

Condensations of Brominated Products of *o*-Acetylbenzophenone with Several Primary Amines

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2-Bromo-3-phenylinden-1-one **2** reacted with phenylthiourea to produce 2-phenylimino-8-phenylindenol[1,2-*d*]thiazole (heteropentalene) **4** in moderate yield and bis-substituted-indenyl sulfide **5** in low yield. Whereas, from the reaction of **2** with thiourea or its methyl derivative only **5** was obtained in moderate yield. Another brominated compound, dibromoacetylbenzophenone and several primary amines afforded iminoindanone derivatives **6**.

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In previous study [1], attempts to brominate the acetyl group of *o*-acetylbenzophenone **1** produced 2-bromo-3-phenylinden-1-one **2**. When the bromination of **1** was carried out in the tetrachloromethane with bromine under ultraviolet irradiation, dibromoacetylbenzophenone **3** was newly obtained. This compound **3** afforded **2** by prolonged stirring under irradiation or by refluxing in acetic acid. The reaction of **2** with several primary amines allowed us to synthesize substituted indene oximes, indenothiazine and indenoazabenzothiazine derivatives [1,2]. In this paper, the reactions of **2** with thiourea derivatives and **3** with cyclohexylamine as well as aniline derivatives are reported.

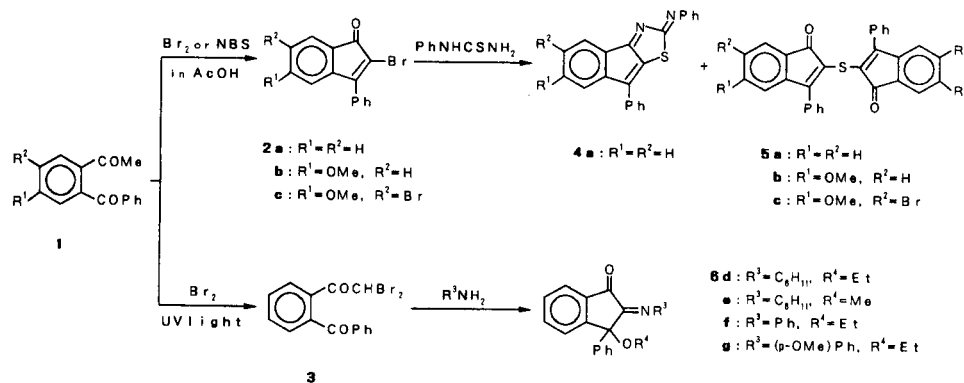
The reaction of **2a** with phenylthiourea in the presence of potassium acetate in ethanol under reflux produced 2-phenylimino-8-phenylindenol[1,2-*d*]thiazole **4a** in moderate yield and bis-2-(1-oxo-3-phenyl)indenyl sulfide **5a** in low yield. Whereas, in the case of 2-bromo-5-methoxy- (**2b**) and 2,6-dibromo-5-methoxy-3-phenylindene-1-ones (**2c**) with phenylthiourea under the above conditions none of the **4b** and **4c** were obtained, instead **5b** and **5c** were isolated in

moderate yield. The failure to obtain **4b** and **4c** presumably due to the substituents present on the benzene nucleus of the indenone derivatives. Furthermore, in the case of **2a-2c** with thiourea, only bisindenyl sulfide **5** and none of the corresponding 2-iminoindenthiazole (heteropentalene) **4** could be isolated.

To enhance the nucleophilicity of one of the amino groups by introducing methyl substitution [3] with the hope to obtain thiazole derivatives in good yields, the reaction of **2a** with methylthiourea was carried out under the above conditions. Surprisingly, in this case also only bisindenyl sulfide **5a** was obtained in 41% yield. Solvents and the reagents attempted for the analogous reactions are listed in the Experimental. Formation of **5a** was confirmed chemically by reacting **2a** with sodium sulfide.

The reaction of **3** with cyclohexylamine in ethanol at room temperature produced 2-cyclohexylimino-3-ethoxy-3-phenylindan-1-one **6d**. In the case of **3** with methylamine only decomposition products were obtained even in an ice-bath. From **3** and aromatic amines, aniline as well as *p*-anisidine refluxing in ethanol 3-ethoxy-2-phenylimino

Scheme 1



(6f) and 3-ethoxy-2-*p*-methoxyphenylimino-3-phenylindan-1-one (6g) were isolated respectively. These reactions are available for the preparation of several iminoindanones and differing from the condensations of **1** with primary amines affording isoindole derivatives [4].

EXPERIMENTAL

Melting points were determined on Yanaco micromelting point apparatus and are uncorrected. The infrared spectra were taken on a JASCO A-102 spectrometer using potassium bromide pellets and ultraviolet spectra were recorded with JASCO UVIDEK-505 in methanol solution. The ¹H and ¹³C nmr spectra were measured on a Varian Gemini-200 or Hitachi R-90 (¹H only) spectrometers, using tetramethylsilane as the internal standard. Mass spectra were obtained with Hitachi M-2000 spectrometer. For column chromatography, silica gel (Kieselgel 60, Merck, 70-30 mesh ASTM) was used. Elemental analyses were performed at the Elemental Analysis Center in Kyoto University.

o-Dibromoacetylbenzophenone (**3**).

To a tetrachloromethane solution (20 ml) of *o*-acetylbenzophenone (2 mmoles) a tetrachloromethane solution (2 ml) of bromine (2 mmoles) was added dropwise with stirring. The resulting mixture was stirred at room temperature under ultraviolet irradiation for 30 minutes. After evaporating the solvent under reduced pressure, the residue was chromatographed on a silica gel column using benzene-ethyl acetate (97:3) as the eluent. From the second fraction **3** was obtained in the yield of 68%. With prolonged stirring **3** [1] was isolated as a by-product.

Compound **3** had mp 168.8-170.2° (from ethanol); ir: 1725 cm⁻¹ (ν C=O); uv: λ max, nm (log ϵ), 294 (sh), 268 (sh), 262 (sh), 250 (3.83); ¹H nmr (deuteriochloroform): δ 8.01 (m, 1H), 7.82-7.75 (m, 1H), 7.67-7.58 (m, 2H), 7.33-7.15 (m, 5H), 3.58 (s, 1H, CHBr₂); ms: m/z 303/301 (M-Br)⁺, 302/300 (M-HBr)⁺.

Anal. Calcd. for C₁₅H₁₀Br₂O₂ (382.05): C, 47.15; H, 2.64; Br, 41.82. Found: C, 47.37; H, 2.59; Br, 41.59.

2-Phenylimino-8-phenylindeno[1,2-*d*]thiazole (**4a**) and Bis-2-(1-oxo-3-phenyl)indenyl Sulfide (**5a**).

A solution of **2a** (1 mmole), phenylthiourea (2 mmoles) and potassium acetate (3 mmoles) in ethanol was heated under reflux for three days. After evaporating the solvent, the residue was extracted with chloroform and was washed with water. The extract was chromatographed on a silica gel column using benzene as the eluent. From the first red fraction 7% of **5a** [1] and from the next violet fraction **4a** was obtained in 22% yield. Solvents and the reagents attempted for the analogous reactions were i) ethanol/acetic acid reflux; ii) Pyridine/potassium carbonate at 80°; iii) Methanol/potassium carbonate reflux; iv) Methanol/potassium hydroxide reflux: all the cases 30-40% of bisindenyl sulfide **5** was obtained.

Compound **4a** had mp 139-140° (needles from hexane-ethyl acetate); ir: 1605, 1560, 1480, 1440 cm⁻¹; uv: λ max, nm (log ϵ) 537 (3.73), 410 (sh, 3.71), 336 (4.16), 263 (4.67); ¹H nmr (deuteriochloroform): δ 7.87-7.06 (m, 14H, arom H); ms: m/z 338 (M⁺).

Anal. Calcd. for C₂₂H₁₄N₂S (338.43): C, 78.08; H, 4.17; N, 8.28. Found: C, 78.16; H, 4.00; N, 8.25.

Compound **5a** had mp 85-87° and the spectra (ir, uv and ¹H nmr) were identical with the authentic compound [1].

Bis-2-(1-oxo-5-methoxy-3-phenyl)indenyl sulfide (**5b**) was ob-

tained in 35% yield and had mp 213-215° (from ethanol); ir: 1700 cm⁻¹; uv: λ max, nm (log ϵ), 488 (3.53), 347 (4.08), 267 (4.72); ¹H nmr (deuteriochloroform): δ 3.80 (s, 6H, OCH₃), 6.50-6.61 (m, 4H), 7.33-7.62 (m, 12H); ms: m/z 502 (M⁺).

Anal. Calcd. for C₃₂H₂₂O₄S (502.59): C, 76.47; H, 4.41; S, 6.38. Found: C, 76.42; H, 4.45; S, 6.41.

Bis-2-(1-oxo-6-bromo-5-methoxy-3-phenyl)indenyl Sulfide (**5c**) was obtained in 42% yield and had mp 276-278° (from ethanol); ir: 1702, 1255 and 1025 cm⁻¹; uv: λ max, nm (log ϵ) 510 (3.58), 277 (4.78); ¹H nmr (deuteriochloroform): δ 3.89 (s, 6H, OCH₃), 6.64 (m, 2H), 7.43-7.61 (m, 12H); ms: m/z 658/660/662 (M⁺, 45/100/60%).

Anal. Calcd. for C₃₂H₂₀Br₂O₄S (660.38): C, 58.20; H, 3.05; S, 4.85. Found: C, 58.11; H, 2.82; S, 4.83.

2-Cyclohexylimino-3-ethoxy-3-phenylindan-1-one (**6d**).

To an ethanol solution (5 ml) of **3** (0.3 mmole), cyclohexylamine (5 mmoles) was added and the mixture was stirred at room temperature for 6 hours. After concentrating the mixture the residue was shaken with benzene. The extract was chromatographed on silica gel column using benzene as the eluent to give 25 mg (24%) of pure **6d** as colorless needles.

Compound **6d** had mp 130-131° (from ethanol); ir: 1675 (CO), 1072 (COC) cm⁻¹; uv: λ max, nm (log ϵ), 362 (sh), 358 (4.38), 258 (4.54), 231 (4.38); ¹H nmr (deuteriochloroform): δ 8.18 (m, 1H), 7.54-7.41 (m, 5H), 7.26 (m, 2H), 7.01 (m, 1H), 4.46 (q, 2H, J = 7.2 Hz, OCH₂CH₃), 2.34 (br, 2H, cyclohexyl), 1.82 (m, 5H, cyclohexyl), 1.59 (m, 1H, cyclohexyl), 1.52 (t, 3H, J = 7.2 Hz, OCH₂CH₃), 1.25 (m, 3H, cyclohexyl); ms: m/z 347 (M⁺), 265 (M-cyclohexyl + 1)⁺.

Anal. Calcd. for C₂₃H₂₃NO₂ (347.46): C, 79.51; H, 7.25; N, 4.03. Found: C, 79.27; H, 7.28; N, 4.01.

2-Cyclohexylimino-3-methoxy-3-phenylindan-1-one (**6e**).

From a methanol solution of **3** and cyclohexylamine **6e** was obtained in 19% yield as pure needles by treatment in a similar manner as described above.

Compound **6e** had mp 185-187° (from ethanol); ir: 1670 (CO), 1075 (COC) cm⁻¹; uv: λ max, nm (log ϵ), 362 (sh), 357 (4.24), 258 (4.41), 230 (4.24); ¹H nmr (deuteriochloroform): δ 8.15 (m, 1H), 7.54-7.42 (m, 5H), 7.26 (m, 2H), 7.01 (m, 1H), 3.99 (s, 3H, OCH₃), 2.34 (br, 1H, cyclohexyl), 1.82 (m, 5H, cyclohexyl), 1.59 (m, 2H, cyclohexyl), 1.25 (m, 3H, cyclohexyl); ms: m/z 333 (M⁺), 251 (M-cyclohexyl + 1)⁺.

Anal. Calcd. for C₂₂H₂₃NO₂ (333.43) + 1/10H₂O: C, 78.82; H, 6.98; N, 4.18. Found: C, 78.59; H, 6.93; N, 4.17.

3-Ethoxy-3-phenyl-2-phenyliminoindan-1-one (**6f**).

A mixture of **3** (0.4 mmole) and aniline (5 mmoles) in ethanol was refluxed for three days. Treating the mixture in a similar manner to that for **6d** using benzene-ethyl acetate (9:1) as the eluent, **6f** was obtained in 21% yield as a pure yellow crystalline substance.

Compound **6f** had mp 167-168°; ir: 1695 cm⁻¹; ¹H nmr (deuteriochloroform): δ 8.26 (m, 1H), 7.67 (m, 1H), 7.39-7.12 (m, 12H), 4.27 (q, 2H, J = 7.0 Hz, OCH₂CH₃), 1.30 (t, 3H, J = 7.0 Hz, OCH₂CH₃); ¹³C nmr (deuteriochloroform): δ 161.2 (CO), 139.3, 133.4, 130.6, 129.1, 128.6, 128.4, 128.3, 128.2, 127.8, 127.3, 126.2, 123.7, 122.9, 121.2, 120.7, 113.1, 59.6 (OCH₂), 14.5 (OCH₂CH₃); ms: m/z 341 (M⁺).

Anal. Calcd. for C₂₃H₁₉NO₂ (341.41) + 1/2H₂O: C, 78.83; H, 5.75; N, 4.00. Found: C, 78.79; H, 5.57; N, 3.85.

3-Ethoxy-2-*p*-methoxyphenylimino-3-phenylindan-1-one (**6g**).

The mixture of **3** and *p*-anisidine in ethanol was refluxed for 10 hours. By treatment of the resulting mixture as described above, **6g** was obtained in 20% yield as a pure pale yellow crystalline substance.

Compound **6g** had mp 221-223.5°; ir: 1695, 1610, 1255, 1045 cm^{-1} ; uv: λ max, nm (log ϵ), 355 (4.43), 254 (4.63), 227 (4.56); ^1H nmr (deuteriochloroform): δ 8.24 (m, 1H), 7.65 (m, 1H), 7.38-7.24 (m, 6H), 7.18-7.10 (m, 3H), 6.86 (m, 2H), 4.29 (q, 2H, $J = 7.2$ Hz, OCH_2CH_3), 3.82 (s, 3H, OCH_3), 1.33 (t, 3H, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C nmr (deuteriochloroform): δ 161.1 (CO), 159.1 (COCH_3), 133.5, 131.8, 130.4, 129.1, 128.8, 128.1, 127.6, 126.0, 123.5, 122.6, 121.0, 120.5, 113.3, 59.5 (OCH_2), 55.2 (OCH_3), 14.4 (OCH_2CH_3); ms: m/z 371 (M^+).

Anal. Calcd. for $\text{C}_{24}\text{H}_{21}\text{NO}_3$ (371.44): C, 77.61; H, 5.70; N, 3.77. Found: C, 77.47; H, 5.43; N, 3.79.

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