Preparation of 5,5-Bis(ethoxycarbonyl)-5,6-dihydro-3,7-diaryl-4*H*-1,2-diazepines and Their Halogenations[1)]

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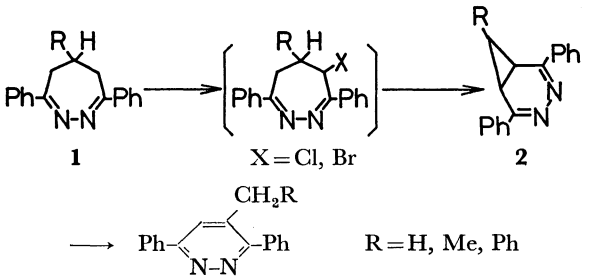
5,5-Bis(ethoxycarbonyl)-5,6-dihydro-3,7-diaryl-4*H*-1,2-diazepines (**4**) were prepared by the condensation of α-bromoacetophenone azines with diethyl malonate in the presence of sodium ethoxide. Halogenation of **4** afforded 7,7-bis(ethoxycarbonyl)-2,5-diaryl-3,4-diazanorcaradiene, 4,6-dihalodihydrodiazepines, 1-halodiazanorcaradienes, and/or 4,4,6,6-tetrachlorodihydrodiazepine, whose relative yields depended upon the reaction conditions. Dehalogenation of the halogenated products was also investigated.

It has been reported that the treatment of 3,7-diphenyl-5,6-dihydro-4*H*-1,2-diazepines (**1**) with halogenation-reagents resulted in ring contraction to pyridazines. The isolation of 3,4-diazanorcaradienes (**2**, R=H,[2)] Ph[3)]) has been cited as evidence for their intermediacy in the contraction reaction which presumably proceeds by a halogenation-dehydrohalogenation process. However, halogenated intermediates have not been isolated (Scheme 1).



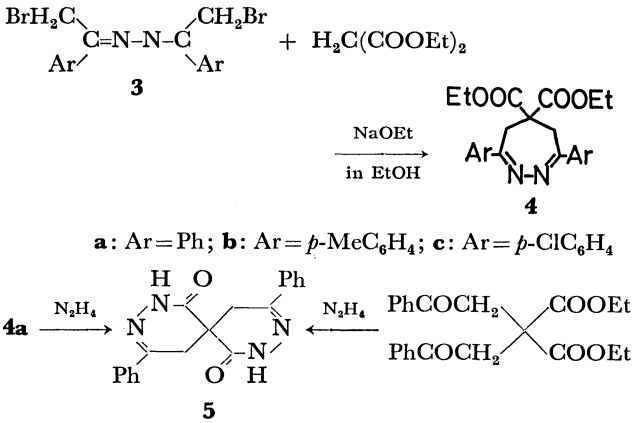
Scheme 1.

This paper is concerned with the preparation of 5,5-bis(ethoxycarbonyl)-5,6-dihydro-3,7-diaryl-4*H*-1,2-diazepines, and with their halogenations which afforded halogenated intermediates and diazanorcaradienes in good yields.

Results and Discussion

Preparation of 5,5-Bis(ethoxycarbonyl)-5,6-dihydro-3,7-diaryl-4H-1,2-diazepines (4). 5,5-Disubstituted 5,6-dihydro-4*H*-1,2-diazepines have not been reported in literature. α-Bromoacetophenone azine (**3a**)[4)] which was prepared by the bromination of acetophenone azine, would be expected to react with active methylene compounds, affording the corresponding 5,6-dihydro-4*H*-1,2-diazepines. In fact, **3a** reacted with diethyl malonate in the presence of sodium ethoxide to give the expected 5,5-bis(ethoxycarbonyl)-5,6-dihydro-3,7-diphenyl-4*H*-1,2-diazepine (**4a**). Similarly, 3,7-di(*p*-tolyl) and 3,7-bis(*p*-chlorophenyl) derivatives, **4b** and **4c**, were prepared from the corresponding azines, **3b** and **3c**, respectively.

Structural elucidation of **4** was accomplished on the basis of spectral data and the results of microanalyses,



Scheme 2.

Table 1. 5,5-Bis(ethoxycarbonyl)-5,6-dihydro-3,7-diaryl-4*H*-diazepines **4**[a)]

	Yield %	Mp, °C	IR, $\nu_{C=O}$ cm^{-1}	NMR ($CDCl_3$) δ ppm	Found (Calcd) % C	H	N
4a	77	124—125	1760, 1740	1.15 (6H, t, CH_2CH_3), 3.30 (4H, s, CH_2) 4.13 (4H, q, CH_2Me), 7.3—8.0 (10H, m, ArH)	70.44 (70.39)	6.12 (6.16)	7.13 (7.14)
4b	45	103—104	1760, 1740	1.18 (6H, t, CH_2CH_3), 2.36 (6H, s, CH_3) 3.23 (4H, s, CH_2), 4.15 (4H, q, CH_2Me) 7.1—7.8 (8H, m, ArH)	71.40 (71.41)	6.73 (6.71)	6.65 (6.66)
4c	58	129—130	1750, 1730	1.17 (6H, t, CH_2CH_3), 3.21 (4H, s, CH_2) 4.11 (4H, q, CH_2Me), 7.2—7.9 (8H, m, ArH)	59.90 (59.87)	4.82 (4.80)	6.09 (6.07)

a) All **4** are colorless prisms.

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which are given with the yields and melting points in Table 1.

Treatment of **4a** with hydrazine hydrate in acetic acid afforded 5,5′-spirobi(1*H*-3-phenyl-4,5-dihydropyridazin-6-one) (**5**), which was identical with an authentic sample prepared from diethyl diphenacylmalonate and hydrazine hydrate (Scheme 2).

Bromination. When **4a** was treated with an equimolar amount of bromine in methanol at room temperature, 7,7-bis(ethoxycarbonyl)-2,5-diphenyl-3,4-diazanorcaradiene (**7a**), mp 120—121 °C, was obtained in excellent yield. The reaction of **4a** with two molar amounts of bromine in methanol gave 5,5-bis(ethoxycarbonyl)-4,6-dibromo-5,6-dihydro-3,7-diphenyl-4*H*-1,2-diazepine (**8a**) and/or 1-bromo-7,7-bis(ethoxycarbonyl)-2,5-diphenyl-3,4-diazanorcaradiene (**9**); whose relative yields greatly depended upon the reaction time. That is, the reaction for 10 min gave **8a** and **9** in 83 and 16% yields respectively, whereas the reaction for 2 h exclusively produced **9**. On the other hand, the reactions of **4a** with two molar amounts of bromine in methylene dichloride, chloroform, and acetic acid, and with excess *N*-bromosuccinimide (NBS) in carbon tetrachloride did not give **8a** and **9**, but instead **7a** was only formed.

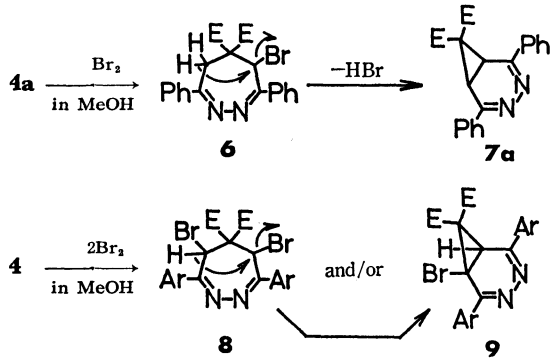
Similarly, the reaction of 3,7-di(*p*-tolyl)- **4b** and 3,7-bis(*p*-chlorophenyl)dihydrodiazepine **4c** with two molar amounts of bromine in methanol for 5 min afforded the corresponding dibromides **8b** and **8c** respectively. In these cases, the corresponding 1-bromodiazanorcaradines were not obtained.

Hydrolysis of **7a** with ethanolic potassium hydroxide afforded the half ester **10**, which on heating in ethanol or ethanol-d_1 underwent decarboxylation to give 7-*exo*-ethoxycarbonyl-2,5-diphenyl-3,4-diazanorcaradiene (**11**) or its 7-deuterio derivative **11**-d_1 respectively. When **10** was heated at 130—140 °C without solvent, ring opening occurred to yield 4-ethoxycarbonylmethyl-3,6-diphenylpyridazine (**12**) (Scheme 3).

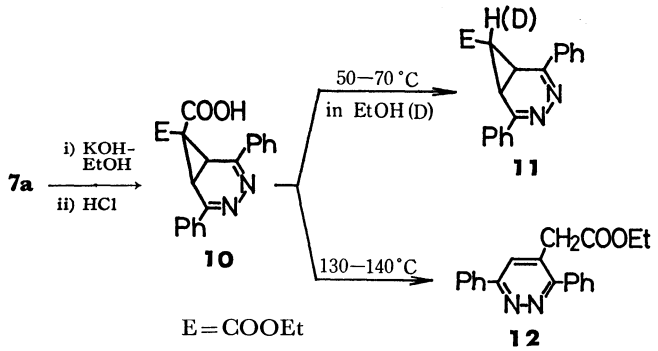
The structures of all products, **7**—**12**, were confirmed on the basis of their spectral data.

Although the monobromide **6** has not been isolated, it is clear that the diazanorcaradienes **7a** and **9** are formed *via* internal nucleophilic displacement of the monobromide **6** and dibromide **8** respectively as delineated in Scheme 3.

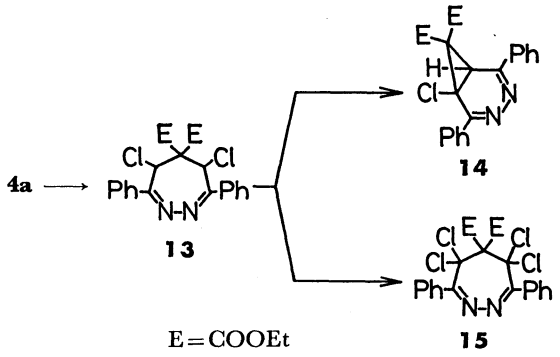
Chlorination. The treatment of **4a** with an equimolar amount of sulfuryl chloride in methylene dichloride at room temperature afforded traces of an unidentified compound, together with recovery of **4a**. However, **4a** reacted with two molar amounts of sulfuryl chloride to give 5,5-bis(ethoxycarbonyl)-4,6-dichloro-5,6-dihydro-3,7-diphenyl-4*H*-1,2-diazepine (**13**) and/or 7,7-bis(ethoxycarbonyl)-1-chloro-2,5-diphenyl-3,4-diazanorcaradiene (**14**); whose relative yields depended upon the reaction time again. Further chlorination of the dichloride **13** with sulfuryl chloride afforded the 4,4,6,6-tetrachlorodihydrodiazepine **15** in good yield. The tetrachloride **15** was formed directly from chlorination of **4a** with excess sulfuryl chloride or chlorine gas. Structural elucidation of **13**—**15** was accomplished on the basis of their spectral data.



a: Ar=Ph; **b**: Ar=*p*-MeC$_6$H$_4$; **c**: Ar=*p*-ClC$_6$H$_4$



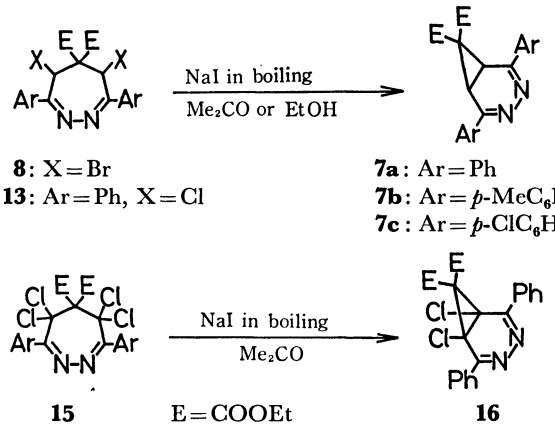
Scheme 3.



Scheme 4.

It is considered that activation of the methylene groups at positions 4 and 6 in **4** to halogenation is attributable to the electron-withdrawing azine and ethoxycarbonyl groups. As shown above. 7,7-bis(ethoxycarbonyl)diazanorcaradienes, **7**, **9**, and **14**, were isolated in good yields respectively; this fact suggests that the diazanorcaradienes are stabilized by the extended π-electron conjugation.

Dehalogenations of the Halogenated Products. When dibromides, **8a**—**8c**, were treated with sodium iodide in boiling acetone for 2 h, the corresponding diazanorcaradienes, **7a**—**7c**, were obtained in good yields. Although the dichloride **13** was unchanged under similar conditions, **13** was also converted to **7a** on prolonged heating with sodium iodide in ethanol. Similarly, treatment of the tetrachloride **15** with sodium iodide in boiling acetone afforded the 1,6-dichlorodiazanorcaradiene **16** quantitatively (Scheme 5).



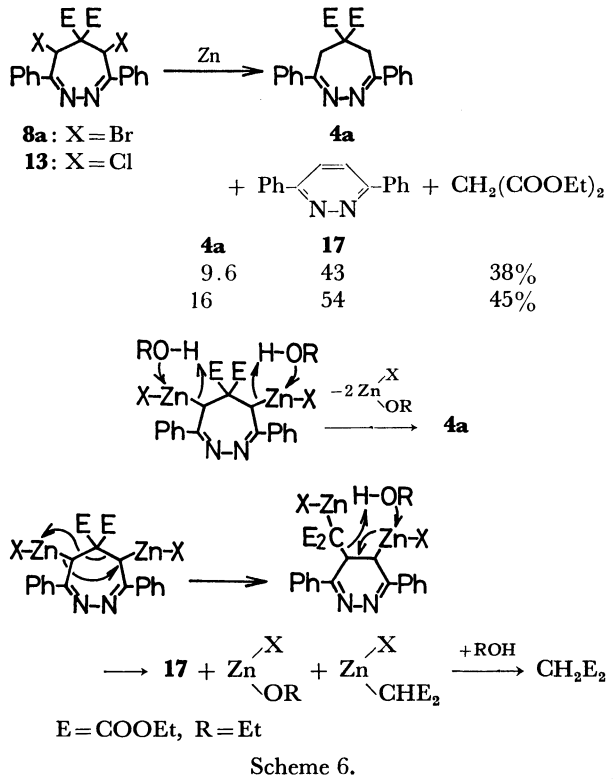
8: X=Br
13: Ar=Ph, X=Cl

7a: Ar=Ph
7b: Ar=*p*-MeC$_6$H$_4$
7c: Ar=*p*-ClC$_6$H$_4$

15 E=COOEt **16**

Scheme 5.

Next, we have investigated the dehalogenation with zinc dust in boiling ethanol. In contrast to the above dehalogenation using sodium iodide, the dihalides, **8a** and **13**, did not give the diazanorcaradines **7a**, but instead the dihydrodiazepine **4a**, 3,6-diphenylpyridazine (**17**), and diethyl malonate were formed in the respective yields shown in Scheme 6. As illustrated in Scheme 6, these reactions proceed through two different pathways from the organozinc halide; one is direct decomposition by ethanol to give **4a**, and the other is ring contraction, followed by decomposition to afford **17** and diethyl malonate.



8a: X=Br
13: X=Cl

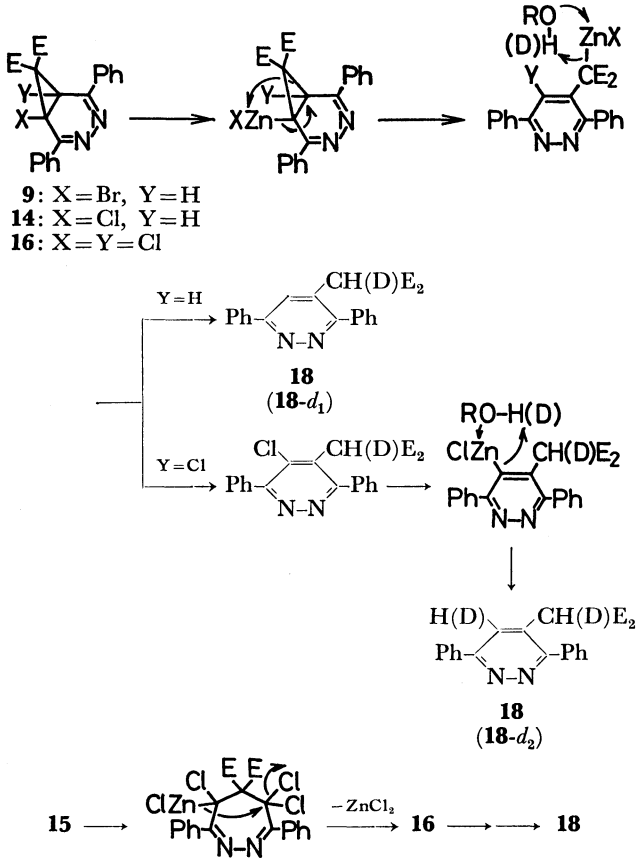
4a **17**

9.6	43	38%
16	54	45%

E=COOEt, R=Et

Scheme 6.

On the other hand, similar treatments of halogenated diazanorcaradienes, **9**, **14**, and **16**, afforded 4-[bis(ethoxycarbonyl)methyl]-3,6-diphenylpyridazine (**18**) in 47, 51, and 13% yields respectively. The pyridazine **18** was also obtained in 16% yield from the tetrachloride



9: X=Br, Y=H
14: X=Cl, Y=H
16: X=Y=Cl

18 (**18**-d_1)

18 (**18**-d_2)

E=COOEt, R=Et

Scheme 7.

15. The dehalogenation of **14** and **15** with zinc dust in boiling ethanol-d_1 afforded the pyridazines, **18**-d_1 and **18**-d_2, respectively.

On the basis of the above results, the pathways for the formation of **18** from **9** and **14**—**16** are interpreted as depicted in Scheme 7.

Experimental

All the melting points are uncorrected. The NMR spectra were determined with a Hitachi R-20 Model spectrometer, with TMS as the internal standard. The IR spectra were measured as KBr disks, and the MS were obtained on a Hitachi RMS-4 mass spectrometer with a direct inlet and an ionization energy of 70 eV.

α-Bromoacetophenone Azines (3). α-Bromoacetophenone azine (**3a**), mp 151—152 °C (lit,[4] mp 151—152 °C), was prepared by the bromination of acetophenone azine. Similarly, α-bromo-*p*-methylacetophenone azine (**3b**) and α-bromo-*p*-chloroacetophenone azine (**3c**) were prepared from the corresponding acetophenone azine.

3b: mp 182—183 °C; IR 1590 cm^{-1} (C=N). Found: C, 51.23; H, 4.15; N, 6.75%. Calcd for $C_{18}H_{18}N_2Br_2$: C, 51.19; H, 4.27; N, 6.63%.

3c: mp 186—187 °C; IR 1597 cm^{-1} (C=N). Found: C, 41.14; H, 2.67; N, 6.31%. Calcd for $C_{16}H_{12}N_2Br_2Cl_2$: C, 41.47; H, 2.60; N, 6.05%.

5,5-Bis(ethoxycarbonyl)-5,6-dihydro-3,7-diaryl-4H-1,2-diazepines (4). A solution of the azine **3a** (3.94 g, 0.01 mol) in benzene (50 ml) was added to a solution of diethyl malonate (3.2 g, 0.02 mol) and sodium ethoxide (1.4 g, 0.02 mol) in

ethanol (20 ml), and then the reaction mixture was refluxed for 1 h. The mixture was poured into water (100 ml) and the benzene layer was separated and evaporated *in vacuo* to leave crystals. Recrystallization from ethanol gave 3.0 g (77%) of the dihydrodiazepine **4a**.

Similarly, 3,7-di(*p*-tolyl) and 3,7-bis(*p*-chlorophenyl) derivatives, **4b** and **4c**, were prepared from the corresponding azines, **3b** and **3c**, respectively. The yields, physical data, and results of microanalyses of **4** are given in Table 1.

5,5'-Spirobi(1H-3-phenyl-4,5-dihydropyridazine-6-one) (5). A solution of the dihydrodiazepine **4a** (3.92 g, 0.01 mol) and hydrazine hydrate (1.0 g, 0.02 mol) in acetic acid (50 ml) was heated at 60—70 °C for 2 h. The mixture was poured into water (10 ml) and was allowed to stand at room temperature to give crystals. Recrystallization from ethanol gave 0.66 g (20%) of **5**, mp 315 °C (dec), as colorless prisms. NMR (pyridine-d_5) δ 3.19, 3.90 (each 2H, CH_2, J=17.4 Hz), 7.2—8.1 (10H, m, aromatic protons), 12.86 ppm (2H, br, NH).

Found: C, 68.78; H, 4.88; N, 17.02%. Calcd for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.86%.

The spirobipyridazinone **5** was identical with an authentic sample prepared by the following manner. A solution of diethyl diphenacylmalonate (1.33 g) and hydrazine hydrate (0.5 g) in acetic acid (10 ml) was heated at 60—70 °C for 2 h, and a similar work-up gave 0.65 g (59%) of **5**.

Bromination of the Dihydrodiazepines 4. *i*) A solution of bromine (0.8 g, 5 mmol) in methanol (40 ml) was added, drop by drop, over a period of 1 h to a suspension of the dihydrodiazepine **4a** (1.96 g, 5 mmol) in methanol (20 ml), and then the reaction mixture was stirred at room temperature for 2 h. The mixture was added to water (200 ml), and was extracted with benzene (40 ml×2). The benzene extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo* to leave crystals, which on recrystallization from petroleum ether (bp 60—80 °C) afforded 1.91 g (98%) of 7,7-bis(ethoxycarbonyl)-2,5-diphenyl-3,4-diaza-2,4-norcaradiene (**7a**), mp 120—121 °C, as yellow prisms. IR 1725, 1735 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.82, 1.35 (each 3H, t, CH_2CH_3), 3.38 (2H, s, ≥CH), 3.89, 4.40 (each 2H, q, CH_2Me), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* 390 (M^+).

Found: C, 70.79; H, 5.69; N, 7.18%. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.18%.

Bromination of **4a** in acetic acid, chloroform, and carbon tetrachloride under similar conditions afforded **7a** in excellent yields respectively.

ii) Bromine (3.2 g, 0.02 mol) was added to a suspension of the dihydrodiazepine **4a** (3.92 g, 0.01 mol) in methanol (60 ml), and the reaction mixture was stirred at room temperature. The mixture changed to a solution and then yellow crystals separated out after about 5 min. Filtration gave crystals which were washed with methanol (30 ml). Recrystallization from ethanol afforded 4.5 g (83%) of 5,5-bis(ethoxycarbonyl)-4,6-dibromo-5,6-dihydro-3,7-diphenyl-4*H*-1,2-diazepine (**8a**), mp 150—151 °C, as yellow prisms. NMR ($CDCl_3$) δ 1.15 (6H, t, CH_2CH_3), 4.18 (4H, q, CH_2Me), 5.73 (2H, s, ≥CH), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* 548, 550, 552, 554 (M^+).

Found: C, 50.22; H, 4.04; N, 5.15%. Calcd for $C_{23}H_{22}N_2O_4Br_2$: C, 50.20; H, 4.04; N, 5.09%.

The filtrate and methanol washing were combined, poured into water (300 ml), and extracted with benzene (80 ml×2). The benzene extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo* to leave 0.74 g (16%) of crystals. Recrystallization from petroleum ether (bp 60—80 °C) afforded 1-bromo-7,7-bis(ethoxycarbonyl)-2,5-diphenyl-3,4-diazanorcaradiene (**9**), mp 133—134 °C, as yellow prisms. NMR ($CDCl_3$) δ 0.87, 1.44 (each 3H, t, CH_2CH_3), 3.88 (1H, s, ≥CH), 3.95, 4.54 (each 2H, q, CH_2Me), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* 468, 470 (M^+).

Found: C, 59.01; H, 4.52; N, 5.94%. Calcd for $C_{23}H_{21}N_2O_4Br$: C, 58.86; H, 4.51; N, 5.97%.

Similar reactions of the dihydrodiazepines **4b** and **4c** with bromine in methanol for 5 min afforded the corresponding dibromodihydrodiazepines **8b** and **8c** in 75 and 86% yields respectively.

8b: Mp 151—152 °C, yellow prisms. NMR ($CDCl_3$) δ 1.21 (6H, t, CH_2CH_3), 2.41 (6H, s, CH_3), 4.20 (4H, q, CH_2Me), 5.70 (2H, s, ≥CH), 7.2—8.1 ppm (8H, m).

Found: C, 51.89; H, 4.52; N, 4.85%. Calcd for $C_{25}H_{26}N_2O_4Br_2$: C, 51.92; H, 4.53; N, 4.84%.

8c: Mp 149—150 °C, yellow prisms. NMR ($CDCl_3$) δ 1.17 (6H, t, CH_2CH_3), 4.07 (4H, q, CH_2Me), 5.60 (2H, s, ≥CH), 7.3—8.1 ppm (8H, m).

Found: C, 44.63; H, 3.28; N, 4.50%. Calcd for $C_{23}H_{20}N_2O_4Br_2Cl_2$: C, 44.61; H, 3.26; N, 4.52%.

iii) When a mixture of **4a** (1.96 g, 5 mmol) and bromine (1.6 g, 10 mmol) in methanol (30 ml) was stirred at room temperature for 1 h, the precipitated dibromide **8a** dissolved. After the reaction mixture was stirred for another 1 h, it was evaporated *in vacuo* to leave crystals which on recrystallization from petroleum ether gave 2.31 g (98.5%) of the 1-bromodiazanorcaradiene **9**.

7-exo-Ethoxycarbonyl-2,5-diphenyl-3,4-diphenyl-3,4-diazanorcaradine (11). After a solution of the 7,7-bis(ethoxycarbonyl)-diazanorcaradiene **7a** (3.9 g) in ethanol (50 ml) was stirred with potassium hydroxide (4.0 g) at room temperature for 3 h, the mixture was acidified with dil. hydrochloric acid to give 2.5 g (70%) of the half ester **10**. A solution of the half ester **10** (1.0 g) in ethanol (5 ml) was warmed at 50—70 °C for 15 min, and then allowed to stand at room temperature, giving 0.47 g (54%) of the mono(ethoxycarbonyl)diazanorcaradiene **11**, mp 233—234 °C, as yellow needles. NMR ($CDCl_3$) δ 1.35 (3H, t, CH_2CH_3), 1.41 (1H, t, ≥CH, J=4.2 Hz), 3.25 (2H, d, 2×≥CH, J=4.2 Hz), 4.34 (2H, q, CH_2Me), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* 318 (M^+).

Found: C, 75.35; H, 5.61; N, 8.92%. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80%.

A similar treatment of **10** with ethanol-d_1 gave the 7-deuterio derivative **11**-d_1, mp 233—234 °C, in 60% yield. NMR ($CDCl_3$) δ 1.35 (3H, t, CH_2CH_3), 3.22 (2H, s, ≥CH), 4.43 (2H, q, CH_2Me), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* (rel. intensity %) 319 (M^+, 88), 318 (15), 246 (M^+−COOEt, 12).

4-Ethoxycarbonylmethyl-3,6-diphenylpyridazine (12). The half ester **10** (1.0 g) was heated at 130—140 °C (bath temperature) for 5 min, and then the residue was recrystallized from ethanol to give 0.54 g (63%) of the pyridazine **12**, mp 139—140 °C, as colorless prisms. NMR ($CDCl_3$) δ 1.20 (3H, t, CH_2CH_3), 3.72 (2H, s, CH_2), 4.15 (2H, q, CH_2Me), 7.85 (1H, s, pyridazine ring proton), 7.4—8.3 ppm (10H, m); MS *m/e* 318 (M^+).

Found: C, 75.31; H, 5.68; N, 8.72%. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80%.

Chlorination of the Dihydrodiazepine 4a. A solution of **4a** (1.96 g, 5 mmol) and sulfuryl chloride (1.35 g, 10 mmol) in methylene dichloride (40 ml) was stirred at room temperature for 5 min, and then the solvent was removed *in vacuo*. The residue was triturated with methanol (10 ml) and filtration gave crystals which on recrystallization from petroleum ether (bp 60—80 °C) afforded 2.97 g (64%) of 5,5-bis(ethoxycarbonyl)-4,6-dichloro-5,6-dihydro-3,7-diphenyl-4*H*-1,2-di-

azepine (**13**), mp 112—113 °C, as colorless prisms. NMR ($CDCl_3$) δ 1.15 (6H, t, CH_2CH_3), 4.18 (4H, q, CH_2Me), 5.73 (2H, s, $\geq CH$), 7.3—7.7 (6H, m), 7.8—8.3 ppm (4H, m); MS *m/e* 460, 462, 464 (M^+).

Found: C, 59.70; H, 4.78; N, 6.05%. Calcd for $C_{23}H_{22}N_2O_4Cl_2$: C, 59.88; H, 4.81; N, 6.07%.

The methanol filtrate was poured into water and extracted with benzene (40 ml×2). The benzene extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo* to give crystals. Recrystallization from petroleum ether (bp 60—80 °C) afforded 1.27 g (30%) of 7,7-bis(ethoxycarbonyl)-1-chloro-2,5-diphenyl-3,4-diazanorcaradiene (**14**), mp 130—131 °C, as yellow prisms. NMR ($CDCl_3$) δ 0.86, 1.41 (each 3H, t, CH_2CH_3), 3.88 (1H, s, $\geq CH$), 3.94, 4.50 (each 2H, q, CH_2Me), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* 424, 426 (M^+).

Found: C, 64.77; H, 4.92; N, 6.57%. Calcd for $C_{23}H_{21}N_2O_4Cl$: C, 65.02; H, 4.98; N, 6.59%.

The same reaction for 2 h afforded 1.87 g (88%) of **14**.

*5,5-Bis(ethoxycarbonyl)-5,6-dihydro-3,7-diphenyl-4,4,6,6-tetrachloro-4H-1,2-diazepine (**15**).* A solution of the dichloride **13** (0.46 g, 1 mmol) and sulfuryl chloride (0.27 g, 2 mmol) in methylene dichloride (10 ml) was stirred at room temperature for 2 h. The reaction mixture was evaporated *in vacuo* to leave crystals which on recrystallization from ethanol afforded 0.45 g (85%) of the tetrachloride **15**, mp 143—144 °C, as colorless prisms. NMR ($CDCl_3$) δ 1.21 (6H, t, CH_2CH_3), 4.35 (4H, q, CH_2Me), 7.3—7.7 (6H, m), 7.8—8.1 ppm(4H, m); MS *m/e* 528, 530, 532, 534, 536 (M^+).

Found: C, 51.82; H, 3.72; N, 5.22%. Calcd for $C_{23}H_{20}N_2O_4Cl_4$: C, 52.09; H, 3.81; N, 5.28%.

The tetrachloride **15** was directly obtained from chlorination of the dihydrodiazepine **4a** with excess sulfuryl chloride or chlorine gas. A solution of **4a** (1.96 g, 5 mmol) and sulfuryl chloride (2.7 g, 20 mmol) in methylene dichloride (40 ml) was stirred at room temperature for 2 h. A similar work-up of the reaction mixture as above gave 1.68 g (63%) of the tetrachloride **15**.

Chlorination of **4a** with excess chlorine gas in methanol, acetic acid, carbon tetrachloride, chloroform, and methylene dichloride afforded **15** in 45, 79, 79, 87, and 47% yields respectively.

Dehalogenation of the Dihalodihydrodiazepines with Sodium Iodide. *i*) A solution of the dibromide **8a** (1.1 g, 2 mmol) and sodium iodide (0.75 g, 5 mmol) in acetone (20 ml) was refluxed for 2 h. The reaction mixture was poured into water (100 ml) and extracted with benzene (40 ml×2). The benzene extract was washed with sodium thiosulfate aqueous solution, water, and dried over sodium sulfate, and then evaporated *in vacuo* to leave 0.76 g (97%) of the diazanorcaradiene **7a**.

Similarly, treatment of the dibromides **8b** and **8c** with sodium iodide in boiling acetone afforded 7,7-bis(ethoxycarbonyl)-2,5-di(*p*-tolyl)- (**7b**) and 7,7-bis(ethoxycarbonyl)-2,5-bis(*p*-chlorophenyl)-3,4-diaza-2,4-norcaradiene (**7c**) in 83 and 90% yields respectively.

7b: Mp 128—129 °C, yellow prisms. NMR ($CDCl_3$) δ 0.86, 1.36 (each 3H, t, CH_2CH_3), 2.45 (6H, s, CH_3), 3.35 (2H, s, $\geq CH$), 3.88 4.41 (each 2H, q, CH_2Me), 7.2—8.1 ppm (8H, m).

Found: C, 71.71; H, 6.20; N, 6.67%. Calcd for $C_{25}H_{26}N_2O_4$: C, 71.75; H, 6.26; N, 6.69%.

7c: Mp 165—166 °C, yellow prisms. NMR ($CDCl_3$) δ 0.85, 1.35 (each 3H, t, CH_2CH_3), 3.25 (2H, s, $\geq CH$), 3.85, 4.36 (each 2H, q, CH_2Me), 7.3—8.1 ppm (8H, m).

Found: C, 60.10; H, 4.36; N, 6.08%. Calcd for $C_{23}H_{20}N_2O_4Cl_2$: C, 60.14; H, 4.38; N, 6.09%.

ii) A solution of the dichloride **13** (0.92 g, 2 mmol) and sodium iodide (0.75 g, 5 mmol) in ethanol (20 ml) was refluxed for 24 h. A similar work-up as above afforded 0.75 g (96%) of the diazanorcaradiene **7a**.

*7,7-Bis(ethoxycarbonyl)-1,6-dichloro-2,5-diphenyl-3,4-diaza-2,4-norcaradiene (**16**).* A solution of the tetrachloride **15** (1.06 g, 2 mmol) and sodium iodide (0.75 g, 5 mmol) in acetone (20 ml) was refluxed for 2 h. A similar work-up as above and recrystallization of the product from petroleum ether (bp 60—80 °C) gave 0.88 g (97%) of the 1,6-dichlorodiazanorcaradiene **16**, mp 118—119 °C, as yellow prisms. NMR ($CDCl_3$) δ 0.89, 1.45 (each 3H, t, CH_2CH_3), 4.0, 4.5 (each 2H, q, CH_2Me), 7.3—7.7 (6H, m), 7.9—8.3 ppm (4H, m); MS *m/e* 458, 460, 462 (M^+).

Found: C, 60.09; H, 4.38; N, 6.15%. Calcd for $C_{23}H_{20}N_2O_4Cl_2$: C, 60.15; H, 4.38; N, 6.10%.

Dehalogenation of the Dibromide 8a with Zinc Dust. A solution of **8a** (1.1 g) in ethanol (40 ml) was refluxed with zinc dust (1.0 g) for 2 h. The reaction mixture was filtered and the residue was washed with hot ethanol (30 ml). The ethanol filtrate and washing were combined, concentrated to about 30 ml, and allowed to stand at room temperature. Filtration gave 0.2 g (43%) of 3,6-diphenylpyridazine (**17**), mp 223 °C (lit,[5] mp 222 °C), as colorless prisms. The filtrate was further concentrated to about 5 ml to give 75 mg (9.6%) of the dihydrodiazepine **4a**. The solution which was removed **4a** was chromatographed on silica gel to give 0.12 g (38%) of diethyl malonate.

A similar treatment of the dichloride **13** with zinc dust afforded the dihydrodiazepine **4a**, pyridazine **17**, and diethyl malonate; the yields are shown in Scheme 6.

*Dehalogenation of the 1-Bromodiazanorcaradiene **9** with Zinc Dust.* A solution of **9** (0.94 g) in ethanol (30 ml) was refluxed with zinc dust (1.0 g) for 2 h. A similar work-up as above afforded 0.38 g (47%) of 4-bis(ethoxycarbonyl)methyl-3,6-diphenylpyridazine (**18**), mp 131—132 °C, as colorless needles. IR 1740, 1760 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.23 (6H, t, CH_2CH_3), 4.25 (4H, q, CH_2Me), 4.93 (1H, s, $\geq CH$), 7.4—7.8 (6H, m), 8.0—8.4 (4H, m), 8.23 ppm (1H, s, pyridazine ring-H); MS *m/e* 390 (M^+).

Found: C, 70.82; H, 5.69; N, 7.21%. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.18%.

Similarly, the chlorodiazanorcaradiene **14**, tetrachloride **15**, and dichlorodiazanorcaradiene **16** afforded the pyridazine **18** in 51, 16, and 13% yields respectively. Treatments of **14** and **15** with zinc dust in ethanol-d_1 under similar conditions afforded the pyridazines **18**-d_1 and **18**-d_2 in 54 and 13% yields respectively. **18**-d_1: NMR (DMSO-d_6) δ 1.20 (6H, t, CH_2CH_3), 4.20 (4H, q, CH_2Me), 7.4—7.8 (6H, m), 8.25 ppm (1H, s, pyridazine ring-H); MS *m/e* 391 (M^+). **18**-d_2: NMR (DMSO-d_6) δ 1.20 (6H, t, CH_2CH_3), 4.20 (4H, q, CH_2Me), 7.4—7.8 (6H, m), 8.0—8.4 ppm (4H, m); MS *m/e* 392 (M^+).

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