# Reactions of 2-Acyl-1,3-indandiones with Monosubstituted Hydrazines and Hydrazides

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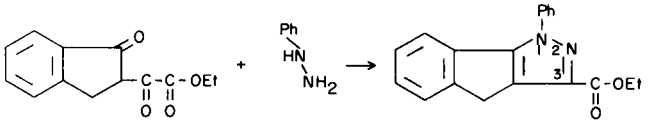
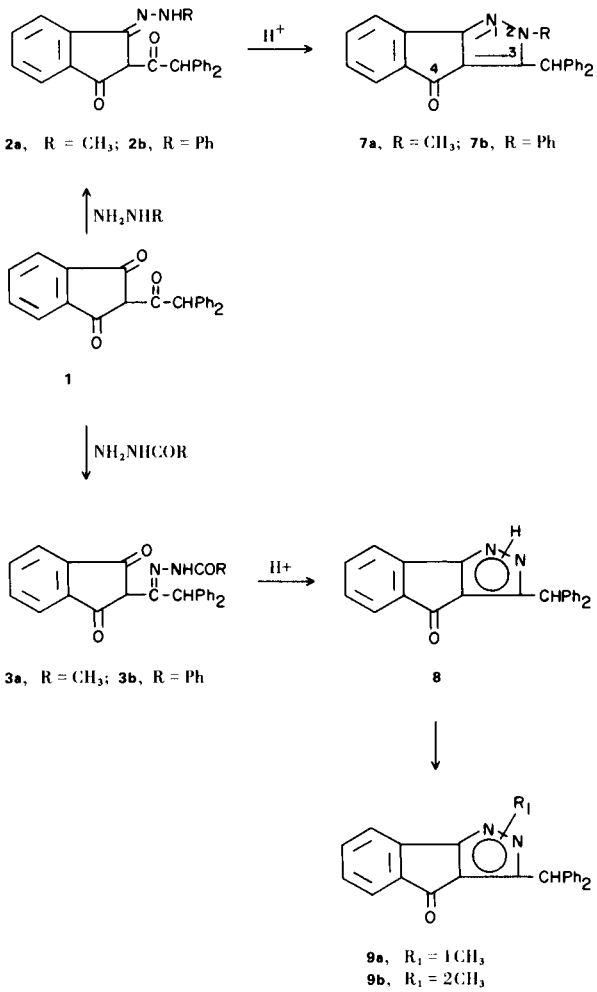
Methyl- and phenylhydrazines react with 2-(diphenylacetyl)-1,3-indandione (**1**) to yield respectively the 1-(methylhydrazone) and the 1-(phenylhydrazone) of 2-(diphenylacetyl)-1,3-indandione (**2a** and **2b**). In comparison, acetic and benzoic acid hydrazides react with **1** to give respectively the α-(acetylhydrazone) and the α-(benzoylhydrazone) of 2-(diphenylacetyl)-1,3-indandione (**3a** and **3b**). Cyclization of **2a** and **2b** gives 2,3-disubstituted indeno[1,2-*c*]pyrazol-4(2*H*)-ones (**7a** and **7b**). Cyclization of **3a** and **3b**, followed by methylation, gives 1-methyl- and 2-methyl-3-(diphenylmethyl)indeno[1,2-*c*]pyrazol-4(1 and 2*H*)-ones (**9a** and **9b**). 2-Isovaleryl-1,3-indandione reacts with phenylhydrazine to give directly 3-isobutyl-1-phenylindeno[1,2-*c*]-pyrazol-4(1*H*)-one (**10**).

In earlier work in this laboratory it was shown that hydrazine reacts with 2-acyl-1,3-indandiones to give monohydrazones (1) or indeno[1,2-*c*]pyrazol-4(1*H*)-ones (2), depending upon the structure of the acyl group. In the present study the reactions of monosubstituted hydrazines and hydrazides with 2-acyl-1,3-indandiones have been investigated.

Numerous examples are reported in the literature concerning the reactions of β-diketones with monosubstituted hydrazines to form the corresponding *N*-substituted pyrazoles (3). When the β-dicarbonyl compound is unsymmetrical, two isomeric pyrazoles are usually obtained if a substituted hydrazine is used. There is no record, however, of the reaction of 2-acyl-1,3-indandiones with substituted hydrazines or hydrazides. A closely related reference reports the reaction of ethyl 1-hydrindone-2-oxalate with phenylhydrazine giving a compound to which the structure of ethyl 1-phenylindeno[1,2-*c*]pyrazole-3-carboxylate was assigned without experimental support (4,5).



Methyl- and phenylhydrazines reacted with 2-(diphenylacetyl)-1,3-indandione (**1**) to give the corresponding monomethyl- and monophenylhydrazones with the hydrazono group on the indan ring (**2a** and **2b**), whereas the reactions of acetic and benzoic acid hydrazides with **1** yielded the monoacetyl- and monobenzoylhydrazones with the hydrazono group on the side chain (**3a** and **3b**).

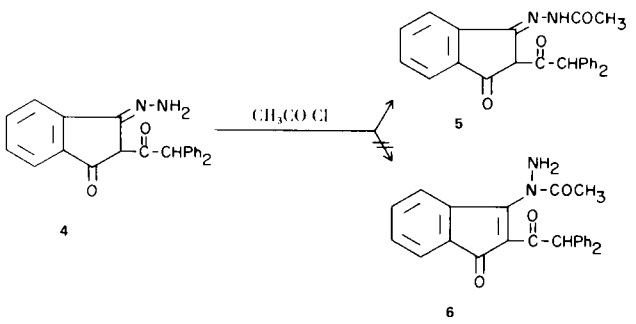


The methylhydrazone **2a** was more difficult to prepare than the phenylhydrazone **2b**. However, the reaction

conditions for preparing hydrazones **3a** and **3b** were the same.

The structural assignments were based on the similarities of the spectral and chemical properties of **2a** and **2b** with those of the known 1-hydrazone of 2-(diphenylacetyl)-1,3-indandione (**4**) and on the similarities of the properties of **3a** and **3b** with those of the known α-hydrazone of 2-acetyl-1,3-indandione (1).

As further evidence to support structures **3a** and **3b**, the isomer **5** was prepared from an authentic sample of **4** by the following route:




It was found that **5** possesses properties quite different from those of **3a** and therefore structure **5** was discounted. Structure **6**, another possible isomer from the reaction of **4** with acetyl chloride, was ruled out, since the infrared spectrum of **3a** showed a single N-H stretching band, indicating the absence of a primary amino group.

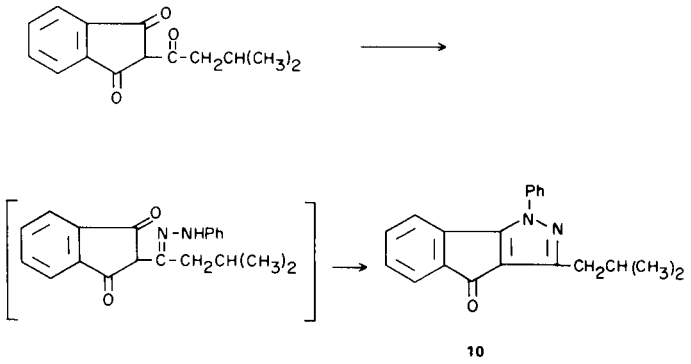
Cyclization of the monomethyl- and monophenylhydrazones **2a** and **2b**, in the presence of *p*-toluenesulfonic acid, gave the corresponding 2-substituted-3-(diphenylmethyl)indeno[1,2-*c*]pyrazol-4(2*H*)-ones (**7a** and **7b**). The structures of compounds **7a** and **7b** are based upon elemental analyses and spectral data.

Monoacetylhydrazone **3a**, as well as monobenzoylhydrazone **3b**, upon refluxing in acidic medium, cyclized to yield 3-(diphenylmethyl)indeno[1,2-*c*]pyrazol-4(1*H* or 2*H*)-one (**8**).

The cyclization of **3b** was more difficult than that of **3a**, requiring refluxing in 99% formic acid, instead of refluxing in methanol in the presence of *p*-toluenesulfonic acid.

Alkylation of the sodium salt of **8** with methyl iodide yielded a mixture of two methyl derivatives, easily separated by fractional crystallization. The major fraction (68% of the alkylated product) melted at 159° and the minor fraction (32%) melted at 143°. Structure **9b** was assigned to the lower melting compound, since it was found to be identical with an authentic sample of 3-(diphenylmethyl)-2-methylindeno[1,2-*c*]pyrazol-4-(2*H*)-one (**7a**), prepared from **2a** by the independent route described above. This structural proof of **9b** is obviously an indirect proof for the structure of **9a**, since the latter can have only the alternative structure.

The reaction of phenylhydrazine with 2-isovaleryl-1,3-indandione was also investigated. It was found that in this reaction, as in that between hydrazine and some 2-aroyl-1,3-indandiones reported by Braun and Mosher (2), a compound is formed for which structure **10** would appear to be the most probable, although our data do not completely rule out the 2-phenyl isomer structure.




The results of this study provide a basis for a general method for preparing 1 or 2 substituted indeno[1,2-*c*]-pyrazol-4(1*H* or 2*H*)-ones, from the monohydrazones of 2-acyl-1,3-indandiones, the substitution being determined by the structure of the hydrazone precursor.

Further studies are in progress on various aspects of this synthetic method and will be the subject of a later communication.

## EXPERIMENTAL (6)

**2-(Diphenylacetyl)-1,3-indandione, 1-methylhydrazone (2a).**

2-(Diphenylacetyl)-1,3-indandione (7) (1.0 g., 0.003 mole), dimethylformamide (10.0 ml.) and methylhydrazine (0.3 ml., 0.0056 mole) were immersed in an oil bath at 200° for exactly 1 minute. The red solution was then cooled to room temperature and water was added until the solution became cloudy. Sufficient methanol was then added to dissolve the precipitate and the clear solution was cooled in a freezer for 0.5 hour. The resulting precipitate was collected by filtration and recrystallized from alcohol-water mixture to give 0.41 g. (37%) of **2a**, as yellow fluorescent needles, m.p. 195°; ir 3350, 1680 and 1600 $cm^{-1}$. The infrared spectrum of 2-(diphenylacetyl)-1,3-indandione, 1-hydrazone shows the same peaks with some slight shifts to lower frequencies (3400-3200; 1650 and 1550 $cm^{-1}$). Compound **2a** does not give a positive Tollens test and does not form a red solution upon treatment with 10% aqueous sodium hydroxide. This behavior is identical to that shown by 2-(diphenylacetyl)-1,3-indandione, 1-hydrazone (1).

*Anal.* Calcd. for $C_{24}H_{20}N_2O_2$: C, 78.26; H, 5.43; N, 7.61. Found: C, 78.13; H, 5.61; N, 7.50.

2-(Diphenylacetyl)-1,3-indandione, 1-phenylhydrazone (**2b**).

A mixture of 2.0 g. (0.0056 mole) of **1**, 1.0 ml. of phenylhydrazine and 50 ml. of methanol was refluxed for 4 hours. The solution was concentrated to half volume, cooled in a refrigerator and the yellow precipitate was collected and recrystallized from methanol. An 81% yield (1.95 g.) of **2b** was obtained, as yellow fluorescent crystals, m.p. 173°. The ir spectrum was similar to that of **2a**. Compound **2b** does not give a positive Tollens test and does not form a red solution with 10% aqueous sodium hydroxide (1).

*Anal.* Calcd. for $C_{29}H_{22}N_2O_2$: C, 80.93; H, 5.12; N, 6.51. Found: C, 80.95; H, 5.22; N, 6.51.

2-(Diphenylacetyl)-1,3-indandione, α-acetylhydrazone (**3a**).

A mixture of acetic acid hydrazide (3.0 g.), compound **1** (5.0 g.) and chloroform (50 ml.) was refluxed for 2 hours. After removal of the solvent under reduced pressure, the residue was crystallized from methanol. A 73% yield (4.0 g.) of **3a** was obtained, as white crystals, m.p. 192°; λ max (methanol), mμ 207 (ε, 44,000), 295 (ε, 30,000), 337 (ε, 5,000); ir 3400, 1725 and 1700 $cm^{-1}$. It is not fluorescent and is very soluble in 10% aqueous sodium hydroxide giving a red solution. This behavior is characteristic of 2-acyl-1,3-indandione hydrazones, with the hydrazono group on the side chain (1).

*Anal.* Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.75; H, 5.05; N, 7.07. Found: C, 75.61; H, 5.04; N, 7.12.

2-(Diphenylacetyl)-1,3-indandione, α-benzoylhydrazone (**3b**).

A mixture of **1** (2.0 g.), an excess of benzoic acid hydrazide and chloroform (50 ml.) was refluxed for 2 hours. The red solution was evaporated to a small volume under reduced pressure, methanol was added and the mixture cooled in a refrigerator. The collected precipitate, recrystallized from 75:25 alcohol-chloroform mixture, gave 2.3 g. (85%) of **3b**, as yellow needles, m.p. 230°. The infrared spectrum of **3b** was in agreement with the structure.

*Anal.* Calcd. for $C_{30}H_{22}N_2O_3$: C, 78.60; H, 4.80; N, 6.11. Found: C, 78.89; H, 4.98; N, 6.57.

2-(Diphenylacetyl)-1,3-indandione, 1-acetylhydrazone (**5**).

A mixture of 2-(diphenylacetyl)-1,3-indandione 1-hydrazone (7) (1.0 g.), acetyl chloride (1 ml.) and chloroform (30 ml.) was refluxed for 10 minutes, or until the solution turned red. After removal of the solvent under reduced pressure, the residue was washed with carbon tetrachloride and then crystallized from methanol to give 0.66 g. (60%) of **5**, as yellowish fluorescent crystals, m.p. 215°; λ max (methanol), 210 mμ (ε, 16,000), 280 (ε, 13,000), 292 (ε, 14,600) and 350 (ε, 6,000). Compound **5** is slightly soluble in 10% aqueous sodium hydroxide giving a yellow solution.

*Anal.* Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.75; H, 5.05; N, 7.07. Found: C, 75.58; H, 5.05; N, 7.12.

3-(Diphenylmethyl)-2-methylindeno[1,2-*c*]pyrazol-4(2*H*)-one (**7a**).

A mixture of **2a** (0.3 g.), *p*-toluenesulfonic acid (0.3 g.) and methanol (30 ml.) was refluxed for 48 hours. The solution was filtered to remove insoluble matter and then decolorized with charcoal. The filtrate was evaporated to half volume, water was added to the cloud point and the mixture allowed to cool in a refrigerator overnight. A 70% yield (0.2 g.) of **7a** was obtained, as white crystals, m.p. 143° and greenish-yellow fluorescence; ir 1700, 1600 and a strong singlet at 900 $cm^{-1}$; nmr shows aromatic peaks at 7.1-7.6 ppm, in addition to chemical shifts at 5.48 ppm for Ph-CH-Ph and at 3.67 ppm for $CH_3$.

*Anal.* Calcd. for $C_{24}H_{18}N_2O$: C, 82.28; H, 5.14; N, 8.00. Found: C, 82.44; H, 5.44; N, 7.53.

3-(Diphenylmethyl)-2-phenylindeno[1,2-*c*]pyrazol-4(2*H*)-one (**7b**).

A mixture of **2b** (1.0 g.), catalytic amounts of *p*-toluenesulfonic acid and ethanol (50 ml.) was refluxed for 2 days. The solution was evaporated to half volume under reduced pressure and allowed to stand at room temperature for 1 day. The resulting precipitate, recrystallized from ethanol, gave 0.70 g. (73%) of **7b**, as faintly yellow crystals, m.p. 170°. The infrared spectrum of **7b** was in agreement with the structure.

*Anal.* Calcd. for $C_{29}H_{20}N_2O$: C, 84.46; H, 4.85; N, 6.79. Found: C, 84.22; H, 4.73; N, 6.53.

3-(Diphenylmethyl)indeno[1,2-*c*]pyrazol-4(1*H* or 2*H*)-one (**8**). From **3a**.

A mixture of **3a** (1.0 g.), catalytic amounts of *p*-toluenesulfonic acid and methanol (50 ml.) was refluxed with stirring for 24 hours, allowed to cool to room temperature and diluted with water to the cloud point. The precipitate was collected and recrystallized from methanol-water mixture to give 0.67 g. (80%) of faintly yellow crystals, m.p. 180°; ir 3100-3000, 1700 and 1600 $cm^{-1}$.

From **3b**.

A mixture of **3b** (1.0 g.) and 99% formic acid (30 ml.) was refluxed for 2 hours. The red solution was cooled to room temperature, diluted with water and the precipitate collected, washed with water, dried and recrystallized to give faintly yellow crystals, m.p. 180°; the ir spectrum was identical with that of the compound prepared from **3a**.

*Anal.* Calcd. for $C_{23}H_{16}N_2O$: C, 82.14; H, 4.76; N, 8.33. Found: C, 81.67; H, 4.73; N, 8.33.

1-Methyl- and 2-Methyl-3-(diphenylmethyl)indeno[1,2-*c*]pyrazol-4(1*H* and 2*H*)-ones (**9a** and **9b**).

A mixture of 0.50 g. (0.0014 mole) of the sodium salts of **8** (prepared by mixing at room temperature equivalent amounts of **8** and sodium methoxide in 20 ml. methanol, evaporating to dryness under reduced pressure and drying the residue under vacuum for 12 hours) an excess of methyl iodide and methanol (30 ml.) was refluxed for 5 hours. The solution was evaporated to half volume and cooled overnight in a refrigerator. The resulting precipitate was collected and recrystallized from alcohol-water mixture to give 0.29 g. (68% of the alkylated product) of **9a**, as crystals of m.p. 159°; ir 1700, 1600 and a doublet at 880 $cm^{-1}$; nmr shows aromatic peaks at 7.1-7.6 ppm, in addition to the chemical shifts at 5.57 ppm for the methynyl proton PhCHPh and at 3.9 for the methyl protons.

*Anal.* Calcd. for $C_{24}H_{18}N_2O$: C, 82.28; H, 5.14; N, 8.00. Found: C, 82.24; H, 5.22; N, 7.73.

The filtrate was diluted with water and the resulting precipitate collected to give 0.13 g. (32% of the alkylated product) of **9b**, as greenish-yellow crystals, m.p. 143°. The identity of this compound with **7a** was established by infrared and nmr spectra.

*Anal.* Calcd. for $C_{24}H_{18}N_2O$: C, 82.28; H, 5.14; N, 8.00. Found: C, 82.24; H, 5.22; N, 7.73.

3-Isobutyl-1-phenylindeno[1,2-*c*]pyrazol-4(1*H*)-one (**10**).

A mixture of 2-isovaleryl-1,3-indandione (8) (1.0 g., 0.0043 mole), phenylhydrazine (1.1 g.), catalytic amounts of *p*-toluenesulfonic acid and ethanol (30 ml.) was refluxed for 2 days. The solution was cooled in a refrigerator for 2-3 hours. The precipitate was recrystallized from alcohol to give 0.91 g. (70%) of **10**, as yellow fluorescent needles, m.p. 169°. The infrared spectrum of

**10** was in agreement with the structure.

*Anal.* Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.24; H, 6.21; N, 8.95.

Acknowledgment.

We gratefully acknowledge the valuable assistance of Dr. Mario F. Sartori in connection with this research.

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Received January 9, 1970 Newark, Delaware 19711