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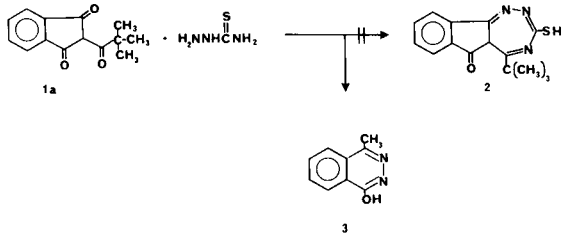
Received June 9, 1980

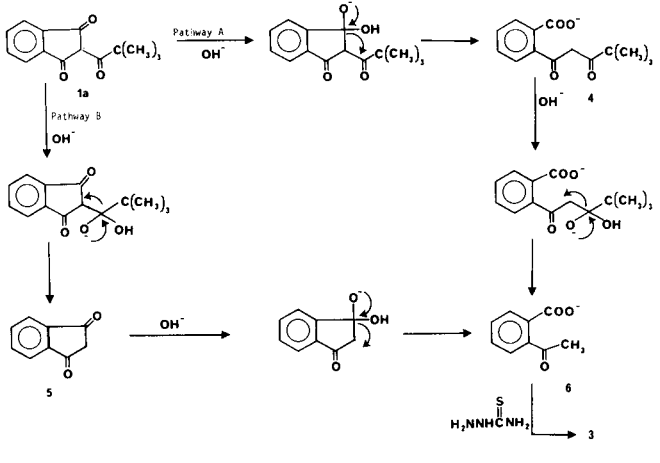
2-Pivaloyl-1,3-indandione reacts with thiosemicarbazide in aqueous base, through two successive retro-Claisen reactions, to yield 1-hydroxy-4-methylphthalazine. The mechanism of this reaction is described. Under similar conditions, 2-benzoyl and 2-acetyl-1,3-indandione, did not undergo the same reaction, a steric factor is considered.

J. Heterocyclic Chem., **17**, 1519 (1980).

While the reaction of 2-acyl-1,3-indandiones with hydrazines has been studied in considerable depth (2), the chemistry resulting from the combination of 2-acyl-1,3-indandiones with thiosemicarbazide has not previously been reported. Losse (3) reported that β-ketoesters are converted to heptriazinones upon reaction with thiosemicarbazide and therefore we applied the same procedure to 2-pivaloyl-1,3-indandione (**1**). Instead of obtaining the expected heptriazine (**2**), 1-hydroxy-4-methylphthalazine (**3**) resulted as the only identified product.

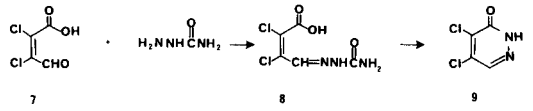


Two mechanisms can be proposed to account for formation of **3** (Scheme I). To test the proposed mechanisms, **1**

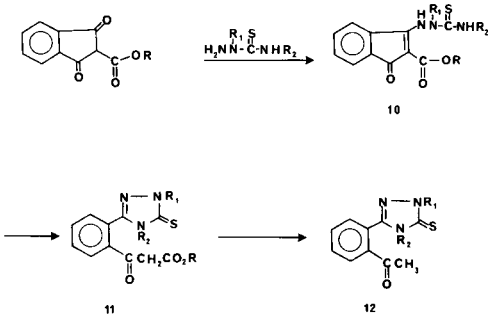


Scheme I

was heated with aqueous sodium carbonate and 2-acetylbenzoic acid (**6**) was recovered in 60-70% yield. Treatment of **6** with thiosemicarbazide resulted in formation of **3** in approximately 70% yield. It is presumed that this final step proceeds through the thiosemicarbazone in light of a similar reaction reported by Mowry (4) in which mucochloric acid (**7**) gives rise to the semicarbazone **8**, which upon heating decomposes to the pyridazone **9**.



When 1,3-indandione (**5**) was treated under the reaction conditions, a salt of **5** formed but none of the acid **6** was obtained These results support Pathway A, which involves two successive reto-Claisen reactions. Our results are similar to those reported by Mosher and Toothill (5) who obtained 3-(*o*-acetylphenyl)-Δ^2-1,2,4-triazoline-5-thiones through the intermediacy of **10** and **11** when 2-alkoxycarbonyl-1,3-diones were treated with thiosemicarbazide and aqueous base. This reaction presumably involving reto-Claisen reactions.

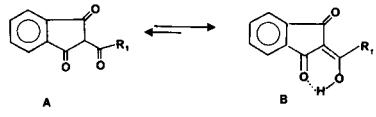


When the above reaction was attempted with 2-benzoyl-1,3-indandione or 2-acetyl-1,3-indandione we were surprised to find that the only identifiable material was recovered starting material. This is unexpected in that the nature of the acyl substituent was not expected to influence the course of the reaction. These results suggest that the size of the acyl substituent has a profound influence on the stability of the indandione ring in aqueous carbonate.

Work by Forsen, Nerenyi and Nilsson (6) suggests that 2-acyl-1,3-indandiones exist exclusively in the enol form (1B), and this has been confirmed by the single crystal

0022-152X/80/071519-02$02.25

X-ray diffraction studies of Csöregh and Norrestam (7) and Korp, Bernal and Lemke (8). A comparison of the crystal structure of **1a** with **1c** has shown small but significant differences in bond lengths and angles which are indicative of steric repulsion in the pivaloyl derivative (**1a**). In addition, H^1 nmr and ir spectra further substantiate the enolic nature of the 2-acyl-1,3-indandiones as well as differences between the derivatives (**1a-c**). The exchangeable proton on **1a** appears at δ 16 (w ½ 10 Hz), while for **1b** and **1c** the protons appear at δ 14.9 (w ½ 4 Hz) and 13.2 δ (w ½ 4 Hz), respectively. This is interpreted to mean that **1a** exhibits stronger H-bonding than either **1b** or **1c** (5). The peak half width (w ½) may also be a measure of the strength of H-bonding. The w ½ for **1a** was larger than for **1b** or **1c** in various solvents. The ir data likewise shows differences between the various derivatives; *i.e.*, the *t*-butyl "carbonyl" bands are found at 1700, 1640, and 1570 cm^{-1}, while the methyl derivative's "carbonyl" band appear at 1705, 1660, 1630, and 1590 cm^{-1}. The phenyl compound is complicated by additional aromatic absorption, but does appear similar to the methyl compound. The band at 1700 cm^{-1} has been assigned the non-bonded carbonyl, while 1630-1660 cm^{-1} band corresponds to the "chelated carbonyl". The 1590-1570 cm^{-1} region has been assigned the enolic double bond, which at lower frequency in **1a**, suggests a greater amount of extended resonance in this derivative.



A B

1

1 a $R_1 = C(CH_3)_3$
b $R_1 = C_6H_5$
c $R_1 = CH_3$

Using the previously reported crystal structure (8) and the solution nmr data, it can be postulated that the strain in the five-membered ring in **1a** can be relieved when the ring is opened by a base catalyzed retro-Claisen reaction. Because **1b** and **1c** are more acidic (weaker intramolecular H-bond), and possess less strain in the five membered ring due to nonrepulsive conformations, salt formation occurs which inhibits the base attack on a ring carbonyl carbon.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover unimelt apparatus and are uncorrected. The infrared spectra were recorded on a Perkin Elmer 283 as potassium bromide pellets. All ^1H nmr spectra were recorded on a Varian EM 360 spectrometer in deuteriochloroform using tetramethylsilane as an internal reference or DMSO-d_6. Chemical shifts are quoted in parts per million (s = singlet, m = multiplet).

1-Hydroxy-4-methylphthalazine (**3**).

A mixture of 2.3 g. (0.01 mole) of **1**, 1.0 g. (0.011 mole) of thiosemicarbazide, 2.1 g. (0.02 mole) of sodium carbonate (or 2.76 g., 0.02 mole of potassium carbonate) in 50 ml. of water was heated under reflux with stirring for 24 hours. Upon cooling a brown solid was present which was collected by filtration and dried giving 0.9 g. of product. The solid was recrystallized from ethyl acetate to give white crystals of **3**, m.p. 221-222° (lit. (8) m.p. 220-222°). Proof of structure consisted of independent synthesis of **3** from 2-acetylbenzoic acid and hydrazine and comparison of nmr spectra and chemical analysis; nmr (DMSO-d_6): δ 8.18-8.43 (m, 1), 7.93 (m, 3), 3.53 (s, 1), 2.67 (s, 3).

Anal. Calcd. for $C_9H_8N_2O$: C, 67.5; H, 5.0; N, 17.5. Found: C, 67.3; H, 5.1; N, 17.5.

An alternate two step procedure consists of heating under reflux a mixture of 2.3 g. (0.01 mole) of **1** and 2.1 g. (0.02 mole) of sodium carbonate in 50 ml. of water for 24 hours. Acidification of the reaction mixture with 18% hydrochloric acid, concentration *in vacuo*, and extraction with chloroform led to recovery of 2.2 g. of crude **6** after drying. The product was recrystallized from benzene to give 1.0 g. of 2-acetylbenzoic acid, m.p. 114.5°. The normal procedure does not involve isolation of **6**, but rather consists of addition of 1.0 g. (0.011 mole) of thiosemicarbazide followed by an additional heating under reflux for 48 hours. The reaction mixture was cooled and 1.2 g. of crude **3** was recovered, m.p. 221-222°.

1-Hydroxy-4-methylphthalazine (**3**).

A mixture of 1.64 g. (0.01 mole) of 2-acetylbenzoic acid, 1.82 g. (0.02 mole) of thiosemicarbazide, 3.72 g. (0.03 mole) of sodium carbonate monohydrate, and 50 ml. of water was heated under reflux with stirring for 20 hours. The solid which was present after cooling was collected by filtration and recrystallized from ethyl acetate to give 1.1 g. of **3**, m.p. 221-223°.

Acknowledgement.

Support of this research by the Robert A. Welch Foundation (Grant E-791) is gratefully acknowledged.

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