**12**) and 1-methoxycarbonyl-3-methyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**13**) were obtained by the reaction of **8a** and **9a** with methyl propiolate (MP), respectively. These results are shown in Table 3.

Table 4

Preparation of [*ef*]Condensed Cycl[3.2.2]azine Derivatives **14** and **15**



Cyclazines	n	R	Yield (%)
14a	2	Me	86
14b	2	Ph	92
15a	1	Me	68
15b	1	Ph	52

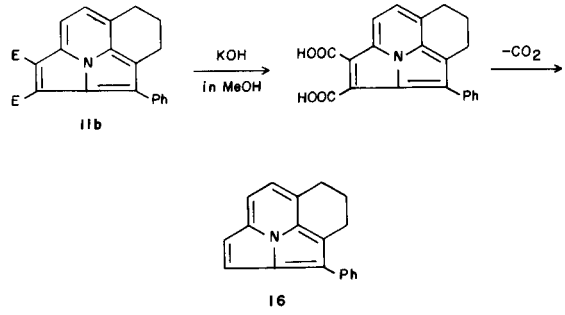
However, in the reaction of the indolizines with dibenzoyl acetylene (DBZA) under similar conditions, formation of the cyclazines carried too deliberately [4]. This problem was easily solved by the use of DDQ instead of palladium-charcoal as an oxidant. The use of DDQ, however, required the relatively limited reaction conditions, *i.e.*, the temperature must be kept exactly below 0° and the prolonged reaction time must be avoided [5].

When an equimolar DDQ was added bit by bit to a mixture of reddish THF solution of **9a** and DBZA and then reaction mixture was stirred for additional ten minutes, 1,2-dibenzoyl-3-methyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl-[3.2.2]azine (**14a**) was obtained in 86% yield by the usual working-up. Similarly, the 1,2-dibenzoyl substituted [*ef*]-condensed cycl[3.2.2]azines **14b**, **15a** and **15b** were obtained in 52-92% yields. These results are shown in Table 4.

The structural elucidation of these cyclazines **10-15** were accomplished also by the basis of analytical and spectral data. Especially, AB quartets with similar chemical shifts and coupling constants, which were supporting the cyclazine structures, were always observed in those pmr spectra.

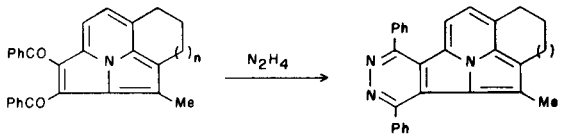
While the preparation of mono-substituted [*ef*]condensed cycl[3.2.2]azine from the indolizine **9b** with phenylvinylsulfoxide as an equivalent of acetylene was examined under several conditions, the starting materials were recovered in every case. Thus, the saponification of **11b** with methanolic potassium hydroxide and the successive decarboxylation in quinoline in the presence of copper dust gave 3-phenyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**16**) in 78% yield based on **11b** (Scheme 2). The structure of **16** was confirmed by its pmr spectrum, which showed the signals centered on aromatic region, typical of the cycl[3.2.2]azine nuclei [6].

Scheme 2



Finally, the reaction of 1,2-dibenzoyl substituted cyclazines **14a** and **15a** with hydrazine hydrate in alcohol afforded the corresponding pyridazino derivatives **17** and **18** (Scheme 3).

Scheme 3



Compound	n
17	2
18	1

EXPERIMENTAL

All melting and boiling points are uncorrected. The ir spectra were measured on a Nippon Bunko IRA-1 spectrometer as potassium bromide pellets. The pmr spectra were obtained at 100 MHz using a Nippon Denshi JEOL JNM-MH-100 spectrometer with tetramethylsilane as an internal standard in deuteriochloroform unless otherwise stated. Mass spectra were determined with JEOL JMS-D and JMS-01 SG-2 mass spectrometers equipped with direct inlets and at an ionization energy of 75 eV.

General Procedure for the Preparation of Pyridinium Salts **5-7**.

All these reactions were carried out under nitrogen atmosphere. Bromoacetone (**4a**) (50 mmoles) in dry acetone (20 ml) was added dropwise for one hour to a stirred solution of 2,3-cycloheptenopyridine (**1**) (50 mmoles) in dry acetone (30 ml). The reaction mixture was heated at reflux for two hours and allowed to stand at room temperature overnight. The resultant precipitate of **5a** was collected by filtration and washed with dry acetone to give 13.2 g of **5a** (93%). Pure **5a** was obtained by recrystallization as colorless prisms from ethanol.

N-Acetonyl-2,3-cycloheptenopyridinium Bromide (**5a**).

This compound had mp 181-182°; ir: ν CO 1730 cm^{-1}; pmr: δ 1.7-1.9 (m, 6H), 2.56 (s, 3H, CH_3), 3.0-3.2 (m, 4H), 6.70 (s, 2H, CH_2-CO), 7.69 (dd, 1H, $J_{45} = J_{56} = 7$ Hz, H-5), 8.16 (d, 1H, J = 7 Hz, H-4), 9.28 ppm (d, 1H, J = 7 Hz, H-6).

Anal. Calcd. for $C_{13}H_{18}BrON$: C, 54.92; H, 6.39; N, 4.93. Found: C, 54.82; H, 6.27; N, 4.87.

N-Phenacyl-2,3-cycloheptenopyridinium Bromide (**5b**).

This compound was obtained as colorless needles (ethanol), mp 211-212°; ir: ν CO 1965 cm^{-1}; pmr: δ 1.4-1.9 (m, 6H), 3.0-3.1 (m, 4H), 7.14 (s, 2H, CH_2-CO), 7.3-7.7 (m, 4H, H-5 and phenyl), 8.94 (m, 3H, H-4 and phenyl), 9.36 ppm (d, 1H, J = 7 Hz, H-6).

Anal. Calcd. for $C_{18}H_{20}BrON$: C, 62.42; H, 5.83; N, 4.05. Found: C, 62.41; H, 5.85; N, 4.06.

N-Acetonyl-2,3-cyclohexenopyridinium Bromide (**6a**).

This compound is known, mp 135-136° (lit [7], mp 134-136°).

N-Phenacyl-2,3-cyclohexenopyridinium Bromide (**6b**).

This compound was obtained as colorless prisms (ethanol), mp 205-206° dec; ir: ν CO 1685 cm^{-1}; pmr: δ 1.8-2.0 (m, H), 2.9-3.1 (m, 4H), 7.04 (s, 2H, CH_2-CO), 7.3-7.8 (m, 4H, H-5 and phenyl), 8.2 (m, 3H, H-4 and phenyl), 9.19 ppm (d, 1H, J = 6 Hz, H-6).

Anal. Calcd. for $C_{17}H_{18}BrON$: C, 61.46; H, 5.46; N, 4.22. Found: C, 61.51; H, 5.46; N, 4.29.

N-Phenacyl-2,3-cycloheptenopyridinium Bromide (**7**).

This compound was obtained as colorless prisms (ethanol-ethyl acetate), mp 168-169°; ir: ν CO 1690 cm^{-1}; pmr: δ 2.1-2.5 (m, 2H), 3.1-3.4 (m, 4H), 7.02 (s, 2H, CH_2-CO), 7.4-7.9 (m, 4H, H-5 and phenyl), 8.13 (m, 2H, phenyl), 8.26 (d, 1H, J = 7 Hz, H-4), 9.27 ppm (d, 1H, J = 7 Hz, H-6).

Anal. Calcd. for $C_{16}H_{16}BrON$: C, 60.39; H, 5.07; N, 4.40. Found: C, 60.25; H, 5.08; N, 4.55.

General Procedure for the Preparation of [*hi*]Condensed Indolizines **8** and **9**.

A vigorously stirred suspension of sodium hydrogencarbonate (150 mmoles) in ethanol (200 ml) containing pyridinium salt **5a** (50 mmoles) was heated at reflux overnight. After cooling, the solution was filtered and the filtrate was evaporated *in vacuo*. The residue was poured in water and extracted with ether (50 ml × 4). The ether extract was dried and concentrated *in vacuo* to give 9.17 g of the oily crude product **8a** (99%). Pure **8a** was obtained by distillation under vacuum in 78% yield.

1-Methyl-7,8,9,10-tetrahydrocyclohepta[*hi*]indolizine (**8a**).

This compound was obtained as colorless oil, bp 116°/3 mm; pmr: δ 1.8-2.0 (m, 4H, H-8 and H-9), 2.17 (s, 3H, CH_3), 2.7-3.0 (m, 4H, H-7 and H-10), 6.1-6.3 (m, 2H, H-5 and H-6), 7.03 (s, 1H, H-2), 7.54 ppm (d, 1H, J = 6 Hz, H-4); ms: m/e 185.1204 (M^+), Calcd. for $C_{13}H_{15}N$: 185.1204.

Satisfactory analytical values for **8a** were not obtained because of its instability to heat, light and air.

1-Methyl-8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinoline (**9a**).

This compound was known, bp 95-97°/2.5 mm (lit [7], bp 87°/0.2 mm).

Indolizine derivatives **8b** or **9b** was obtained in solid state together with sodium hydrogencarbonate and sodium bromide. Thus, the precipitates were collected and washed with 50% aqueous ethanol (50 ml × 5) and the expected **8b** and **9b** was isolated.

1-Phenyl-7,8,9,10-tetrahydrocyclohepta[*hi*]indolizine (**8b**).

This compound was obtained as colorless plates (ethanol), mp 117-118°; pmr: δ 1.8-2.0 (m, 4H, H-8 and H-9), 2.8-3.0 (m, 4H, H-7 and H-10), 6.0-6.3 (m, 2H, H-5 and H-6), 7.1-7.4 (m, 6H, H-2 and phenyl), 7.52 ppm (d, 1H, J = 6 Hz, H-4).

Anal. Calcd. for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.67; H, 7.06; N, 5.65.

1-Phenyl-8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinoline (**9b**).

This compound was obtained as colorless plates (ethanol), mp 118-119°; pmr δ 1.9-2.1 (m, 2H, H-8), 2.80 (br t, 2H, J = 6 Hz, H-7), 3.03 (t, 2H, J = 6 Hz, H-9), 6.2-6.4 (m, 2H, H-5 and H-6), 7.2-7.6 ppm (m, 7H, H-2, H-4 and phenyl).

Anal. Calcd. for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.00. Found: C, 87.63; H, 6.60; N, 5.97.

General Procedure for the Preparation of [*ef*]Condensed Cycl[3.2.2]azine Derivatives **10-13**.

All these reactions were carried out under nitrogen atmosphere. A toluene solution (20 ml) of indolizine **8a** (2 mmoles) and DMAD (3 mmoles) was heated at reflux in the presence of palladium-charcoal (100 mg) for fifty hours. The reaction was pursued with tlc (Merck, Kieselgel $60F_{254}$) and its ending point was determined by the full consumption of the primarily formed orange and red spots. While still warm, the solution was filtered and the filtrate was evaporated *in vacuo*. The residue was treated with column chromatography on silica gel to give the cyclizine **10a** as chloroform eluent. The chloroform solution of **10a** showed a characteristic fluorescence.

1,2-Dimethoxycarbonyl-3-methyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl-[3.2.2]azine (**10a**).

This compound was obtained as yellow prisms (ethanol), mp 101-102°; ir: ν CO 1730, 1710 cm^{-1}; ms: m/e (relative intensity) 325 (M^+, 100), 297 (M^+-C_2H_4, 15), 294 (M^+-OCH_3, 35); pmr: δ 2.0-2.2 (m, 4H, H-5 and H-6), 2.56 (s, 3H, CH_3), 3.02, 3.32 (2 br t, 2H each, J = 6 Hz each, H-4 and H-7), 4.00, 4.08 (2 s, 3H, CO_2CH_3), 7.54 (d, 1H, J = 8 Hz, H-8), 8.14 ppm (d, 1H, J = 8 Hz, H-9).

Anal. Calcd. for $C_{19}H_{19}O_4N$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.20; H, 5.91; N, 4.37.

1,2-Dimethoxycarbonyl-3-phenyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl-[3.2.2]azine (**10b**).

This compound was obtained as pale yellow needles (ethanol), mp 161-162°; ir: ν CO 1725, 1705 cm^{-1}; ms: m/e (relative intensity) 387 (M^+, 100), 359 (M^+-C_2H_4, 40), 352 (M^+-OCH_3, 19), 269 (M^+- 2 × CO_2CH_3, 14); pmr: δ 2.0-2.3 (m, 4H, H-5 and H-6), 3.23, 3.43 (2 t, 2H each, J = 6 Hz each, H-4 and H-7), 3.74, 4.00 (2 s, 3H each, CO_2CH_3), 7.4-7.6 (m, 5H, phenyl), 7.69 (d, 1H, J = 8 Hz, H-8), 8.30 ppm (d, 1H, J = 8 Hz, H-9).

Anal. Calcd. for $C_{24}H_{21}O_4N$: C, 74.40; H, 5.46; N, 3.62. Found: C, 74.17; H, 5.54; N, 3.74.

1,2-Dimethoxycarbonyl-3-methyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**11a**).

This compound was obtained as yellow prisms (ethanol), mp 116-117°; ir: ν CO 1730, 1705 cm^{-1}; ms: m/e (relative intensity) 311 (M^+, 100), 280 (M^+-OCH_3, 55), 279 (50), 193 (M^+- 2 × CO_2CH_3, 32); pmr: δ 2.1-2.4 (m, 2H, H-5), 2.55 (s, 3H, CH_3), 2.9-3.1 (m, 4H, H-4 and H-6), 3.16, 4.01 (2s, 3H each, CO_2CH_3), 7.20 (d, 1H, J = 8 Hz, H-7), 8.02 ppm (d, 1H, J = 8 Hz, H-8).

Anal. Calcd. for $C_{1617}O_4N$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.50; H, 5.61; N, 4.53.

1,2-Dimethoxycarbonyl-3-phenyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**11b**).

This compound was obtained as yellow needles (ethanol), mp 164-165°; ir: ν CO 1720, 1700 cm^{-1}; ms: m/e (relative intensity) 373 (M^+, 100), 342 (M^+-OCH_3, 24), 255 (M^+- 2 × CO_2CH_3, 19); pmr: δ 2.3-2.4 (m, 2H, H-5), 3.21, 3.30 (2 t, 2H each J = 6 Hz each, H-4 and H-6), 3.95, 4.01 (2 s, 3H each, CO_2CH_3), 7.3-7.5 (m, 3H, phenyl), 7.64 (d, 1H, J = 8 Hz, H-7), 7.71 (m, 2H, phenyl), 8.23 ppm (d, 1H, J = 8 Hz, H-8).

Anal. Calcd. for $C_{28}H_{19}O_4N$: C, 73.98; H, 5.13; N, 3.75. Found: C, 73.71; H, 5.16; N, 3.70.

1-Methoxycarbonyl-3-methyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl[3.2.2]-azine (**12**).

This compound was obtained as yellow prisms (ethanol), mp 122-124°; ir: ν CO 1690 cm^{-1}; ms: m/e (relative intensity) 267 (M^+, 100), 239 (M^+-C_2H_4, 84), 236 (M^+-OCH_3, 27), 208 (M^+-CO_2CH_3, 23); pmr: δ 2.1-2.2 (m, 4H, H-5 and H-6), 2.56 (s, 3H, CH_3), 3.05, 3.45 (2 br t, 2H each, J = 6 Hz each, H-4 and H-7), 4.00 (s, 3H, CO_2CH_3), 7.56 (d, 1H, J = 8 Hz, H-8), 7.87 (s, 1H, H-2), 8.15 ppm (d, 1H, J = 8 Hz, H-9).

Anal. Calcd. for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.60; H, 6.42; N, 5.44.

1-Methoxycarbonyl-3-methyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**13**).

This compound was obtained as yellow needles (ethanol), mp 150-151°; ir: ν CO 1690 cm^{-1}; ms: m/e (relative intensity) 253 (M^+, 100), 222 (M^+-OCH_3, 50), 194 (M^+-CO_2CH_3, 20); pmr: δ 2.2-2.4 (m, 2H, H-5), 3.99 (s, 3H, CO_2CH_3), 7.52 (d, 1H, J = 8 Hz, H-7), 7.88 (s, 1H, H-2), 8.11 ppm (d, 1H, J = 8 Hz, H-8).

Anal. Calcd. for $C_{16}H_{15}O_2N$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.93; H, 5.96; N, 5.65.

General Procedure for the Preparation of [*ef*]Condensed Cycl[3.2.2]azine Derivatives **14** and **15**.

All these reactions were carried out under nitrogen atmosphere. To a solution of indolizine **5a** (2 mmoles) in dry THF (20 ml) cooled with ice-salt bath was added dropwise DBZA (2 mmoles) in the same solvent (10 ml). The solution turned reddish violet in color. After confirming the complete consumption of starting materials, the reaction mixture was kept below 0°. To this solution DDQ (2.2 mmoles) was added bit by bit for one hour and the reaction mixture was allowed to stand at the same temperature for additional ten minutes. After removing the resultant hydroquinone, the THF solution was concentrated *in vacuo*. The residue was treated with the column chromatography on silica gel to give the cyclazine **14a** as chloroform eluent. Also, the chloroform solution of **14a** showed a characteristic fluorescence.

1,2-Dibenzoyl-3-methyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl[3.2.2]azine (**14a**).

This compound was obtained as yellow prisms (ethanol-benzene), mp 161.5-163°; ir: ν CO 1635, 1620 cm^{-1}; ms: m/e (relative intensity), 417 (M^+, 100), 416 (12), 389 (M^+-C_2H_4, 16), 340 (M^+-Ph, 22), 312 (M^+-PhCO, 20); pmr: δ 2.1-2.3 (m, 4H, H-5 and H-6), 2.49 (s, 3H, CH_3), 3.09, 3.40 (2 br t, 2H each, J = 6 Hz each, H-4 and H-7), 7.2-7.6 (m, 10H, phenyl), 7.63 (d, 1H, J = 8 Hz, H-8), 7.79 ppm (d, 1H, J = 8 Hz, H-9).

Anal. Calcd. for $C_{29}H_{23}O_2N$: C, 83.43; H, 5.55; N, 3.36. Found: C, 83.10; H, 5.69; N, 3.35.

1,2-Dibenzoyl-3-phenyl-4,5,6,7-tetrahydrocyclohepta[*ef*]cycl[3.2.2]azine (**14b**).

This compound was obtained as yellow prisms (ethanol-benzene), mp 205-206°; ir: ν CO 1655, 1615 cm^{-1}; ms: m/e (relative intensity) 479 (M^+, 100), 478 (12), 451 (M^+-C_6H_2, 21), 402 (M^+-Ph, 22), 312 (M^+-PhCO, 14); pmr: δ 2.1-2.3 (m, 4H, H-5 and H-6), 3.24, 3.46 (2 br t, 2H each, J = 6 Hz each, H-4 and H-7), 7.1-7.5 (m, 11H, phenyl), 7.6-7.7 (m, 5H, H-8 and phenyl), 7.92 ppm (d, 1H, J = 8 Hz, H-9).

Anal. Calcd. for $C_{34}H_{25}O_2N$: C, 85.15; H, 5.25; N, 2.92. Found: C, 85.48; H, 5.41; N, 3.03.

1,2-Dibenzoyl-3-methyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**15a**).

This compound was obtained as yellow prisms (ethanol), mp 153-155°; ir: ν CO 1640 cm^{-1}; ms: m/e (relative intensity) 403 (M^+, 100), 402 (10), 326 (M^+-Ph, 39), 298 (M^+-PhCO, 29); pmr: δ 2.1-2.4 (m, 2H, H-5), 2.40 (s, 3H, CH_3), 2.8-3.1 (m, 4H, H-4 and H-6), 7.1-7.8 ppm (m, 12H, H-7, H-8 and phenyl).

Anal. Calcd. for $C_{28}H_{21}O_2N$: C, 83.35; H, 5.25; N, 3.47. Found: C, 83.05; H, 5.48; N, 3.45.

1,2-Dibenzoyl-3-phenyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**15b**).

This compound was obtained as yellow prisms (ethanol-benzene), mp 200-201°; ir: ν CO 1665, 1620 cm^{-1}; ms: m/e (relative intensity), 465 (M^+, 39), 388 (M^+-Ph, 22), 105 ($PhCO^+$, 100); pmr: δ 2.2-2.4 (m, 2H, H-5), 3.0-3.2 (m, 4H, H-4 and H-6), 7.0-7.6 ppm (m, 17H, H-7, H-8 and phenyl).

Anal. Calcd. for $C_{33}H_{23}O_2N$: C, 85.14; H, 4.98; N, 3.01. Found: C, 85.02; H, 5.12; N, 3.00.

Preparation of Mono-substituted Cyclazine **16**.

Cyclazine **11b** (2 mmoles) was treated with a refluxing 5% methanolic potassium hydroxide for two hours. After removing methanol *in vacuo*, the residue was dissolved in water. The aqueous solution was filtered in order to remove tarry materials and the filtrate was made acidic with concentrated hydrochloric acid. The resultant dicarboxylic acid was filtered, dried and treated with the next decarboxylation without further purification. A soluton of the dicarboxylic acid in quinoline (10 ml) was refluxed in the presence of 100 mg of copper dust for ten hours, copper dust was filtered off and quinoline was removed in reduced pressure. The residue was dissolved in ether and washed with 0.5*N* hydrochloric acid (50 ml × 5) in order to remove quinoline completely. The ether layer was dried and evaporated *in vacuo* to give an oily residue. The residue was column chromatographed on silica gel to afford 400 mg of the expected **16** (78% from **11b**) using benzene-hexane (3:1) as an elution.

3-Phenyl-5,6-dihydro-4*H*-benzo[*ef*]cycl[3.2.2]azine (**16**).

This compound was obtained as yellow plates (ethanol), mp 89-90°; ms: m/e (relative intensity) 257 (M^+, 100), 256 (63), 254 (28), 228 (20), 180 (M^+-Ph, 17); pmr: δ 2.3-2.5 (m, 2H, H-5), 3.22, 3.42 (2 t, 2H each, J = 6 Hz each, H-4 and H-6), 7.2-8.0 ppm (m, 9H, H-1, H-2, H-7, H-8 and phenyl).

Anal. Calcd. for $C_{19}H_{15}N$: C, 88.68; H, 5.88; N, 5.44. Found: C, 88.48; H, 5.89; N, 5.55.

Reaction of **14a** and **15a** with Hydrazine Hydrate.

To a solution of **14a** (1 mmole) in ethanol (20 ml) was added hydrazine hydrate (2 ml, excess) and the reaction mixture was heated at reflux for one hour in the presence of a catalytic amount of concentrated hydro-

chloric acid. Ethanol was removed *in vacuo*, the residue was poured in water and extracted with dichloromethane (20 ml × 2). The organic layer was dried and concentrated in reduced pressure to give 393 mg of the corresponding pyridazino derivative **17** (95%).

11-Methyl-1,4-diphenyl-7,8,9,10-tetrahydrocyclohepta[*ef*]pyridazino-[4,5-*a*]cycl[3.2.2]azine (**17**).

This compound was obtained as orange needles (hexane-ethyl acetate), mp 219-221°; ms: m/e (relative intensity), 413 (M^+, 100), 412 (40), 398 (M^+-CH_3, 5), 385 (M^+-C_2H_4, 18), 356 (8); pmr: δ 1.94 (s, 3H, CH_3), 2.1-2.2 (m, 4H, H-8 and H-8), 3.05, 3.46 (2 br t, 2H each, J = 6 Hz each, H-7 and H-10), 7.54 (d, 1H, J = 8 Hz, H-6), 7.6-7.7, 7.9-8.0, 8.1-8.2 ppm (m, total 11H, H-5 and phenyl).

Anal. Calcd. for $C_{29}H_{23}N_3$: C, 84.23; H, 5.61; N, 10.16. Found: C, 84.28; H, 5.68; N, 10.32.

10-Methyl-1,4-diphenyl-8,9-dihydro-7*H*-benzo[*ef*]pyridazino[4,5-*a*]cycl-[3.2.2]azine (**18**).

This compound was obtained as yellow needles (ethanol-benzene), mp 231-232°; ms: m/e (relative intensity), 399 (M^+, 100), 398 (42), 370 (9), 368 (6), 354 (8); pmr: δ 2.04 (s, 3H, CH_3), 2.3-2.4 (m, 4H, H-8) 3.06, 3.25 (2 t, 2H each, J = 6 Hz, H-7 and H-9), 7.47 (d, 1H, J = 8 Hz, H-6), 7.6-7.7, 8.0-8.1, 8.2-8.3 ppm (m, total 11H, H-5 and phenyl).

Anal. Calcd. for $C_{28}H_{21}N_3$: C, 84.18; H, 5.30; N, 10.52. Found: C, 84.17; H, 5.36; N, 10.77.

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