REACTION OF SUBSTITUTED 2,3,4,5,10,11-HEXAHYDRO-3,3-DIMETHYL-11-PHENYL-1H-DIBENZ[b,e][1,4]DIAZEPIN-1-ONES WITH *m*-CHLOROPEROXYBENZOIC ACID

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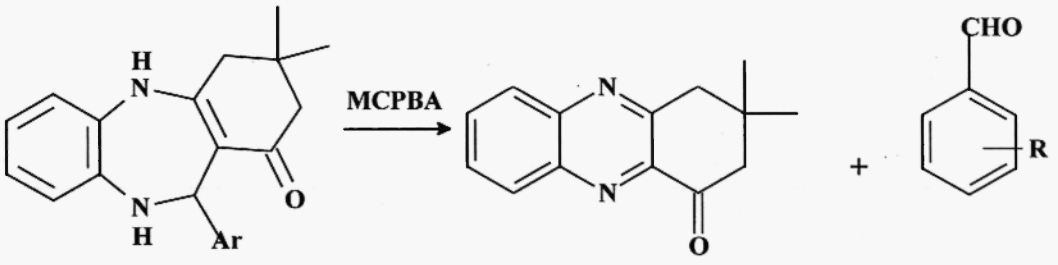
ABSTRACT: The title compounds (readily available from *o*-phenylendiamine, dimedone and substituted benzaldehydes) undergo facile rearrangement into 3,4-dihydrophenazin-1-(2H)-ones.

INTRODUCTION

Phenazine derivatives are of considerable importance as inhibitors, bactericides, dyes and insecticidal (2). Some methods to synthesize phenazines are available, and the most general is the Beirut reaction (3). A more specific cyclization reported by Miyano (4) involves reaction of 3-(*o*-nitroanilino)-2-cyclohexenone and sodium isopropoxide in isopropyl alcohol. As a part of a program directed toward the synthesis and spectral properties of heterocyclic derivatives with possible pharmacological activity we have explored the unknown reactivity of the title compounds **1a-g** under oxidation conditions using *m*-chloroperoxybenzoic acid and dichloromethane as solvent.



1a-g 2 3a-g

EXPERIMENTAL

Melting points were determined in Fisher-Jones melting point apparatus and are uncorrected. The IR spectra were determined in Perkin-Elmer 283-B and Nicolet FT-5SX spectrometer. The ^{1}H-NMR and ^{13}C-NMR were determined in Varian Gemini 200 and Varian-VXR-300S spectrometers

in deuteriochloroform solution containing tetramethylsilane in internal standard with chemical shifts (δ) expressed down field from TMS. Column chromatography was carried out on Merck silica gel 60F-254- Mass spectra were obtained with a Jeol-JMS-SX 102 A mass spectrometer.

Reaction of ortho and para-substituted dibenz[b,e][1,4]diazepin-1-ones 1a-g with *m*-chloroperoxybenzoic acid.

General procedure (R=*o*-NO_2)

A solution of 0.57 g (3.3 x 10^{-3} mole) of *m*-chloroperoxybenzoic acid in 10 ml dichloromethane was added dropwise to a cold solution (0-5 °C) of **1a** (0.3 g, 8.2 x 10^{-4} mole in 10 ml of dichloromethane. The reaction mixture was stirred at this temperature for ten minutes. The solution was then washed with saturated aqueous sodium bicarbonate (2x 20 ml) and water (2x 20 ml), dried (Na_2SO_4), and concentrated (rotatory evaporator). The oil obtained was then separated by column chromatography (*n*-hexane/ethyl acetate, 95:5) into **2a** [0.05 g; 26.7%; mp 169-170 °C, lit 173-175°C (6)] and 3a [0.038g, 30.4%; mp 98-99°C; lit (7a)].

Compound **1b** (R=H; 0.4 g, 12.6 x10^{-4} mole) was allowed to react according to the procedure described above. It gave also **2** compound in 47% (0.133 g) and **3b** (7b) in 37% (0.05g) yield, respectively.

Compound **1c** (R=*o*-Cl; 0.2 g, 5.7x10^{-4} mole) was allowed to react according to the procedure described above. It gave also **2** compound in 37% (0.133 g) and **3c** (7c) in 35% (0.02g) yield, respectively.

Compound **1d** (R=o-OMe; 0.3 g, 8.6 x10^{-4} mole) was allowed to react according to the procedure described above. It gave also **2** compound in 38% (0.133 g) and **3d** (7d) in 35% (0.05g) yield, respectively.

Compound **1e** (R=*p*-NO2; 0.3 g, 8.3 x10^{-4} mole) was allowed to react according to the procedure described above. It gave also **2** compound in 47% (0.09 g) and **3e** (7e) in 45% (0.05g) yield, respectively.

Compound **1f** (R=*p*-Cl; 0.3 g, 8.5x10^{-4} mole) was allowed to react according to the procedure described above. It gave also **2** compound in 37% (0.07 g) and **3f** (7f) in 35% (0.03g) yield, respectively.

Compound **1g** (R=*p*-OMe; 0.4 g, 11.4 x10^{-4} mole) was allowed to react according to the procedure described above. It gave also **2** compound in 27% (0.07 g) and **3g** (7g) in 35% (0.04g) yield, respectively.

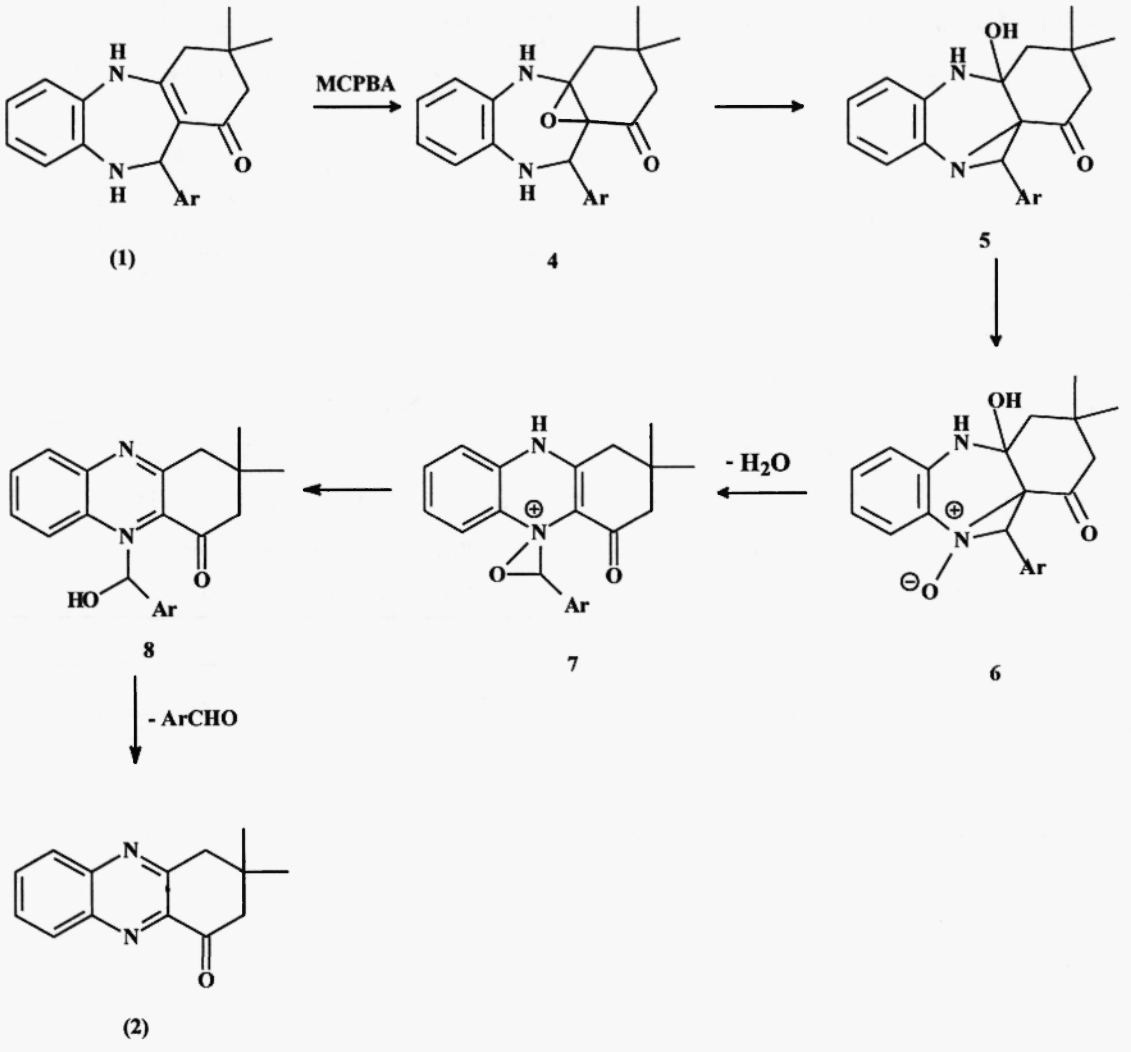
RESULTS AND DISCUSSION

Ortho and *para*-substituted dibenz[b,e][1,4]diazepin-1-ones (a=*o*-NO_2, **b**=H, **c**=*o*-Cl, **d**=o-OMe, e=*p*-NO_2, **f**=*p*-Cl and **g**= *p*-OMe) have been prepared following reported procedures. The identity of these compounds were confirmed by IR, ^1H and ^{13}C-NMR and mass spectral and comparison with the literature data (5).

In a typical procedure 11-(*ortho*-nitrophenyl) dibenz[b,e][1,4]diazepin-1-one **1a** and *m*-chloroperoxybenzoic acid (in a molar ratio 4:1) react at 0-5 °C in dicholoromethane to give **2** and **3a**. Structural assignment of **2** was made on spectroscopic grounds and they agree with the literature data (6). The general run of this reaction was tested with the *ortho* and *para*-phenyl substituted-1,4-benzodiazepin-1-ones **1b-g** that were treated as was compound **1a** and they also afforded **2** and **3b-g** as the only products. The identity of product **3a** was confirmed by NMR, IR, and MS spectra, mp and comparison with the literature data (7).

In a preliminary investigation of the influence of MCPBA concentration in this reaction the molar ratio substrate; MCPBA from 1: 4 to 1: 2 or 1: 3 was changed. In both cases starting material was recovered. This result implies that the MCPBA have to be 1: 4. A possible mechanism for the formation of 3,4-dihydrophenazine-1-(2H)-one **2** and **3a-g** from **1a-g** and aromatic aldehydes on reaction with *m*-chloroperoxybenzoic acid is outlined in scheme 1 (8). The proposed first step involves the formation of epoxide **4**; the cleavage of epoxide by intramolecular attack of N-10 gives the intermediate **5**. The N-oxide **6**, may be formed from the action of a second MCPBA molecule, loses a molecule of water to give **7**. The oxazidirine ring-opening reaction of **7** gives the dihydrophenazinol **8** that can lose a benzaldehyde molecule to yield **2.** Similar ring-contractions of 1,5-benzodiazepines have been reported (9). Further investigation of this mechanism is presently being carried out

Scheme 1



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