

Nüket Öcal, Zuhâl Turgut and Şeniz Kaban*

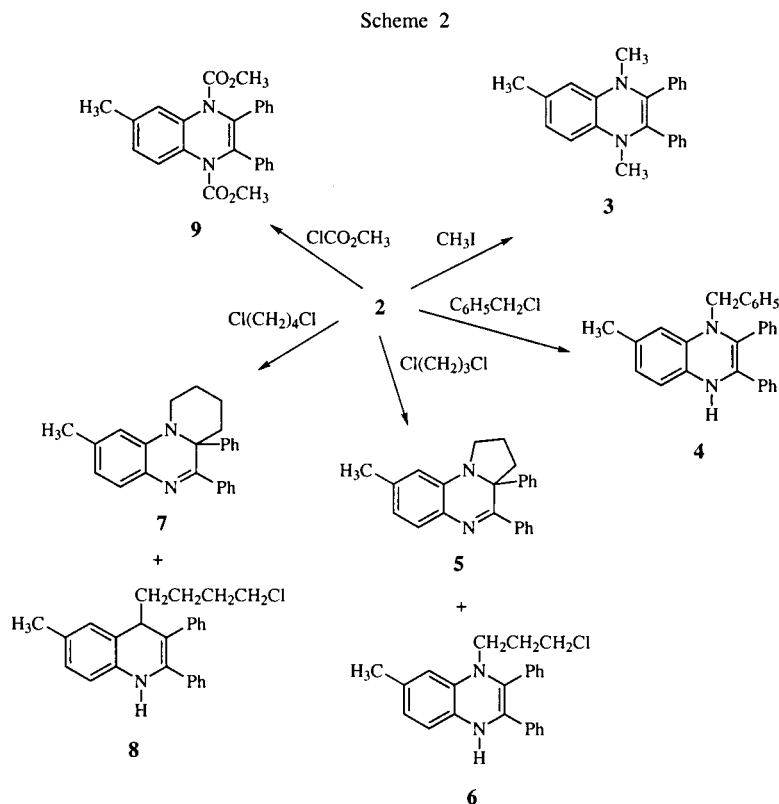
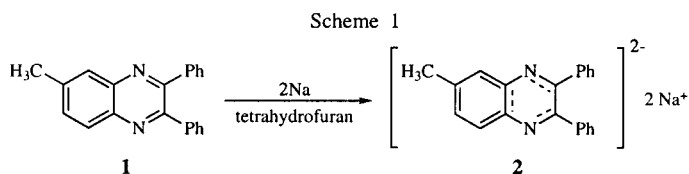
Yildiz Technical University, Department of Chemistry, 80270 Şişli, İstanbul, Turkey
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The reductive metallation of 6-methyl-2,3-diphenylquinoxaline **1** with sodium metal in tetrahydrofuran and inert atmosphere to a monomeric dianion **2** has been explored and the nucleophilicity of this disodium adduct was investigated with various alkylation and acylation reagents. An annulation of the pyrazine ring system was accomplished by treating the dianion with polymethylene chlorides, $\text{Cl}(\text{CH}_2)_n\text{Cl}$, $n = 3,4$.

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Dianions obtained by the reduction of $[4n+2]$ π electron compounds have a $4n\pi$ array of electrons and can, therefore, serve as model compounds for antiaromatic species, thus enabling discussion of the notion of antiaromaticity. On these grounds the effect of the heteroatom on the main characteristics of these charged systems, such as their paratropicity, charge delocalization and ion-pairing, seems interesting. The introduction of a heteroatom into the path of the electron delocalization of the charged system may increase the regioselectivity of their reactions (such as alkylation) and even change their chemistry. The study of π -conjugated charged systems especially the reductive metallation of heterocyclic systems can provide synthetically useful dihydro dianionic derivatives. Although many

carbocyclic systems were reduced by alkali metals to form their respective dianions, most of which were stable enough to be characterized by nmr, only few heterocyclic dianions are known [1,2]. Reduction of some heterocyclic compounds having carbon-nitrogen double bonds and conjugated π electron systems in aprotic solvents by alkali metals have been investigated by our research group in the last decade [3].



In this report, the reductive metalation of the quinoxaline ring is described, using 6-methyl-2,3-diphenylquinoxaline **1**, having conjugated alkene and azo functionalities with electron donating phenyl groups as the example. This compound was metalated by reduction with excess sodium in tetrahydrofuran under an argon atmosphere to form a deep colored solution of dianion **2**. The reactivity of this dianion was examined with several reagents.

Alkylation of dianion **2** with methyl iodide and benzyl chloride produced the 1,4-dihydro-1,4,6-trimethyl-2,3-diphenylquinoxaline **3** and 4-benzyl-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline **4**. The presence of the quaternary benzyl carbons was confirmed by ^1H nmr spectrum. Annulation of a five- and six-membered ring to the 1,2-positions of the pyrazine ring system was effected by alkylating of **2** with 1,3-dichloropropane and 1,4-dichlorobutane. These pyrrolidino- **5** and piperidino- **7** systems were performed through intramolecular Exo-tet ring closures in accordance with Baldwin's rules [4]. Also 4-(3-chloropropyl)-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline **6** and 4-(4-chlorobutyl)-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline **8** were obtained as the second products. In the case of 1,2-dichloroethane, attempts to annulate a four-membered ring were unsuccessful.

Acylation of dianion **2** with methyl chloroformate occurred on the negatively charged nitrogen with the formation of 1,4-dicarbomethoxy-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline **9** as the only isolated product in 89% yield.

In every experiment, some 6-methyl-2,3-diphenylquinoxaline **1** was recovered, probably, because of only partial reduction of **1** to **2**, or conversion of **2** to **1** by traces of the oxygen introduced into the system during the handling of the reaction reagents.

EXPERIMENTAL

Melting points were uncorrected and were measured in open capillaries with an Electrothermal IA 9100 melting point apparatus. Infrared (ir) spectra were recorded on a Philips PU 9714 spectrometer in potassium bromide pellets unless otherwise indicated. The nmr spectra were determined on a Varian 200 MHz Gemini in deuteriochloroform with tetramethylsilane (TMS, δ 0 ppm) as internal standard. Mass spectra were obtained with Shimadzu GC/MS QP 2000 A. Column chromatography was performed with silica gel 60 (70-230 mesh) purchased from E. Merck AG. Thin-layer chromatography (tlc) was effected with Eastman Kodak Chromatogram 13181 silica gel sheets with fluorescent indicator.

6-Methyl-2,3-diphenylquinoxaline was prepared from 4-methyl-1,2-phenyldiamine with 1,2-diphenylethanedione. Tetrahydrofuran [5] as purified by refluxing for at least 8 hours over lithium aluminum hydride under nitrogen, stored over lithium aluminum hydride, and when needed the solvent was refluxed for two hours and the required amount was redistilled

immediately before use. All reactions involving alkali-metal compounds were conducted in an atmosphere of purified and dried argon.

The reductive metallation of **1** on a preparative scale was performed in an argon-filled modified Schlenk tube as described in the literature [6]. Removal of weighed aliquots of the solution during the reaction between **1** and sodium in tetrahydrofuran, quenching the aliquots in 1:1 water/methanol, and titrating with standardized hydrochloric acid, demonstrated that formation of the deep violet solution of the dianion **2** was complete after 20 hours.

A detailed description of one experiment is given here to illustrate the procedures. All crude reaction products were examined by tlc using toluene as the developing solvent and compared with starting material **1** and the reagent in order to follow the progress of the reaction. The purification procedures and additional comments together with the ir, nmr, ms, and analytical data are given in each experiment.

General Procedure.

1,4-Dihydro-1,4,6-trimethyl-2,3-diphenylquinoxaline (**3**).

Dianion **2** was obtained from the reaction of 0.296 g (1 mmole) of **1** in 100 ml of tetrahydrofuran with freshly cut sodium metal (*ca.* 1 g) in a specially designed flask [7]. Under an argon atmosphere, the mixture was shaken about 20 hours and then the excess sodium was removed from the solution of **2**. After the solution was cooled to -78° , 0.283 g (2.0 mmoles) of methyl iodide was injected and stirring was continued at -78° for 3 hours. During the warming of the reaction mixture to the room temperature, the color changed from violet to green. After that, 1 ml of methanol was added to the mixture by injection. The flask was opened and the reaction mixture was diluted with water, extracted with diethyl ether (3 x 100 ml); the ethereal solution was dried over sodium sulfate and evaporated. The crude reaction product was chromatographed on silica gel. Elution of the column with toluene gave colorless needles, 0.205 g (63%), mp 175° , recrystallized from a mixture of 40-60° petroleum ether-diethyl ether (1:1); ir (potassium bromide): ν 3025 (=CH), 2940 (CH_3) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.50 (s, 3, CH_3), 2.75 (s, 3, CH_3), 2.93 (s, 3, CH_3), 7.12-7.63 (m, 13, phenyl protons); ms: m/z 326 (35), 311 (100), 296 (30).

Anal. Calcd. for $\text{C}_{23}\text{H}_{22}\text{N}_2$: C, 84.62; H, 6.79; N, 8.58. Found: C, 84.66; H, 6.81; N, 8.59.

4-Benzyl-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline (**4**).

Benzyl chloride (0.253 g, 2.0 mmoles) was added to the dianion **2** solution at -78° and the resulting solution stirred for two hours. The crude reaction product was isolated as described above and chromatographed on silica gel. Elution with toluene gave a colorless oil which was crystallized from a mixture of 40-60° petroleum ether-diethyl ether (1:1) as yellow crystals, 0.287 g (74%), mp 154° ; ir (potassium bromide): ν 3420 (NH), 3020 (=CH), 2900 (CH_2) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.45 (s, 3, CH_3), 4.55 (s, 2, CH_2), 7.26-7.53 (m, 18, phenyl protons); ms: m/z 388 (88), 325 (98), 297 (35), 201 (45).

Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{N}_2$: C, 86.56; H, 6.22; N, 7.21. Found: C, 86.58; H, 6.23; N, 7.18.

3a,4-Diphenyl-8-methyl-1,2,3,3a-tetrahydropyrrolo[1,2-*a*]quinoxaline (**5**).

The deep violet solution of **2** prepared from **1** (0.296 g, 1 mmole) was treated with 1,3-dichloropropane (0.226 g,

2.0 mmoles) at -78° in an argon atmosphere. Stirring was continued for 2 hours at this temperature. After being allowed to warm to room temperature, the color of the resulting solution changed from green to yellow. Water (ca. 1 ml) was injected through the septum and the mixture of two products was isolated as an oil by diethyl ether (3 x 100 ml) extraction. After purification by column chromatography (silica/toluene), evaporation of the eluate first gave **5** (0.267 g, 79%) as colorless plates, mp 130° ; ir (potassium bromide): ν 3040 (=CH), 2910 (CH_2) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.90-2.90 (m, 4, 2- CH_2 and 3- CH_2), 2.40 (s, 3, CH_3), 3.40-3.60 (m, 2, 1- CH_2), 7.10-7.65 (m, 13, phenyl protons); ^{13}C nmr (deuteriochloroform): δ 22 (C-2), 30 (C-3), 38 (C-1), 47 (C-3a), 111-130 (phenyl carbons); ms: m/z 338 (18), 261 (100), 234 (30).

Anal. Calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_2$: C, 85.17; H, 6.55; N, 8.27. Found: C, 85.21; H, 6.54; N, 8.28.

The second fraction was identified as 4-(3-chloropropyl)-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline **6**.

This compound (0.067 g, 18%) was obtained as bright colorless plates, mp 68° ; ir (potassium bromide): ν 3400 (NH), 3040 (=CH), 2910 (CH_2) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.13-2.39 (p, 2, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Cl}$), 2.61 (s, 3, CH_3), 3.39-3.70 (m, 4, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Cl}$), 7.30-7.96 (m, 13, phenyl protons), 7.81 (s, 1, NH); ms: m/z 374.5 (18), 353 (16), 337 (100), 310 (45).

Anal. Calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_2\text{Cl}$: C, 76.88; H, 6.18; N, 7.47. Found: C, 76.85; H, 5.74; N, 7.42.

4a,5-Diphenyl-9-methyl-1,2,3,4-tetrahydro-4aH-pyrido-[1,2-a]quinoxaline (**7**).

The preceding reaction was repeated with dianion **2** derived from **1** (0.296 g, 1 mmole) in tetrahydrofuran and 1,4-dichlorobutane (0.254 g, 2.0 mmoles) at -78° . The mixture of two products was isolated as an oil by diethyl ether (3 x 100 ml) extraction. After purification by column chromatography (silica gel-toluene), evaporation of the eluate first gave **7** (0.232 g, 66%) as a viscous oil which was crystallized from 40-60 $^{\circ}$ petroleum ether to afford bright colorless crystals, mp 76° ; ir (potassium bromide): ν 3040 (=CH), 2940 (CH_2) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.82-2.02 (m, 4, 3- CH_2 and 4- CH_2), 2.59 (s, 3, CH_3), 3.27-3.66 (m, 4, 2- CH_2 and 3- CH_2), 7.15-7.95 (m, 13, phenyl protons); ^{13}C nmr (deuteriochloroform): δ 28.16 (C-2), 29.31 (C-3), 31.90 (C-4a), 34.74 (C-4), 46.99 (C-1), 128.14-153.85 (phenyl carbons); ms: m/z 352 (100), 338 (94), 309 (66), 297 (36).

Anal. Calcd. for $\text{C}_{25}\text{H}_{24}\text{N}_2$: C, 85.19; H, 6.86; N, 7.95. Found: C, 85.21; H, 6.84; N, 7.96.

The second fraction was identified as 4-(4-chlorobutyl)-1,4-dihydro-6-methyl-2,3-diphenylquinoxaline **8**.

This compound (0.090 g, 23%) was obtained as bright colorless plates, mp 168° ; ir (potassium bromide): ν 3420 (NH), 3040 (=CH), 2910 (CH_2) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.70-1.94 (m, 4, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$), 2.55 (s, 3, CH_3), 3.24-3.27 (t, 2, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$), 3.31-3.65 (t, 2, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$), 7.30-7.57 (m, 13, phenyl protons), 7.66 (s, 1, NH); ms: m/z 388 (37), 374 (12), 351 (100), 337 (60), 323 (62), 309 (40).

Anal. Calcd. for $\text{C}_{25}\text{H}_{25}\text{N}_2\text{Cl}$: C, 77.19; H, 6.47; N, 7.20. Found: C, 77.21; H, 6.44; N, 7.21.

1,4-Bismethoxycarbonyl-1,4-dihydro-2,3-diphenyl-6-methylquinoxaline (**9**).

The general procedure applied to **2** by using methyl chloroformate (0.189 g, 2.0 mmoles) as the reagent gave the *N*-acylated product. Thus, **9** was obtained from the major eluent, (0.370 g, 89%), bright colorless crystals, mp 140° ; ν 3020 (=CH), 2940 (CH_3) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.45 (s, 3, CH_3), 3.60 (s, 3, N-COOCH₃), 3.71 (s, 3, N-COOCH₃), 7.12-7.63 (m, 13, phenyl protons); ms: m/z 414 (92), 355 (94), 341 (15), 323 (40), 311 (100).

Anal. Calcd. for $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_4$: C, 72.45; H, 5.35; N, 6.76. Found: C, 72.47; H, 5.31; N, 6.78.

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