Simple regioselective synthesis of spiro[2*H*-indene-2,3′-[3*H*]pyrazoles]

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A.S. Girgis[a], Y.A. Ibrahim[b], I.S. Ahmed Farag[a] and N. Mishriky[a]*

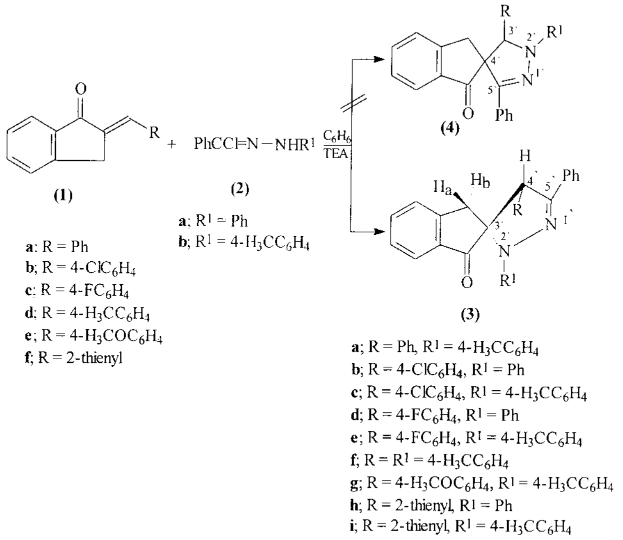
[a]*National Research Centre, Dokki, Cairo, Egypt*

[b]*Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt*

1,3-Dipolar cycloaddition of nitrilimines to a variety of 2-arylmethylidene-1-indanones **1** or 2-arylmethylidene-1,3-indandiones **5** gave the corresponding spiro[2*H*-indene-2,3′-[3*H*]pyrazol]-1(3*H*)-one **3** and their 1,3-dione derivatives **6** in high regioselectivity. The stereo-configuration of **3** (3′R, 4′S or its enantiomeric form) was established by nOe-difference technique as well as single crystal X-ray diffraction analysis.

1,3-Dipolar cycloaddition is a general method to synthesize five membered ring systems. Particularly, nitrilimines have been widely used to obtain pyrazoline derivatives.[1–3] In the present work, it is intended to investigate the 1,3-dipolar cycloaddition reaction of nitrilimines to the exocyclic double bond of arylidenes derived from 1-indanone and 1,3-indandione in an attempt not only to isolate the corresponding spiro-containing pyrazoline derivatives but also to determine the regioselectivity of these reactions.

Reaction of a variety of 2-arylmethylidene-1-indanones **1a–f** with the appropriate nitrilimines (generated *in situ* by triethylamine dehydrohalogenation of the corresponding hydrazonoyl chlorides **2**) in refluxing dry benzene afforded only one-regioisomer, the structure of which was established to be spiro[2*H*-indene-2,3′-[3*H*]pyrazol]-1(3*H*)-ones **3** rather than spiro[2*H*-indene-2,4′-[4*H*]pyrazol]-1(3*H*)-ones **4** based on spectroscopic and analytical data. ^{1}H-NMR spectra of **3a–i** exhibit the presence of singlet signals at (δ) = 4.91–5.27 assignable to the pyrazole H-4′. The appearance of this signal ruled out the presence of the other regioisomer **4**.[9–13]



Scheme 1

^{13}C-NMR spectra of **3a,h** show the presence of the pyrazole CH-4′ and spiro carbon at (δ) = 61.2, 56.2 and 78.2, 78.4 respectively. These chemical shift values are consistent with other similar structures which add good support for the proposed structure.[12,13] The stereo configuration of **3** (3′R, 4′S or its enantiomeric form) was established through nuclear Overhauser effect difference technique (nOe-difference) of **3h** as a representative example. Thus, irradiation of the singlet signal of H-4′ at δ = 5.27 gives more enhancement for the H_a signal at δ = 3.00 than for the H_b signal at δ = 3.47. This observation indicates that the more downfield shift position of H_b than H_a could be attributed to the positioning of the pyrazole N-2′ closer to H_b than H_a

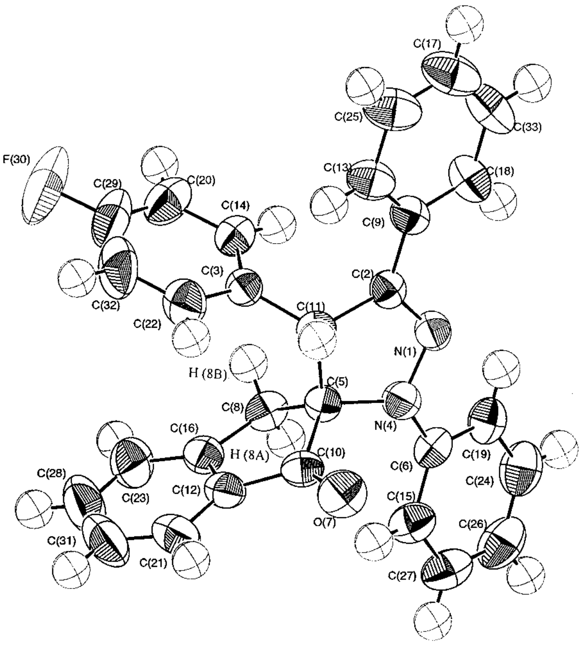


Fig. 1 Single crystal X-ray diffraction of **3d**

Single crystal X-ray diffraction of **3d** add a sharp evidence not only for the proposed structure but also for the stereochemical configuration.[14] From the data obtained (cf. Fig. 1) it is obvious that the distance between H(11) and H(8A) = 4.1223 Å is greater than the distance between H(11) – H(8B) = 3.489 Å. However, the distance between N(4) and H(8B) = 3.020 Å is greater than the distance between N(4) and H(8A) = 2.648 Å. These data support the previously described stereo-configuration as well as the reason of H_b [H(8A)] deshielding effect than H_a [H(8B)] in ^{1}H-NMR spectra.

Similarly, the reaction of 2-arylmethylidene-1,3-indanediones **5a-f** with nitrilimines in refluxing dry benzene gave the corresponding spiro[2*H*-indene-2,3′-[3*H*]pyrazole]-1,3-diones **6** in a high regioselectivity. The structure of **6** was established through IR, ^{1}H-NMR, ^{13}C-NMR as well as elemental analysis data. The ^{1}H-NMR spectra of **6a-l** reveal the presence of the pyrazole H-4′ at δ = 5.14-5.48. The downfield shift difference of H-4′ in the case of **6** as compared with the corresponding **3** was attributed to the deshielding effect of the two carbonyl groups in **6**. The ^{13}C-NMR spectrum of **6k** (ON-resonance, DEPT) adds further evidence for the proposed

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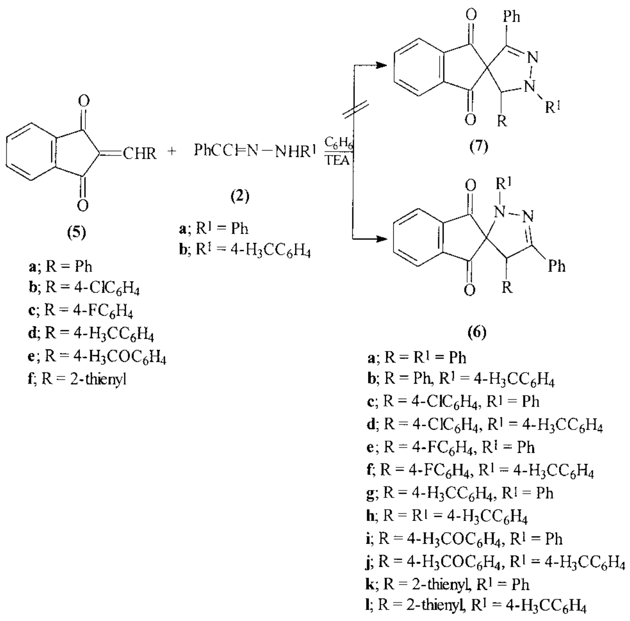
* To receive any correspondence.



(5)
a; R = Ph
b; R = $4\text{-ClC}_6\text{H}_4$
c; R = $4\text{-FC}_6\text{H}_4$
d; R = $4\text{-H}_3\text{CC}_6\text{H}_4$
e; R = $4\text{-H}_3\text{COC}_6\text{H}_4$
f; R = 2-thienyl

(2)
a; R^1 = Ph
b; R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$

(6)
a; R = R^1 = Ph
b; R = Ph, R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$
c; R = $4\text{-ClC}_6\text{H}_4$, R^1 = Ph
d; R = $4\text{-ClC}_6\text{H}_4$, R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$
e; R = $4\text{-FC}_6\text{H}_4$, R^1 = Ph
f; R = $4\text{-FC}_6\text{H}_4$, R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$
g; R = $4\text{-H}_3\text{CC}_6\text{H}_4$, R^1 = Ph
h; R = R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$
i; R = $4\text{-H}_3\text{COC}_6\text{H}_4$, R^1 = Ph
j; R = $4\text{-H}_3\text{COC}_6\text{H}_4$, R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$
k; R = 2-thienyl, R^1 = Ph
l; R = 2-thienyl, R^1 = $4\text{-H}_3\text{CC}_6\text{H}_4$

Scheme 2

structure, revealing the presence of CH-4′ and spiro-C at δ = 58.0 and 80.0 respectively.

Attempts to identify or isolate of the other regio-isomers **4, 7** from the reaction mother liquors were unsuccessful.

Techniques used: Elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR, nOe-difference, X-ray diffraction

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14 Full crystallographic details, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre (CCDC).