

3-Cycloalkyl- and 3-Heterocyclic Substituted Indeno[1,2-c]pyrazol-4(1H)ones

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As a continuation of our earlier work on the reaction of 2-alkanoyl and 2-arylcarbonyl-1,3-indandiones with hydrazine (1,2), we report the results of the reaction of 2-cycloalkylcarbonyl-1,3-indandiones and of their heterocyclic analogs (**1a-j**) with hydrazine.

The indandiones (**1a-j**) were prepared by the sodium methoxide-catalyzed condensation of dimethyl phthalate with the appropriate methyl ketone according to the procedure described by Kilgore, Ford and Wolfe for preparing compound **1d** (3). In some instances, sodium hydride was used in place of sodium methoxide as the catalyst. The structures of the new indandiones **1** are based on the elemental analyses and the similarities of their infrared spectra with those of the known indandiones **1a** and **1d**.

Condensation of equimolar quantities of compounds **1** with hydrazine hydrate in boiling ethanol gave the 3-substituted indeno[1,2-c]pyrazol-4(1H)ones (**2a-h**) in yields varying from 16 to 88%. Presumably first the hydrazine adds to the side chain carbonyl or to one of the

structures. The infrared spectra are consistent with the structures assigned. A shift of the carbonyl bands to lower frequencies is observed when R in compounds **2** is changed from alicyclic to heterocyclic. The hydrazones of compounds **2** were obtained by reacting one mole of compounds **1** with 2.5 moles of anhydrous hydrazine in refluxing ethanol. These compounds are white crystalline products, which decompose on heating to form the corresponding azines. However, if heated rapidly they melt before decomposing.

Treatment of indandiones **1** with a large excess of hydrazine hydrate in boiling ethanol gave the corresponding 3-substituted 1,4-dihydroindeno[1,2-c]pyrazoles (**3**). This unusual reaction, in which the catalyst used in the Wolff-Kishner reduction is omitted, is not of general application. The indandiones **1b** (R = cyclobutyl), **1d** (R = cyclohexyl) and **1i** (R = 2-pyrrolyl) did not form the expected indenopyrazoles **3b**, **3d** and **3g**, but **1b** and **1d** gave the corresponding indenopyrazolone hydrazones and **1i** formed a highly complex yellow solid, which could not be recrystallized or chromatographed. The indenopyrazoles **3b**, **3d** and **3g** were obtained, however, when the indandiones **1b**, **1d** and **1i** were treated with hydrazine and potassium hydroxide under the conditions of the Wolff and Kishner reduction.

EXPERIMENTAL

Melting points are uncorrected. The infrared spectra were taken on a Baird Model B. recording spectrophotometer, using potassium bromide pellets, except for compound **1f** where sodium chloride plates were used. Elemental analyses were performed by Dr. A. Bernhardt, Microanalytisches Laboratorium, Max Planck Institute für Kohlenforschung, Mülheim (Ruhr), West Germany.

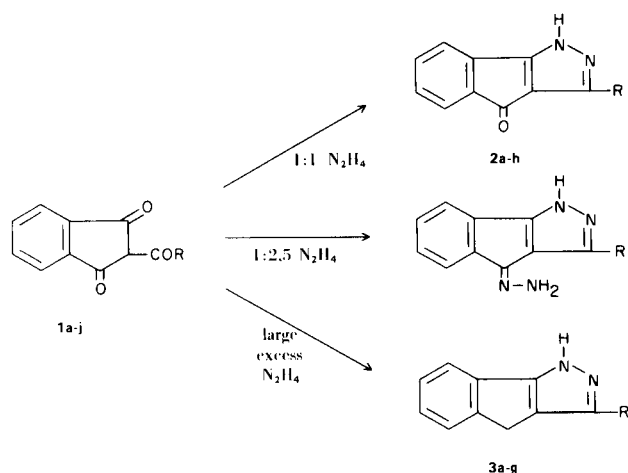
2-Cycloalkyl Methyl Ketones and their Heterocyclic Analogs.

The following compounds were prepared by previously described methods: cyclobutyl- (4), cyclopentyl- (5), cycloheptyl- (6), cyclooctyl- (7), 3-thienyl- (8), 2-pyrrolyl- (9) and 2-picoly- (10) methyl ketones.

2-Cycloalkylcarbonyl-1,3-indandiones and their Heterocyclic Analogs (**1a-j**).

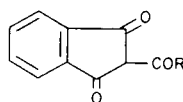
Method A.

The following general procedure was used: a solution of the



indan carbonyls, depending upon the size and the electronic properties of the radical R of compounds **1**, forming the corresponding monohydrazones which then ring close to yield **2a-h**. No attempts have been made to isolate the intermediate monohydrazones or to determine their struc-

Table I
2-Cycloalkylcarbonyl-1,3-indandiones and their Heterocyclic Analogs (1a-j)



Compound	R	Method Preparation	Yield %	M.p., °C	Recryst. Solvent
1a	cyclopropyl	A	26	128-129 (a)	MeOH
b	cyclobutyl	A	4	215-216	EtOH-2-Butanone
c	cyclopentyl	A	2	163-164	EtOH-2-Butanone
d	cyclohexyl	B	15	77-79 (b)	EtOH
e	cycloheptyl	A	1	192.5-193	EtOH-2-Butanone
f	cyclooctyl	B	20	oil	-----
g	2-thienyl	A	17	145 (c)	EtOH-2-Butanone
h	3-thienyl	B	9.3	130.5-131	EtOH
i	2-pyrrolyl	A	36	152.5-153	MeOH-Benzene
j	2-picolyl	B	2	195-196 (d)	EtOH-CHCl ₃

(a) Reported 132-134° (12). (b) Reported 79-80° (3). (c) M.p. not reported (13). (d) Sealed tube melting point.

Table IA
Elemental Analyses of Compounds Listed in Table I

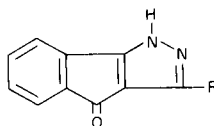
Compound	Formula	% C		% H		% N		% S	
		Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
1a	C ₁₃ H ₁₀ O ₃	----	----	---	---	---	---	----	----
b	C ₁₄ H ₁₂ O ₃	73.67	73.77	5.30	5.58	---	---	----	----
c	C ₁₅ H ₁₄ O ₃	74.36	74.77	5.82	5.86	---	---	----	----
d	C ₁₆ H ₁₆ O ₃	----	----	---	---	---	---	----	----
e	C ₁₇ H ₁₈ O ₃	75.53	75.70	6.71	6.81	---	---	----	----
f	C ₁₈ H ₂₀ O ₃ (a)	----	----	---	---	---	---	----	----
g	C ₁₄ H ₈ O ₃ S	----	----	---	---	---	---	----	----
h	C ₁₄ H ₈ O ₃ S	65.61	65.89	3.15	3.47	---	---	12.51	12.33
i	C ₁₄ H ₉ NO ₃	70.29	69.97	3.79	3.97	5.86	5.98	----	----
j	C ₁₆ H ₁₁ NO ₃	72.44	72.20	4.18	4.46	---	---	----	----

(a) This compound was not easily purified for analysis. However, analyses of the hydrazone of 2e, obtained from 1f (see Table IIB), agree with structure 1f.

appropriate methyl ketone (0.5 mole) and dimethyl phthalate (0.5 mole) in anhydrous benzene (100 ml.) was added to a stirred dispersion of sodium hydride (50% in mineral oil, 24 g., 0.5 mole) in anhydrous benzene (500 ml.) and the mixture heated at reflux for 4 hours. The methanol was removed by azeotropic distillation and

the residual reddish reaction mixture cooled in an ice bath. The precipitate was collected, washed, dried and dissolved in water (500 ml.). The red solution acidified with concentrated hydrochloric acid gave a yellow product, which was recrystallized from a suitable solvent (see Table I).

Table II

3-Substituted Indeno[1,2-*c*]pyrazol-4(1*H*)ones (**2a-h**) and their Hydrazones

Compound	R	Yield %	M. p., °C.	Recryst. Solvent	Hydrazone M. p., °C.	Recryst. Solvent	Yield %
2a	cyclopropyl	82	222-223	MeOH	246-248	EtOH	91
b	cyclobutyl	75	160-161	EtOH-H ₂ O	227-228	EtOH	68
c	cyclopentyl	84	113-114	MeOH-H ₂ O	234-235	MeOH	64
d	cyclohexyl	40	156-157	EtOH	215-216	MeOH	79
e	cyclooctyl	16	338-340 (a)	EtOH	220	EtOH	62
f	2-thienyl	79	248 (subl)	MeOH	227	EtOH- <i>t</i> -BuOH	43
g	3-thienyl	88	240-241	EtOH	-----	-----	--
h	2-pyrrolyl	62	265-267 (dec)	EtOH	-----	-----	--

(a) Melting point of the 2,4-dinitrophenylhydrazone of **2e**.

Table II A

Elemental Analyses of Compounds Listed in Table II
3-Substituted Indeno[1,2-*c*]pyrazol-4(1*H*)ones (**2a-h**)

Compound	R	Formula	% C		% H		% N	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
2a	cyclopropyl	C ₁₃ H ₁₀ N ₂ O	74.27	74.45	4.79	5.09	13.33	13.62
b	cyclobutyl	C ₁₄ H ₁₂ N ₂ O	74.98	74.91	5.40	5.38	12.49	12.49
c	cyclopentyl	C ₁₅ H ₁₄ N ₂ O	75.60	75.72	5.92	6.07	11.76	11.81
d	cyclohexyl	C ₁₆ H ₁₆ N ₂ O	76.16	75.83	6.39	6.24	-----	-----
e	cyclooctyl (a)	C ₁₈ H ₂₀ N ₂ O	62.59	62.34	5.25	5.31	18.75	18.21
f	2-thienyl (b)	C ₁₄ H ₈ N ₂ OS	66.65	66.78	3.19	3.23	11.11	10.97
g	3-thienyl (c)	C ₁₄ H ₈ N ₂ OS	66.65	66.48	3.19	3.07	11.11	11.18
h	2-pyrrolyl	C ₁₄ H ₉ N ₃ O	71.47	71.17	3.86	4.17	17.87	17.65

(a) Analyses of the 2,4-dinitrophenylhydrazone of **2e**. (b) % S: Calcd. 12.71. Found 12.71. (c) % S: Calcd. 12.71. Found 12.52.

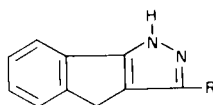
Table II B

Elemental Analyses of Compounds Listed in Table II Hydrazones of **2a-e**

Compound	R	Formula	% C		% H		% N	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
2a	cyclopropyl	C ₁₃ H ₁₂ N ₄	69.92	69.51	5.39	5.22	24.99	25.25
b	cyclobutyl	C ₁₄ H ₁₄ N ₄	70.56	71.00	5.92	5.81	23.52	23.17
c	cyclopentyl	C ₁₅ H ₁₆ N ₄	-----	-----	---	---	22.21	22.09
d	cyclohexyl	C ₁₆ H ₁₈ N ₄	72.15	71.81	6.81	6.63	21.04	21.22
e	cyclooctyl	C ₁₈ H ₂₂ N ₄	73.43	73.25	7.53	7.65	19.03	18.92
f	2-thienyl	C ₁₄ H ₁₀ N ₄ S (a)	63.13	63.05	3.78	3.92	21.04	21.00

(a) % S: Calcd. 12.04. Found 11.82.

Table III

3-Substituted 1,4-Dihydroindeno[1,2-*c*]pyrazoles (**3a-g**)

Compound	R	Method Preparation	Yield %	M. p. °C	Recryst. Solvent
3a	cyclopropyl	A	69	182-183	MeOH
b	cyclobutyl	B	72	143-144	EtOH-H ₂ O
c	cyclopentyl	A	82	139-140	MeOH
d	cyclohexyl	B	64	157-158	EtOH
e	2-thienyl	A	45	219-220	EtOH
f	3-thienyl	A	53	223-224	EtOH
g	2-pyrrolyl	B	22	232-234	EtOH

Table IIIA

Elemental Analyses of Compounds Listed in Table III

Compound	R	Formula	% C		% H		% N	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
3a	cyclopropyl	C ₁₃ H ₁₂ N ₂	79.56	79.35	6.16	6.18	14.28	14.28
b	cyclobutyl	C ₁₄ H ₁₄ N ₂	79.96	79.42	6.71	6.63	13.33	13.52
c	cyclopentyl	C ₁₅ H ₁₆ N ₂	80.32	80.15	7.19	7.07	12.49	12.58
d	cyclohexyl	C ₁₆ H ₁₈ N ₂	80.63	80.55	7.61	7.67	11.75	11.59
e	2-thienyl (a)	C ₁₄ H ₁₀ N ₂ S	----	----	---	---	11.76	11.32
f	3-thienyl (b)	C ₁₄ H ₁₀ N ₂ S	70.56	70.35	4.23	4.05	----	----
g	2-pyrrolyl	C ₁₄ H ₁₁ N ₃	76.02	76.21	4.57	4.62	19.08	18.91

(a) % S: Calcd. 13.46. Found 13.08. (b) % S: Calcd. 13.46. Found 13.58.

Method B.

The general procedure used is illustrated by the synthesis of 2-(3-thienyl)-1,3-indandione (**1h**). A solution of methyl 3-thienyl ketone (14 g., 0.111 mole) and dimethyl phthalate (22 g., 0.0111 mole) in anhydrous benzene (125 ml.) was added slowly to a solution of sodium methoxide (6.0 g.) in anhydrous benzene (125 ml.) and the mixture worked up as in method A with the exception that before acidification the red solution was extracted with ether. The gummy precipitate obtained upon acidification of the aqueous layer and cooling was chromatographed (chloroform as eluent) to give 2.65 g. of **1h**, as yellow crystals.

The yields and melting points of compounds **1a-j** are listed in Table I. The infrared spectra in the region between 1800 and 1550 cm⁻¹ show bands at 1700-1680 (conjugated C=O), 1638-1611 (C=O and C=C) and 1592-1562 cm⁻¹ [C=O in "conjugated chelation" (11)]. The infrared spectrum of the known compound **1a** shows bands at 1690, 1645 and 1590 cm⁻¹, and that of **1d** at 1682, 1626 and 1575 cm⁻¹.

3-Substituted Indeno[1,2-*c*]pyrazol-4(1*H*)ones (**2a-h**).

A mixture of the appropriate indandione **1** (0.001 mole), hydrazine hydrate (0.001 mole) and ethanol (10 ml.) was refluxed for 24 hours then poured into 50 ml. of ice-water sodium chloride mixture. The white precipitate was collected by filtration and recrystallized to give **2a-h**. The yields and melting points of compounds **2a-h** are listed in Table II. The infrared spectra show bands at 3050-3000 (compound **2h** at 3125) (NH); at 1697-1692 (compounds **2a-d**) and 1685-1680 (compounds **2f-h**) (C=O); 1612-1605 (C=C) and 1591-1570 cm⁻¹ (C=N). Compounds **1g** and **1h** show only one band at 1610 for C=N and C=C.

3-Substituted Indeno[1,2-*c*]pyrazol-4(1*H*)one, Hydrazones.

These compounds were obtained by refluxing for 60 hours a solution of the appropriate indandione **1** (0.003 mole) and 95% hydrazine (0.24 g.) in ethanol (20 ml.), adding water and recrystallizing the precipitate from a suitable solvent (see Table II). The melting points of these compounds were taken on a Fisher-Johns

melting point apparatus. Upon heating slowly from room temperature, these products decompose to give compounds which melt above 300° and are believed to be the corresponding azines. To prevent this decomposition, the samples were placed on the hot stage continuously as the temperature was rapidly raised. The point at which the sample melted rather than converted to the azine is recorded as the melting point. The infrared spectra of the hydrazones of compounds **2** show bands at 3375-3355 (non-bonded N-H), 3140-3105 (bonded N-H), 1612 (C=C) and 1590-1580 cm^{-1} (C=N).

3-Substituted 1,4-Dihydroindeno[1,2-c]pyrazoles (**3a-g**).

Method A.

A mixture of the appropriate indandione **1** (0.005 mole) in 13 ml. of hydrazine hydrate was refluxed for 24 hours, then poured into ice-salt water. The precipitate recrystallized from a suitable solvent (Table III) gave compounds **3** as white crystals.

Method B.

A mixture of the appropriate indandione **1** (0.005 mole) and hydrazine hydrate (1 ml.) was heated at 150° for 1 hour. Potassium hydroxide (1.0 g.) was added and the mixture was held at 160° for an additional hour. Addition of water and recrystallization of the formed precipitate from a suitable solvent (Table III) gave compounds **3** as white crystals. The yields and melting points of compounds **3** are listed in Table III.

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