The Regiospecific Synthesis of *N*-Substituted Pyrazoles. I. 1- and 2-Substituted Indeno[1,2-*c*]pyrazol-4(1*H*)-ones

Thomas L. Lemke* and Kailash N. Sawhney

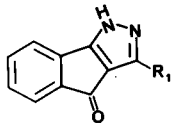
Department of Medicinal Chemistry, College of Pharmacy, University of Houston, Houston, TX 77004 USA

Received April 16, 1982

The reaction of the enaminoketones (**2** or **5**) of 2-acyl-1,3-indandiones with unsymmetrical hydrazines results in the regiospecific synthesis of 1,3- or 2,3-disubstituted indeno[1,2-*c*]pyrazol-4(1*H*)-ones (**4** or **7**). The synthesis of the enaminoketones (**2** or **5**) is accomplished by way of amine addition to the 2-acyl-1,3-indandiones **8a-c** or by reduction of the indenoisoxazole **9**. The structural assignment of the isomeric indenopyrazoles **4** and **7** is based upon ^{1}H-nmr chemical shifts.

J. Heterocyclic Chem., **19**, 1335 (1982).

Previously, we reported the synthesis of a series of 3-substituted indeno[1,2-*c*]pyrazol-4(1*H*)-ones (**1**) (1). It was found that upon alkylation of **1a-b** that the only products



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

obtained were the 1-alkyl-3-substituted indeno[1,2-*c*]pyrazol-4(1*H*)-ones (**4**). When the less stericly restrictive 3-methyl analog **1c** was alkylated, both the 1-alkyl-3-methylpyrazole **4** ($R_1 = CH_3$) and the 2-alkyl-3-methylpyrazole **7** ($R_1 = CH_3$) were obtained. The yield of alkylation product in either case was between 40-50%.

While a variety of synthetic methods are available for the synthesis of *N*-substituted pyrazoles, most are useful for the synthesis of only one of the two possible *N*-substituted isomers in unsymmetrical pyrazoles (2). Compounding the problem is the fact that in much of the older literature arbitrary assignment of the structure of the isomeric pyrazoles was made. As noted by ourselves and others, the ratio of pairs of isomeric pyrazoles obtained on alkylation can be influenced by the nature of the parent compound, the alkylating agent and the experimental conditions. As yet there appears to be no general method for selective or specific synthesis of *N*-substituted unsymmetrical pyrazoles.

We wish to report a method which, at least for the indenopyrazoles, is a regiospecific method for the synthesis of 1,3-disubstituted indeno[1,2-*c*]pyrazol-4(1*H*)-ones (**4**) and the 2,3-disubstituted indeno[1,2-*c*]pyrazol-4(1*H*)-ones (**7**). The procedure consists of the reaction of enaminoketones with unsymmetrical hydrazines as shown in Scheme I. The results suggest that the reaction proceeds *via* Michael addition to the α,β-unsaturated ketone followed by elimination of the amine to yield **3** or **6** which may enolize to the hydrazones **3′** or **6′**, respectively. In several cases the hydrazone intermediates were isolated, while in most cases the intermediates (**3-3′** or **6-6′**) cyclized directly to the indenopyrazoles **4** or **7**. The yield in general is 80-90% with formation of a single isomer (Table I).

The key to this synthesis is the preparation of the enaminoketones **2** and **5**. Several methods are available for

SCHEME-I

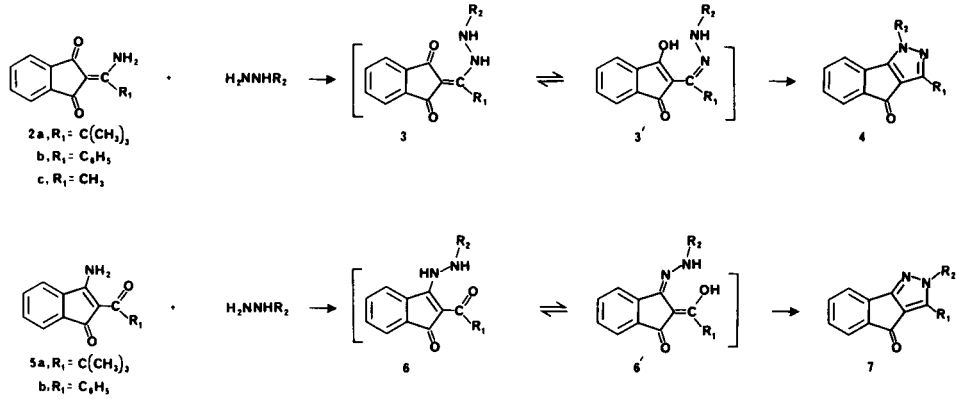
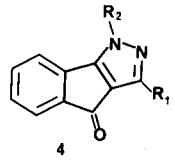
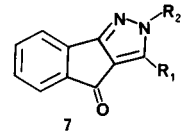


Table I



4

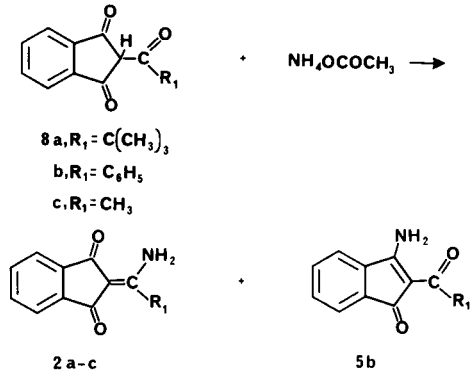


7

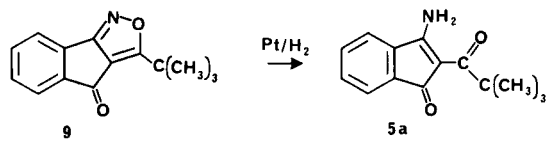
Compound No.	R_1	R_2	Method	Reaction Time (hours)	% Yield	Mp °C	Molecular Formula	Analysis % Clacd./Found C	H	N
4a	$(CH_3)_3C$	CH_3	A	1.5	96	147-148 (a)	$C_{15}H_{16}N_2O$		(1)	
4b	C_6H_5	CH_3	A	2.5	96	193-194 (a)	$C_{17}H_{12}N_2O$		(1)	
4c	CH_3	CH_3	A,B	4.5/2.0	50/78	140-142 (a)	$C_{12}H_{10}N_2O$		(1)	
4d	$(CH_3)_3C$	C_6H_5	A	20	74	147-148 (c)	$C_{20}H_{18}N_2O$	79.44	5.99	9.27
								79.29	6.03	9.20
4e	$(CH_3)_3C$	HOC_2H_4	A	1.5	100	149-151 (a)	$C_{16}H_{18}N_2O_2$	71.08	6.71	10.36
								71.08	6.72	10.33
4f	$(CH_3)_3C$	$(CH_3)_3C$	A	24	91	126-128 (c)	$C_{18}H_{22}N_2O$	76.56	7.85	9.92
								76.64	7.89	9.89
4g	$(CH_3)_3C$	$(CH_3)_2CH$	A	3	86	84-86 (a)	$C_{17}H_{20}N_2O$		(1)	
4h	C_6H_5	C_6H_5	A	22	90	204-205 (b)	$C_{22}H_{14}N_2O$	81.96	4.38	8.69
								81.84	4.40	8.63
4i	C_6H_5	HOC_2H_4	A	1.5	100	186-188 (a)	$C_{18}H_{14}N_2O_2$	74.46	4.86	9.65
								74.48	4.87	9.65
4j	C_6H_5	$(CH_3)_3C$	A	17	86	153-155 (c)	$C_{20}H_{18}N_2O$	79.44	5.99	9.27
								79.33	6.04	9.24
4k	C_6H_5	$(CH_3)_2CH$	A	25	93	175-177 (b)	$C_{19}H_{16}N_2O$		(1)	
4ℓ	CH_3	C_6H_5	C	70/4	74	129-131 (a)	$C_{17}H_{12}N_2O$	78.44	4.65	10.76
								78.46	4.67	10.74
4m	CH_3	HOC_2H_4	A,B	2	55/50	174-176 (a)	$C_{13}H_{12}N_2O_2$	68.40	5.30	12.27
								68.23	5.38	12.24
4n	CH_3	$(CH_3)_3C$	C	16/30	85	180-181 (a)	$C_{15}H_{16}N_2O$	74.97	6.71	11.66
								75.02	6.72	11.61
4p	CH_3	$(CH_3)_2CH$	C	25/4	65	148-149 (c)	$C_{14}H_{14}N_2O$		(1)	
7a	$(CH_3)_3C$	CH_3	A,B	1.5/1	83/94	141-142 (a)	$C_{15}H_{16}N_2O$	74.97	6.71	11.66
								75.01	6.73	11.60
7b	C_6H_5	CH_3	A	1	96	199-201 (a)	$C_{17}H_{12}N_2O$	78.44	4.65	10.76
								78.34	4.68	10.71
7e	$(CH_3)_3C$	HOC_2H_4	A	1	100	107-109 (b)	$C_{16}H_{18}N_2O_2$	71.08	6.71	10.36
								71.18	6.78	10.32
7g	$(CH_3)_3C$	$(CH_3)_2CH$	B	17	65	140-142 (c)	$C_{17}H_{20}N_2O$	76.09	7.51	10.44
								76.12	7.51	10.46
7i	C_6H_5	HOC_2H_4	A	1	93	144-145 (d)	$C_{18}H_{14}N_2O_2$	74.46	4.86	9.65
								74.48	4.86	9.63
7k	C_6H_5	$(CH_3)_2CH$	A	16	46	144-146 (d)	$C_{19}H_{16}N_2O$	79.14	5.59	9.72
								79.28	5.66	9.77

(a) Recrystallized from 95% ethanol. (b) From toluene-petroleum ether (bp 35-60°). (c) From cyclohexane. (d) From toluene.

SCHEME-II

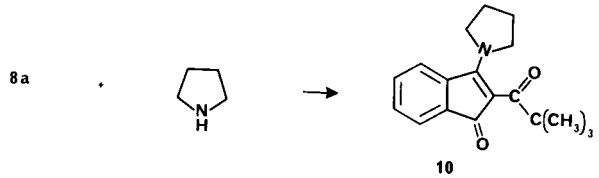


the synthesis of these compounds. The reaction of the β-triketones **8a-c** with ammonium acetate gave the enaminoketones **2a-c** and **5b** (Scheme II) (3). The ammonia prefers to add to the 2-acyl carbonyl giving rise to the exocyclic double bond rather than addition to the ring carbonyl. Only in the case of 2-benzoyl-1,3-indandione was compound **5** obtained as a minor product. An alternative method for preparing the ring amine **5a** was catalytic re-

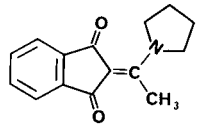


duction of isoxazole **9** (4). Identification of the enaminoketones **2a-c** and **5a-b** was by means of the mass spectral fragmentation pattern. Compounds **5a-b** gave a base peak of m/z 172 resulting from fragmentation alpha to the ketone with loss of R_1. The base peak of the isomeric compounds **2a-c** appeared at $M^+ - 15$, $M^+ - 1$, and M^+, respectively.

Secondary amines such as pyrrolidine, while offering no advantage over ammonium acetate for synthesis of side chain amines, proved valuable for synthesis of the ring amine of the 2-pivaloyl-1,3-indandione. Because of the steric crowding of the pivaloyl group, pyrrolidine adds exclusively to the ring carbonyl to give compound **10**. Reaction of **10** with unsymmetrical hydrazines serves as a more practical method of preparing the 2-substituted indenopyrazoles **7** (R_1 = *t*-Bu) (Method B).



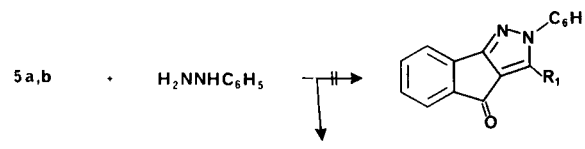
10



11

The reaction of pyrrolidine with 2-acetyl-1,3-indandione gave compound **11**. In the limited cases studied, this enaminoketone proved more susceptible to addition leading to a higher yield of **4c**, but did not improve the yield of **4m** (Table I).

The synthesis of compound **7** (R_1 = *t*-Bu and C_6H_5) was unsuccessful when tertiary butylhydrazine or phenylhydrazine were used. In the former case steric hinderance is suspected as the reason that the reaction does not go to completion. Compounds **6′** (R_1 = *t*-Bu and C_6H_5) was recovered in both of these cases indicating that the Michael addition had occurred, but that cyclization did not occur. When phenylhydrazine was used as the nucleophile, compound **12** was recovered (with **5b** as the substrate, a trace of **13** was also identified). The phenylhydrazine may have undergone the expected Michael addition to give **6** followed by the addition of a second mole of phenylhydrazine to the acylcarbonyl. Elimination of the side chain and addition of a third mole of phenylhydrazine would give rise to **12**. A combination of steric hinderance and reduced nucleophilicity of the phenyl substituted nitrogen could account for the deviation from the expected reaction.



12 **13**

Proof of structure of the indenopyrazoles **4** and **7** is based upon the chemical shift of the protons of R_1 which are influenced by the relative closeness of R_2 (Table II). As previously reported (1), alkylation of 3-*t*-butyl and 3-phenylindeno[1,2-*c*]pyrazol-4(1*H*)-ones give rise to a single product **4**. The chemical shift of the *t*-butyl protons is between δ 1.38-1.39. A similar situation is seen in Table II for compounds **4a,e-g**. With an alkyl substituent at the 2 position, a downfield shift of .11 to .16 ppm is experienced by the *t*-butyl protons. A somewhat different situation is found with the 3-phenyl analogs. 3-Phenylindeno[1,2-*c*]pyrazol-4(1*H*)-one exhibits a characteristic downfield multiplet at δ 8.16-8.36 which integrates for two protons. This two proton multiplet is assigned to the ortho protons on the 3-phenyl substituent on the basis that no such multiplet is seen in any of the 3-alkyl indeno[1,2-*c*]pyrazol-4(1*H*)-ones. The *ortho* protons are deshielded by the 4-ketone provided the 3-phenyl is free to rotate (Figure I). The 1-substituted-3-phenylindeno[1,2-*c*]pyrazol-4(1*H*)-ones **4b,i-k** all show the two proton multiplet (Table II). Compound **4h** not

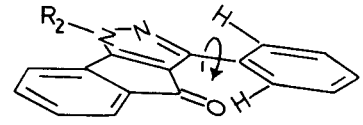


FIGURE - I

shown in Table II has the two proton multiplet at δ 8.16-8.36 with the remaining 12 protons between δ 7.1-7.85. Molecular models show that in the 2-alkyl-3-phenyl derivatives **7b,i,k** that the phenyl ring is not free to rotate and would be expected to exist perpendicular to the pyrazole ring. As such the *ortho* protons of the 3-phenyl are not deshielded by the 4-ketone. Inspection of Table II shows that the aromatic protons are found at δ 7.1-7.9 as a complex multiplet. Although nothing can be said from the present work about the chemical shift of the 3-methyl protons, the previous report (1) found a small downfield shift for the 3-methyl protons when comparing the 1-alkyl to the 2-alkyl substituents (0.07-0.12 ppm).

Present studies underway in our laboratory are directed towards exploring the generality of this stereospecific synthesis to less complex molecules.

Table II

NMR Data for 1- and 2-Alkyl-3-substituted Indeno[1,2-*c*]pyrazol-4(1*H*)-ones

Compound	R_2					R_1
	CH_3	CH_2	CH_2O	CH	OH	
4a	3.92 (s)					1.38 (s) [$(CH_3)_3C$]
4b	3.85 (s)					6.9-7.55 (m) (a) [Ar], 8.03-8.24 (m) [2H]
4c	3.87 (s)					2.28 (s) [CH_3]
4e		4.26 (m)	3.94 (m)		4.87 (m)	1.37 (s) [$(CH_3)_3C$] (b)
4f	1.72 (s)					1.37 (s) [$(CH_3)_3C$]
4g	1.59 (d)			4.60 (m)		1.39 (s) [$(CH_3)_3C$]
4i		4.33 (m)	3.95 (m)		5.00 (m)	7.26-7.61 (m) (a) [Ar] (b), 8.07-8.30 (m) [2H]
4j	1.79 (s)					7.06-7.72 (m) (a) [Ar], 8.23-8.46 (m) [2H]
4k	1.62 (d)			4.60 (m)		7.05-7.63 (m) (a) [Ar], 8.1-8.36 (m) [2H]
4m		4.17 (m)	3.85 (m)		4.93 (m)	2.2 (s) [CH_3] (b)
4n	1.71 (s)					2.35 (s) [CH_3]
4p	1.60 (d)			4.00 (m)		2.32 (s) [CH_3]
7a	3.92 (s)					1.52 (s) [$(CH_3)_3C$]
7b	3.93 (s)					7.1-7.9 (m) (a) [Ar]
7e		4.46 (m)---- 3.35				
		4.3 (m) (c)	4.07 (m) (c)		4.2 (b)	1.53 (s) [$(CH_3)_3C$]
7g	1.53 (d)			4.63 (m)		1.5 (s) [$(CH_3)_3C$]
7i			4.33 (m)----•-3.67		3.8 (b)	7.10-7.77 (m) (a) [Ar]
7k	1.55 (d)			4.64 (m)		7.14-7.81 (m) (a) [Ar]

(a) Includes 4 protons from the indenopyrazole ring. (b) Run in a mixture of deuteriochloroform and hexadeuteriodimethylsulfoxide. (c) After deuterium oxide exchange.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover Unimelt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 283 as potassium bromide pellets unless otherwise stated. All ^{1}H-nmr spectra were recorded on a Varian EM 360 spectrometer in deuteriochloroform using tetramethylsilane as an internal reference unless otherwise stated. Chemical shifts are quoted in parts per million (s = singlet, m = multiplet, d = doublet, t = triplet, b = broad band). Low resolution mass spectra were recorded on a Hewlett-Packard model 5930 GC/MS system equipped with a model 5933A data system using direct probe insertion and an ionizing energy of 70 eV with an ion source temperature of 250°. Microanalyses were performed by Atlantic Microlabs, Atlanta, Georgia.

2-(1'-Amino)benzylidenyl-1,3-indandione (**2b**) and 2-Benzoyl-3-amino-2-inden-1-one (**5b**).

A mixture of 4.0 g (0.032 mole) of 2-benzoyl-1,3-indandione, 40 g of ammonium acetate and 50 ml of glacial acetic acid was heated on a steam bath for 2 hours. The reaction mixture was diluted with 300 ml of ice cold water and the precipitate collected by filtration. The crude product (2.0 g) was chromatographed on silica gel (200 g) using ethyl acetate-toluene (1:4) for elution.

The first compound off the column was 1.2 g of 2-(1'-amino)benzylidenyl-1,3-indandione (**2b**) which was recrystallized from 95% ethanol as greenish yellow needles mp 238-239°; ^{1}H-nmr (hexadeuteriodimethylsulfoxide): δ 7.48 (d, J = 6 Hz, 9H), 8.91 (b, 1, exchangeable), 9.97 (b, 1, exchangeable); ir: 1690, 1630, 1580 cm^{-1}; ms: m/z 249 (M^+, 73.8%), 248 (M^+-1, 100%), 172 (M^+-77, 11.7%), 77 (M^+-172, 38.5%).

Anal. Calcd. for $C_{16}H_{11}NO_2$: C, 77.09; H, 4.45; N, 5.62. Found: C, 77.06; H, 4.47; N, 5.59.

Further elution of the column gave 0.450 g of 2-benzoyl-3-amino-2-inden-1-one (**5b**) which was recrsytallizaed from 95% ethanol as greenish yellow crystals, mp 281-283°; ^{1}H-nmr (hexadeuteriodimethylsulfoxide): δ 7.45-7.92 (m, 8H), 8.05-8.2 (t, J = 3 Hz, 1H), 10.15 (b, 1, exchangeable), 10.35 (b, exchangeable); ir: 1640 (b), 1590 (b) cm^{-1}; ms: m/z 249 (M^+, 37.3%), 248 (M^+-1, 100%), 172 (M^+-77, 100%), 77 (M^+-172, 37%).

Anal. Calcd. for $C_{16}H_{11}NO_2$: C, 77.09; H, 4.45; N, 5.62. Found: C, 77.05; H, 4.48; N, 5.60.

2-(1'-Amino)ethylidenyl-1,3-indandione (**2c**).

A solution of 3 g (0.016 mole) of 2-acetyl-1,3-indandione in 50 ml glacial acetic acid was prepared with heat. Ammonium acetate (30 g) was added and the mixture heated on a steam bath for 2 hours. Ice cold water (300 ml) was added and the precipitate (2.1 g) collected by filtration. The filtrate was made alkaline with aqueous sodium hydroxide and cooled in an ice bath to give an additional 0.70 g of solid. The crude product (2.8 g, 93%) was recrystallized from 95% ethanol to give pure **2c** as greenish yellow needles of mp 227-228°; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 2.53 (s, 3H), 7.61 (s, 4H), 9.06 (b, 1, exchangeable), 9.59 (b, 1, exchangeable); ir: 1690, 1645, 1600 cm^{-1}; ms: m/z 187 (M^+, 100%), 172 (M^+-15, 35.4%).

Anal. Calcd. for $C_{11}H_9NO_2$: C, 70.57; H, 4.84; N, 7.48. Found: C, 70.48; H, 4.89; N, 7.46.

Method A.

1-Methyl-3-*t*-butylindeno[1,2-*c*]pyrazol-4(1*H*)-one (**4a**).

A mixture of 1.05 g (0.0045 mole) of **2a**, 1 g (0.022 mole) of methylhydrazine and 50 ml of 95% ethanol was heated under reflux on a steam bath for 1.5 hours. The solvent was removed, the residue treated with 50 ml of ice cold water, and the precipitate collected by filtration. The crude product was recrystallized from 95% ethanol to give **4a**, mp 147-148°.

Using a similar procedure compounds **4b-k,m** and **7a-e,i,k** were prepared by reaction of the enaminoketones **2** and **5** with the unsymmetrical hydrazine (5). The indenopyrazoles were purified directly by recrystallization with the solvents indicated in Table I or by column chromatography on silica gel followed by recrystallization. The following compounds required an initial purification by chromatography: **4c,d,f-h,k** and **m**. All of the indenopyrazoles showed strong infrared absorption in the regions of 1710-1690, 1610-1600, 890, 770 and 740 cm^{-1}.

2-Pivaloyl-3-pyrrolidino-2-inden-1-one (**10**).

A solution of 1.42 g (0.02 mole) of pyrrolidine in 25 ml of toluene was added dropwise to a solution of 4.6 g (0.02 mole) of 2-pivaloyl-1,3-indandione (**8a**) in 275 ml of toluene containing a catalytic amount of *p*-toluenesulfonic acid. The mixture was heated under reflux for 19 hours while collecting the water using a Dean Stark trap. The solvent was removed and the oily residue was crystallized from 200 ml of cyclohex-

ane as pale yellow crystals. The crude product was collected by filtration and recrystallized from cyclohexane to give 2.5 g of pure crystalline product mp 165-167°. The mother liquor was concentrated and the residue was chromatographed on silica gel using methanol-chloroform (2:98): as eluting solvent. An additional 1.0 g of the product was recovered (61.8% yield); ^{1}H-nmr: δ 1.35 (s, 9), 1.8-2.34 (m, 4), 3.05-3.5 (m, 2), 3.82-4.34 (m, 2), 7.25-7.69 (m, 4); ir: 1660, 1630 cm^{-1}; ms: m/z 283 (M^+, 4.4%), 226 (M^+-57, 100%).

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.41; H, 7.52; N, 4.88.

2-(1'-Pyrrolidino)ethylidenyl-1,3-indandione (**11**).

A solution of 1.1 g (0.015 mole) of pyrrolidine in 20 ml of toluene was added to a solution of 2.5 g (0.013 mole) of 2-acetyl-1,3-indandione in 80 ml of toluene containing a catalytic amount of *p*-toluenesulfonic acid. The mixture was heated under reflux for 3 hours while collecting the water in a Dean Stark trap.

The solvent was removed and the residue recrystallized from benzene-cyclohexane to give 3.0 g (94% yield) of brown crystalline product mp 170-172°; ^{1}H-nmr: δ 1.77-2.34 (m, 4), 2.68 (s, 3), 3.5-4.14 (m, 4), 7.28-7.8 (m, 4); ir: 1730, 1630, 1590 cm^{-1}; ms: m/z 241 (M^+, 100%), 226 (M^+-15, 21.1%), 198 (M^+-43, 59.2%).

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.66; H, 6.27; N, 5.81. Found: C, 74.68; H, 6.29; N, 5.77.

Method B.

2-Methyl-3-*t*-butylindeno[1,2-*c*]pyrazol-4(1*H*)-one (**7a**).

A mixture of 0.283 g (0.001 mole) of **10**, 0.522 g (0.011 mole) of methylhydrazine and 15 ml 95% ethanol was heated under reflux for 1 hour. The solvent was removed, water added, and the crude product (0.225 g, 94% yield) was collected by filtration. The product was recrystallized from 95% ethanol, mp 139-141°.

Using a similar procedure and the appropriate enaminoketones (**10** and **11**), compounds **7g**, **4c** and **4m** were prepared (Table I).

Method C.

1-Phenyl-3-methylindeno[1,2-*c*]pyrazol-4(1*H*)-one (**41**).

(a) Synthesis of Phenylhydrazone **3'**; (R_1 = CH_3, R_2 = C_6H_5).

A mixture of 0.50 g (0.0027 mole) of **5c**, 1.4 g (0.013 mole) of phenylhydrazine and 30 ml of 95% ethanol was heated under reflux on a steam bath for 70 hours. The solvent was removed and the residue treated with ice cold water. The solid product was filtered, washed with water and dried. The crude product (0.70 g) was chromatographed on silica gel (90 g) using ethyl acetate-toluene (5:95) as the eluting solvent.

The initial material from the column (50 mg) was recovered as a yellow solid which gave pale yellow crystals from 95% ethanol, mp 175-177°. Analysis indicated this material to be the phenylhydrazone of **41**. The infrared showed the absence of a carbonyl band.

Anal. Calcd. for $C_{23}H_{18}N_4$: C, 78.83; H, 5.17, N, 15.99. Found: C, 78.87; H, 5.21; N, 15.94.

Elution next with ethyl acetate-toluene (1:9) gave 0.550 g of **3'** (R_1 = CH_3, R_2 = C_6H_5) as a brown solid which was recrystallized from 95% ethanol, m p 185-187°; ^{1}H nmr: δ 2.65 (s, 3), 6.28 (m, 1, exchangeable), 6.68-7.81 (m, 9), 11.6 (s, 1, exchangeable); ir: 1680, 1630, 1580 (br) cm^{-1}.

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.06. Found: C, 73.44; H, 5.11; N, 10.03.

(b) Cyclization of Phenylhydrazone **3'** (R_1 = CH_3, R_2 = C_6H_5) to **41**.

A solution of 0.360 g (0.0013 mole) of **3'** (R_1 = CH_3; R_2 = C_6H_5) in 15 ml 95% ethanol containing a catalytic amount of *p*-toluenesulfonic acid was heated under reflux on a steam bath for 4 hours. The solvent was removed and the residue treated with ice cold water. The precipitate (0.330 g, 98% yield) was collected by filtration and recrystallized from 95% ethanol to give pure **41** mp 129-131°; ^{1}H nmr: δ 2.4 (s, 3), 7.05-7.78 (m, 9).

Compounds **4n** and **4p** were prepared *via* a similar two step procedure. During the synthesis of **4p**, the intermediate hydrazone **3'** (R_1 = CH_3, R_2 = $(CH_3)_2CH$) was isolated but not purified. The crude reaction mixture was directly converted to **4p** which was purified by chromatography and recrystallization. The intermediate hydrazone **3'** (R_1 = CH_3, R_2 = $(CH_3)_3C$) leading to **4n** was recovered in 85% yield following chromatography and recrystallization from 95% ethanol, mp 146-148°; ^{1}H nmr: δ 1.13 (s, 9), 2.69 (s, 3), 3.73 (s, 1, exchangeable), 7.43-7.85 (m, 4), 11.46 (s, 1, exchangeable); ir: 1680, 1640, 1600 (b) cm^{-1}.

Anal. Calcd. for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.85. Found: C, 69.81; H, 7.04; N, 10.79.

1-*t*-Butylhydrazone of 2-Benzoyl-1,3-indandione **6'** (R_1 = C_6H_5; R_2 = $(CH_3)_3C$).

A mixture of 0.30 g (1.2 mmoles) of **5b**, 0.35 ml of *t*-butylhydrazine (Aldrich) and 15 ml of 100% ethanol was heated under reflux for 2 hours. The solvent was removed and the residue was treated with ice cold water. The aqueous layer was extracted with diethylether and the combined ether extract was dried over anhydrous magnesium sulfate. Concentration of the ether resulted in recovery of a semisolid residue which gave crystals from 95% ethanol (0.2 g), mp 182-184°; ^{1}H nmr: δ 1.23 (s, 9), 4.00 (m, 1, exchangeable), 7.17-7.88 (m, 8), 8.30-8.61 (m, 1), 12.50 (s, 1, exchangeable); ir: 1690, 1640 cm^{-1}.

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.97; H, 6.29; N, 8.79. Found: C, 74.97; H, 6.32; N, 8.69.

In a similar manner the reaction of **5a** with *t*-butylhydrazine resulted in recovery of 1-*t*-butylhydrazone of 2-pivaloyl-1,3-indandione **6'** (R_1 = R_2 = $(CH_3)_3C$). The semi-solid residue gave crystals from ethanol-water, mp 70-71°. Unfortunately, the compound was only obtained in the crystalline form as a hydrate with a half mole of ethanol; ^{1}H nmr: δ 1.27 (s, 9), 1.37 (s, 9), 4.00 (b, 1, exchangeable), 7.23-7.80 (m, 3), 8.29-8.57 (m, 1); 12.76 (s, 1, exchangeable); ir: 1680, 1625, 1590 cm^{-1}.

Anal. Calcd. for $C_{16}H_{24}N_2O_2 \cdot \frac{1}{2}C_2H_5OH$: C, 70.55; H, 8.42; N, 8.66. Found: C, 70.63; H, 8.48; N, 8.61.

Reaction of Phenylhydrazine With 2-Benzoyl-3-amino-2-inden-1-one (**5b**).

A mixture of 0.165 g (0.6 mmole) of **5b**, 0.55 g (5.1 mmoles) of phenylhydrazine in 10 ml of 95% ethanol was heated under reflux for 4 hours. The solvent was removed and the residue was treated with water. The precipitate (0.35 g) was collected by filtration, washed with water, and dried. Recrystallization of the solid from toluene gave 0.06 g of *N'*-benzoyl-*N*-phenylhydrazine, mp 169-170° (lit (6a) mp 168°).

The organic mother liquor was evaporated and the residue chromatographed on silica gel (20 g) using toluene as the eluant. The first solid to be eluted gave 0.11 g of pink solid from cyclohexane. The solid was recrystallized from toluene-petroleum ether (bp 35-60°), mp 172-174°. This material was identified as the bisphenylhydrazone of 1,3-indandione (lit (6b) mp 171°); ^{1}H nmr (hexadeuteriodimethylsulfoxide-deuteriochloroform): δ 3.45 (s, 2), 6.60-7.88 (m, 14), 8.45 (s, 2, exchangeable).

Eluting the column with ethyl acetate-toluene (1:3) gave an additional 0.025 g of the *N'*-benzoyl-*N*-phenylhydrazine.

In a similar manner, when **5a** was treated with phenylhydrazine in 95% ethanol, the only product isolated was the bisphenylhydrazone of 1,3-indandione.

Acknowledgement.

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

REFERENCES AND NOTES

(1) T. L. Lemke, M. B. Cramer and K. Shanmugam, *J. Pharm. Sci.*, **67**, 1377 (1978).

(2) R. Fusco in "The Chemistry of Heterocyclic Compounds", A Weissberger, ed, Interscience, New York, NY, 1967, pp 3-174.

(3) V. Zelmens and G. Vanaga, *Latv. PSR Zinat. Akad. Vestis*, 69 (1959); *Chem. Abstr.*, **53** 21830d (1959).

(4) T. L. Lemke, K. N. Sawhney and B. K. Lemke, *J. Hetrocyclic Chem.*, **19**, 363 (1982).

(5) A. N. Kost and R. S. Sagitullin, *Zh. Obshch. Khim.*, **33**, 867 (1963); *Chem. Abstr.*, **59**, 8724f (1963); N. I. Ghali and D. L. Venton, *J. Org. Chem.*, **46**, 5413 (1981).

(6a) Dictionary of Organic Compounds, J. R. A. Pollock and R. Stevens, eds, Oxford University Press, New York, 1965, p 2696; (b) *ibid.*, p 1842.