A New and Convenient Synthesis of 1*H*-Indazoles

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There are three classical ways to prepare 1*H*-indazoles. The most frequently used route to the 1*H*-indazole ring system consists of diazotization of suitably substituted anilines which have a hydrocarbon group in the *ortho*-position[1]. Somewhat similar reactions occur when *N*-nitroso-2-methylanilines are heated in the presence of sodium carbonate[2]. The reaction of *o*-chloro-aromatic ketones having a nitro substituent *para* to the chloro substituent with arylhydrazines also gives 1-aryl-1*H*-indazoles[3]. These methods have several limitations as regards the reaction conditions; therefore, several improved syntheses[4-14] have been proposed or developed. However, to our knowledge, an efficient synthesis of highly substituted 1*H*-indazoles has not been reported so far. We describe here a facile one-pot synthesis of highly substituted 1*H*-indazoles.

Treatment of 1-aryl-4,6,6-trimethyl-3-phenyl-1,6-dihydropyrano[2,3-*c*]pyrazoles **(1a–d)** with dialkyl acetylenedicarboxylates **(2a, b)** in dimethylformamide at reflux temperature results in cycloaddition to give cycloadducts such as **3** which spontaneously eliminate one molecule of acetone to give 1-aryl-6,7-dialkoxycarbonyl-4-methyl-3-phenyl-1*H*-indazoles **(4a–h)** as the final products. The structure of products **4a–h** is supported by the I.R. and ^{1}H-N.M.R. spectra.

The starting compounds **1a–d** are easily prepared from 2-aryl-5-phenyl-3-oxo-3,4-dihydro-2*H*-pyrazoles and acetone[15]; wide variations may be anticipated.

6,7-Dimethoxycarbonyl-4-methyl-1,3-diphenyl-1*H*-indazole (4a); Typical Procedure:

A solution of 4,6,6-trimethyl-1,3-diphenyl-1,6-dihydropyrano[2,3-*c*]pyrazole (**1a**; 3.16 g, 10 mmol) and dimethyl acetylenedicarboxylate (**2a**; 1.92 g, 15 mmol) in dry dimethylformamide (100 ml) is refluxed for 12 h. The mixture is evaporated in vacuo at room temperature to give a dark brown oily residue, which is recrystallized from isopropanol/acetone (10/1) to give **4a**; yield: 3.28 g (82%); m.p. 180–182°C.

$C_{24}H_{20}N_2O_4$	calc.	C 71.98	H 5.03	N 7.00
(400.4)	found	71.72	4.98	6.95

M.S.: $m/e = 400$ (M^+, 100%); 337 (45); 301 (30).

U.V. (C_2H_5OH): $\lambda(\log\varepsilon) = 246$ (4.62); 333 (3.96) nm.

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Table. 1,3-Diaryl-4-methyl-1*H*-indazoles **(4a–h)** prepared

4	R^1	R^2	Yield[a] [%]	m.p. [°C]	Molecular Formula[b]	I.R. (film) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
a	H	CH_3	82	180–182°	$C_{24}H_{20}N_2O_4$ (400.4)	1740, 1710, 1595, 1268	2.38 (s, 3H); 3.29 (s, 3H); 3.80 (s, 3H); 7.4–7.6 (m, 11H)
b	Br	CH_3	80	182–183°	$C_{24}H_{19}BrN_2O_4$ (479.3)	1730, 1725, 1595, 1280	2.39 (s, 3H); 3.40 (s, 3H); 3.90 (s, 3H); 7.35–7.7 (m, 10H)
c	Cl	CH_3	75	151–152°	$C_{24}H_{19}ClN_2O_4$ (434.9)	1730, 1725, 1595, 1290	2.39 (s, 3H); 3.40 (s, 3H); 3.90 (s, 3H); 7.45–7.6 (m, 10H)
d	CH_3	CH_3	85	141–142°	$C_{25}H_{22}N_2O_4$ (414.4)	1735, 1730, 1600, 1280	2.39 (s, 3H); 2.43 (s, 3H); 3.32 (s, 3H); 3.90 (s, 3H); 7.3–7.6 (m, 10H)
e	H	C_2H_5	73	160–162°	$C_{26}H_{24}N_2O_4$ (428.5)	1735, 1715, 1595, 1280	1.07 (t, 3H, J=7 Hz); 1.35 (t, 3H, J=7 Hz); 2.39 (s, 3H); 3.65 (q, 2H, J=7 Hz); 4.35 (q, 2H, J=7 Hz); 7.4–7.6 (m, 11H)
f	Br	C_2H_5	72	191–193°	$C_{26}H_{23}BrN_2O_3$ (507.4)	1725, 1720, 1585, 1260	1.11 (t, 3H, J=8 Hz); 1.37 (t, 3H, J=8 Hz); 2.39 (s, 3H); 3.75 (q, 2H, J=8 Hz); 4.38 (q, 2H, J=8 Hz); 7.35–7.7 (m, 10H)
g	Cl	C_2H_5	70	143–144°	$C_{26}H_{23}ClN_2O_4$ (462.9)	1725, 1715, 1590, 1270	1.12 (t, 3H, J=8 Hz); 1.37 (t, 3H, J=8 Hz); 2.39 (s, 3H); 3.75 (q, 2H, J=8 Hz); 4.37 (q, 2H, J=8 Hz); 7.4–7.6 (m, 10H)
h	CH_3	C_2H_5	80	130–131°	$C_{27}H_{26}N_2O_4$ (442.5)	1735, 1720, 1590, 1280	1.09 (t, 3H, J=8 Hz); 1.38 (t, 3H, J=8 Hz); 2.39 (s, 3H); 2.43 (s, 3H); 3.67 (q, 2H, J=8 Hz); 4.35 (q, 2H, J=8 Hz); 7.3–7.6 (m, 10H)

[a] Yield of isolated product.

[b] The mass spectra and the microanalyses were in satisfactory agreement with the calculated values: C, ±0.26; H, ±0.15; N, ±0.10.