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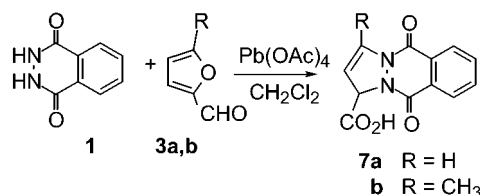
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ABSTRACT



Oxidation of phthalahydrazide (**1**) with lead tetraacetate in the presence of furfural (**3a**) in methylene chloride gives [5,6]benza-3a,7a-diaza-3-carboxylindane-4,7-dione-1-ene (**7a**) in 64% yield. 5-Methylfurfural (**3b**) also reacted similarly to give the product **7b** in 46% yield. Reaction of phthalazine-1,4-dione with thiophene-2-carboxaldehyde gives *N*-(2-formylthiophene)phthalahydrazide.

Diels–Alder type cycloadditions of furan and its derivatives are a well-known reaction.¹ Substituents are known to modify the dienophilic reactivity of the furan system, and especially amines,² hydrazones,³ and acetals⁴ are known to enhance the 4 + 2 addition. The oxabicyclo heptenes thus formed are stable compounds in many cases except for amine and hydrazone derivatives, where they cycloaromatize readily, giving substituted benzenes,^{2,3} and the more stable adducts can be aromatized with acid catalysts.

Diacyl diimides are reactive dienophiles in the 4 + 2 cycloaddition and useful in the preparation of 1,2-pyridazines. The cyclic derivatives of the diacyl diimides class are usually generated in situ by oxidation of the corresponding hydrazide

with *tert*-butyl hypochlorite⁵ or lead tetraacetate.⁶ Phthalazine-1,4-dione (**2**) is known to react with cyclopentadiene to give a stable adduct.⁷ Reaction of furan and 2,5-dimethylfuran with 3,6-pyridazinedione apparently gave⁸ the 4 + 2 adducts but decomposed during the isolations. Adducts from furan and dialkyl azodicarboxylates have also been reported.⁹ Sepulveda-Arques¹⁰ recently reported that the reaction of furfural with diethyl azodicarboxylate gives 6,7-diethoxycarbonyl-6,7-diaza-8-oxabicyclo[3.2.1]oct-3-en-2-one, after the rearrangement of the primary 4 + 2 adduct.

We have found that reaction of phthalahydrazide (**1**) with lead tetraacetate in the presence of excess furfural (**3a**) in

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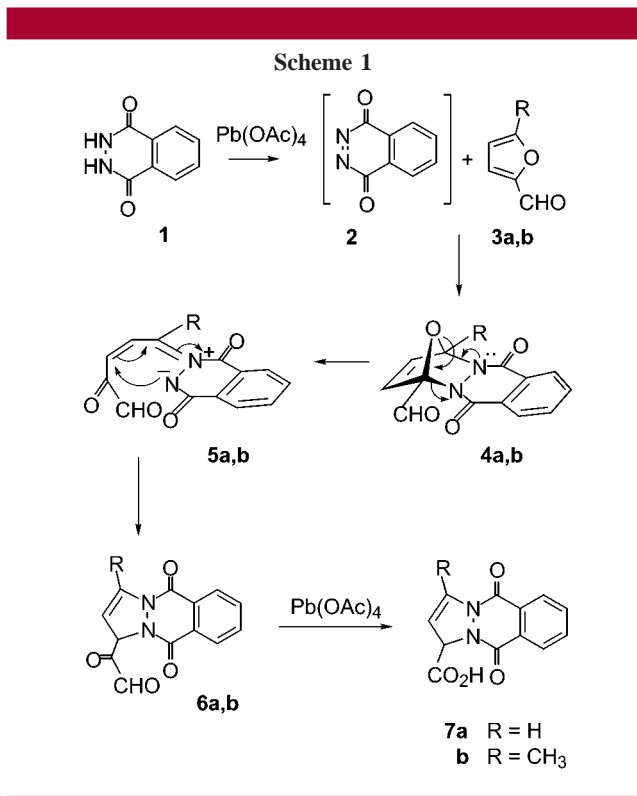
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methylene chloride gives a single compound.¹¹ The product isolated after passing the reaction mixture through a short column of neutral alumina and recrystallization of the residue was identified as [5,6]benza-3a,7a-diaza-3-carboxylindane-4,7-dione-1-ene (**7a**) using spectroscopic data.

¹H NMR spectra of **7a** shows two protons at δ 6.30 (1H, dd, $J = 1.6, 5.6$ Hz) and 7.31 (1H, dd, $J = 1.6, 5.6$ Hz); their coupling was established by an ¹H–¹H COSY experiment. The observed coupling constant of 5.6 Hz is too small for a vicinal H–C=C–H in a six-membered ring. A coupling constant in the region of 10–12 Hz is expected for a six-membered ring, and coupling constants of 4–6 Hz are typical¹² for a five-membered ring vicinal H–C=C–H system. A COSY experiment further showed that these two protons are coupled to the signal at δ 7.61 (1H, dd, $J = 1.6, 1.6$ Hz). It is interesting to note that the two vinylic protons at δ 6.30 and 7.31 have the same coupling constant as the C-3 proton (δ 7.61), which is 1.6 Hz. Similar observations are reported in the literature in the case of an analogous indene system.¹³ For example, two vinylic protons in indene-1-carboxylic acid¹³ are coupled to the C-1 proton (CH–COOH) with the same coupling constant of 2 Hz. Furthermore, a HETCOR spectrum showed that this proton at δ 7.61 is connected to the carbon at δ 86.1. The signal at 172.4 in the ¹³C NMR spectrum and the broad D₂O exchangeable signal at δ 10.5 in the proton NMR were assigned to a carboxylic acid group. On the basis of this spectral evidence, structure **7a** was proposed for the product. The unusually downfield ¹H NMR chemical shift of δ 7.61 for the C-3 proton is due to the deshielding effect of the neighboring nitrogen. An energy-minimized molecular model structure of **7a** as well as the reported X-ray structure of the phthalazine-1,4-dione–cyclopentadiene adduct⁷ show the planar nitrogens in this type of compounds. The formation of the product **7a** can be explained as shown in Scheme 1. Phthalazine-1,4-dione (**2**), generated in situ by the oxidation of **1**, reacts via 4 + 2 cycloaddition with furfural to give 2,3-diza-7-oxabicyclo derivative **4a**. The nitrogen lone pair promoted ring opening of the oxabicyclo system gives the zwitterionic intermediate **5a**, which will ring close again to a more stable 1,2-pyrazoline **6a**. Although this ring closure is a formal violation of Baldwin's rules,¹⁴ many examples are known¹⁵ with similar 5-endo-trig ring closure involving



iminium ions. The α -keto aldehyde function of intermediate **6a** is further oxidized by lead tetraacetate to give the product **7a**. Oxidative cleavage of 1,2-dicarbonyl compounds by lead tetraacetate is a known reaction,¹⁶ and Junculev¹⁷ has reported similar C–C bond cleavages resulting in carboxylic acids as products. The reaction carried out with only 1 equiv of lead tetraacetate failed to yield the intermediate product **6a** and gave only **7a** in reduced yield. The best yield for **7a** was obtained when 2 equiv of lead tetraacetate and an excess of furfuraldehyde (3–5 equiv) are used to trap the reactive phthalazine dione **2**.

5-Methylfurfural (**3b**) also reacted similarly with phthalazine-1,4-dione generated in situ to give the product **7b** in 46% yield (Scheme 1). Further, we have found that 2-furoic acid and methyl 2-furoate also react similarly with 1,4-phthalazinedione generated in situ to give [5,6]benza-3a-7a-diaza-3-carboxylindane-4,7-dione-1-ene (**7a**) in 21 and 26% yields, respectively.

Reaction of **7a** with 1 equiv of diazomethane in ether at 0 °C gave the methyl ester **8**. ¹H NMR of **8** shows a singlet for the methyl group at δ 3.88. Two vinylic protons appear at δ 6.41 (1H, dd, $J = 1.6, 5.6$ Hz) and 7.41 (1H, dd, $J = 1.7, 5.6$ Hz). The proton attached to C-3 is coupled to both these protons with approximately the same coupling constant and appears at δ 7.70 (1H, dd, $J = 1.6, 1.7$ Hz). The reaction of **7a** with a large excess of diazomethane (10 equiv) gave the product **9**. The product **9** is formed as a result of stereoselective dipolar cycloaddition of diazomethane to the C=C double bond of the ester **8** as shown in Scheme 2.

(11) **Experimental procedure for compound 7a:** Phthalaldehyde (324 mg, 2.0 mmol) and furfuraldehyde (576 mmol, 6.0 mmol) were dissolved in 30 mL of methylene chloride, and to this mixture was added lead tetracetate (886 mg, 4 mmol) in small portions during a period of 10 min, while the solution was kept under vigorous stirring at room temperature. The solution was further stirred for 20 min. The resulting mixture was passed through a short column of neutral alumina (2 \times 5 cm) and then the column was washed with 100 mL of methylene chloride. Combined eluent was concentrated under reduced pressure and the residue was recrystallized from ethyl acetate to give **7a** as a white powder, 312 mg, 64% yield, mp 221–3 °C.

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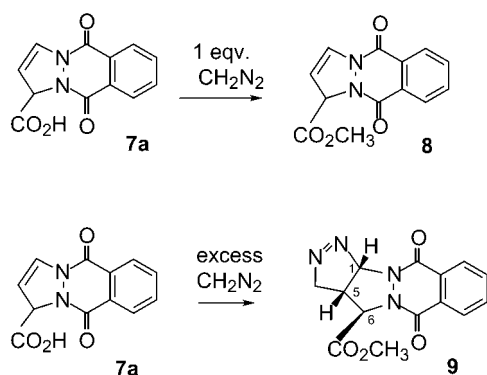
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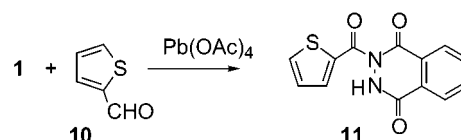
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Scheme 2



The methyl singlet in the ^1H NMR of compound **9** was observed at δ 4.00 and the relative configuration of the adduct was established by analysis of the ^1H NMR spectrum. Methylene protons in **9** are observed at δ 4.95 (1H, ddd, J = 2.6, 5.2, 19.0 Hz) and 5.10 (1H, ddd, J = 1.4, 9.5, 19.0 Hz). These two protons are coupled to the proton attached to C-5 with coupling constants 5.2 and 9.5 Hz, respectively. This C-5 proton is observed at δ 3.30 and is coupled to the C-6 proton at δ 6.85 with a coupling constant of 1.7 Hz. This small coupling indicates the *cis* relative configuration of the C-5 bridgehead proton and the carbomethoxy group as shown in compound **9**.

Scheme 3



Reaction of **1** with thiophene-2-carboxaldehyde (**10**) in the presence of lead tetraacetate in methylene chloride at room temperature gave a single product in 55% yield and was identified as **11** (Scheme 3). This product is formed by reaction of the phthalazine-1,4-dione at the formyl group. Similar reactions of thiophene-2-carboxaldehyde and *N*-methyl-3-formylindole have been reported with diethyl azodicarboxylate as well.¹⁰

In conclusion, these results present a novel rearrangement of the 2,3-diaza-7-oxabicycloheptene system and provide an efficient route to the [5,6]benza-3a,7a-diazaindane ring system.

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Supporting Information Available: Spectral data of compounds **7a**, **7b**, **8**, **9**, and **11**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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