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A One Step Synthesis of 1,3-Disubstituted Indeno[1,2-c] pyrazol-4(1H)-ones

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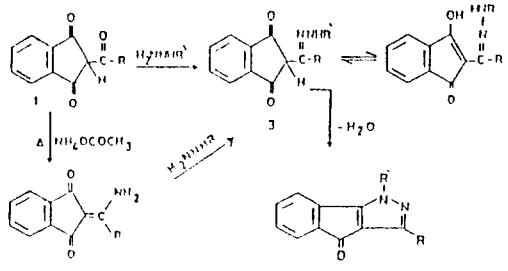
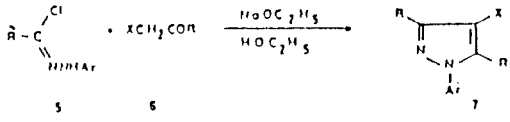
Abstract□A new synthesis of 1,3-disubstituted ideno[1,2-c]-pyrazol-4(1H)-ones has been developed using hydrazonyl halides and 1,3-indanedione.

Keywords□1,3-Indanedione, hydrazonyl halides.

The interesting physiological properties of indeno [1,2-c]pyrazol-4(1H)-ones with substitutents in the pyrazole ring have promoted several authors to investigate their synthesis[1-5]. To date the only practical approach to the synthesis of such compounds involves the reaction of 2-acyl-1,3-indanedione **1** or their enamine derivatives **2** with hydrazine or phenylhydrazine (Scheme 1). The key to such synthesis is the preparation of **1**. As compounds of type **1** are usually prepared by the reaction of dimethyl phthalate and the corresponding methyl ketone[4], the reported methods would be limited to synthesis of **4** with R which is an alkyl or aryl group. In this communication we wish to report a new route to **4** that is based on the reaction of hydrazonyl halides **5** with 1,3-indanedione. This method is an extension of our earlier work on the synthesis of pyrazoles **7** from **5** and active methylene compounds **6** (Scheme 2)[6].



Scheme 1



Scheme 2

RESULTS AND DISCUSSION

Addition of hydrazonly halide **5a** to a solution of the sodium salt of 1,3-indanedione in ethanol at room temperature gave after stirring for 24 h 1,3-diphenyl-indeno[1,2-c]pyrazol-4(1H)-one **10a**. Other hydrazonyl halides **5b-g** reacted similarly with 1,3-indanedione to give the corresponding 1,3-disubstituted indeno[1,2-c]pyrazol-4(1H)-ones **10b-g** respectively (Scheme 3). In no case, the intermediate arylhydrazone of 2-acyl-1,3-indanedione **9** has been isolated. This finding suggests that **9** undergo cyclization as soon as they are formed or probably the reaction follows 1,3-dipolar cycloaddition of the nitrilimine derived from **5** to the C = C double bound of the enol tautomer of 1,3-indanedione followed by the loss of the elements of water[6]. The structure of the compound **10a-g** prepared were supported by elemental analyses and by the similarities of their spectra (^{1}H-NMR, ^{13}C-NMR, IR) with those of known compounds (Tables I and II).

The results of this study provide a basis for a general method for preparing functionalized 1,3-disubstituted indeno[1,2-c]pyrazol-4(1H)-ones. It is an efficient and rapid experimental procedure with necessitates readily available starting materials.

EXPERIMENTAL

Mps. are uncorrected. IR spectra were recorded

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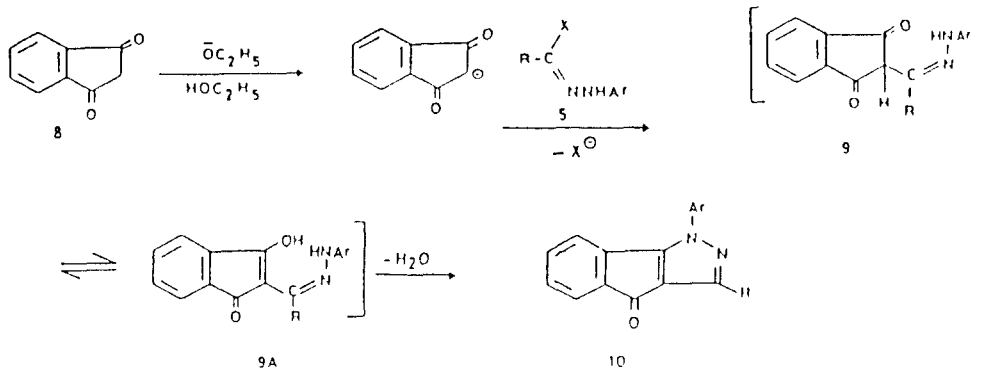

5, 10	X	R	Ar
a	Cl	C_6H_5	C_6H_5
b	Br	2-thienyl	$4-O_2NC_6H_4$
c	Cl	C_2H_5OCO	$4-BrC_6H_4$
d	Cl	C_6H_5NHCO	C_6H_5
e	Cl	C_6H_5NHCO	$4-CH_3C_6H_4$
f	Br	CH_3	$4-O_2NC_6H_4$
g	Cl	C_6H_5NHCO	$4-ClC_6H_4$

Scheme 3.

Table I. Melting points and analytical data of compounds 10a-g

Compound No.	mp.	Molecular formula	Anal. Calcd. (Found) C,%	H,%	N,%
10a	200 (E)[b]	$C_{22}H_{14}N_2O$	81.9 (81.8)	4.4 (4.2)	8.7 (8.7)
10b	253 (A)	$C_{20}H_{11}N_3O_3S$	64.3 (64.1)	2.9 (2.9)	11.3 (10.9)
10c	204 (A)	$C_{19}H_{13}BrN_2O_3$	57.4 (57.5)	3.3 (3.3)	7.0 (6.9)
10d	215 (E)	$C_{23}H_{15}N_3O_2$	75.5 (75.5)	4.1 (4.2)	11.5 (11.4)
10e	213 (D)	$C_{24}H_{17}N_3O_2$	75.9 (76.0)	4.5 (4.4)	11.0 (10.9)
10f	209 (A)	$C_{17}H_{11}N_3O_3$	66.8 (66.8)	3.6 (3.5)	13.7 (13.6)
10g	253 (D)	$C_{23}H_{14}ClN_3O_2$	69.1 (69.1)	3.5 (3.5)	10.5 (10.4)

[a] Solvent of crystallization: A, acetic acid; D, dioxane; E, ethanol.

[b] Lit. m.p. 204-205°C[5]

Table II. Spectral data of compounds 10a-g

Compound No.	$\nu C=O$, cm^{-1}	^1H-NMR δ (ppm)
10a	1695	7.2-8.3 (m, 14H, ArH)
10b	1705	7.1-8.5 (m, 11H, ArH)
10c	1725, 1700	1.40 (t, J=7Hz, 3H, CH_3); 4.35 (q, J=7 Hz, CH_2); 7.2-8.3 (m, 9H, ArH)
10d	1725, 1700	7.2-7.9 (m, 14H, ArH); 9.7 (s, 1H, NH)
10e(a)	1705, 1690	3.0 (s, 3H, CH_3), 7.0-7.8 (m, 13H, ArH); 9.8 (s, 1H, NH)
10f	1695	2.5 (s, 3H, CH_3), 7.0-7.8 (m, 8H, ArH)
10g	1705, 1685	7.3-8.0 (m, 13H, ArH); 9.7 (s, 1H, NH)

(a) ^{13}C-NMR of **10e** in DMSO-d_6: 23.0, 121.8, 122.5, 123.0, 125.4, 126.4, 127.5, 131.1, 132.2, 132.7, 135.1, 136.0, 137.9, 140.3, 141.8, 142.1, 145.6, 159.1, 159.4, 186.6 ppm

on a Beckman IR 4 spectrophotometer. The ^1H-NMR spectra were obtaind in deuterated chloroform on a Varian A 90 NMR spectrometer with tetramethylsilane as the internal standard. The hydrazonyl halides **5a-g** were prepared by known literature procedures[7-11].

1,3-Disubstituted indeno[1,2-c]pyrazol-4(1H)-ones, 10a-g; General procedure

To an ethanolic sodium ethoxide solution (prepared from sodium metal (0.11g, 0.005g. atom) and absolute ethanol (20 ml) was added indane-1,3-dione (0.73g, 5 mmol). After stirring for 15 min at room temperature, the appropriate hydrazonyl halide **5** (5 mmol) was added and stirring continued for 6 h and then left at room temperature overnight. The reaction mixture was diluted with water where the crude product precipitated. In some cases dilution was unnecessary as the product precipitated on standing. It was collected, washed with water and dried. Crystallization from the proper solvent (see Table) gave the corresponding pure indeno[1,2-c]pyrazol-4(1H)-one derivative in 50-60% yield. The compounds prepared together with their physical constants are listed in Table I.

The phenylhydrazone derivative of **10b** was crystallized from aqueous dioxan, mp.249°C. Its infrared spectrum contains NH near 3250 cm^{-1} and no carbonyl in the region 1700-1715 cm^{-1}.

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