SHORT PAPER

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A facile synthesis of 1,3-diphenyl-4-arylspiro[pyrazoline-5, 3′-flavan-4′-one]†

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Synthesis of a series of novel 1,3-diphenyl-4-arylspiro[pyrazoline–5,3′-flavan-4′-ones] has been accomplished in good yields by the regioselective 1,3-dipolar cycloaddition of diphenylnitrilimine with (*E*) 3-benzylideneflavan-4-ones.

Keywords: cycloaddition, spiro compounds, flavanones, pyrazolines, nitrilimines

1,3-Dipolar cycloaddition offers a convenient one-step route for the construction of wide variety of complex five membered heterocycles that are synthetically useful compounds.[1] The regio and stereoselectivities in these reactions have multiplied their utility in the synthesis of natural products.[2] Many pyrazoline derivatives possess important pharmaceutical activities (*e.g.*, as anti-inflammatory, analgesics, and herbicides) and their synthesis has attracted much attention.[3] Flavanoids display widespread biological applications such as antitumoral, antiviral, antibiotic properties, *etc*.[4] Flavanone derivatives have also gained much prominence since they are known to be pharmacologically significant[5] and are excellent anti-oxidants.[6] Many natural products containing the flavanone moiety have been isolated.[7] In continuation of our interest in cycloaddition reactions, and with a view to synthesising a rare class of spiroheterocyclic derivatives[8,9] and also to investigate their biological applications, we have studied the reaction of the versatile 1,3-dipole diphenylnitrilimine (DPNI) with various 3-benzylideneflavan-4-ones.

Reaction of a 3-arylmethyleneflavan-4-one with DPNI (generated *in situ* from N-phenylbenzhydrazonoyl chloride in chloroform solution in the presence of triethylamine at room temperature), led to the formation of 1:1 adducts as a single product in each case, as evidenced by TLC and mass spectral studies (Scheme 1). The reaction yielded a series of novel 4-aryl-1,3-diphenylspiro[pyrazoline-5,3′-flavan-4′-ones] in good yields (79–90%) by the regioselective cycloaddition of the 1,3-dipole across the exocyclic double bond of the 3-benzylideneflavan-4-one in each case. We could not find even a trace of other regioisomers **4a–e** in all the cases studied.

The spectroscopic data of each product **3a–e** are consistent with the asigned regiochemistry of cycloaddition. The carbonyl absorption in the IR spectrum of the product **3a** shows as a peak at 1699 cm^{-1}, an increase of 22 cm^{-1} from that of 3-benzylideneflavan-4-one, indicating the loss of conjugation of the carbonyl group. The ^1H NMR spectrum of the product shows a singlet at δ 4.96 due to benzylic proton and a broad singlet at δ 5.81 due to C-2 proton and a multiplet in the range δ 6.80–7.89 and doublet at δ 8.12 due to aromatic protons. Further confirmation of the spiroheterocyclic structure and the regiochemistry of the cycloaddition was provided by ^{13}C NMR spectra. The presence of a signal at δ 74.02 due to the spiro carbon and a peak at δ 160.84 due to the C=N-N carbon manifests the presence of pyrazoline ring in accordance with the literature value wherein the nitrogen terminal of the 1,3-dipole is attached to the spiro quaternary carbon atom. The structure and stereochemistry and the regiochemistry of cycloaddition were further corroborated by single crystal X-ray analysis of the product **3a**[10] (Fig. 1)

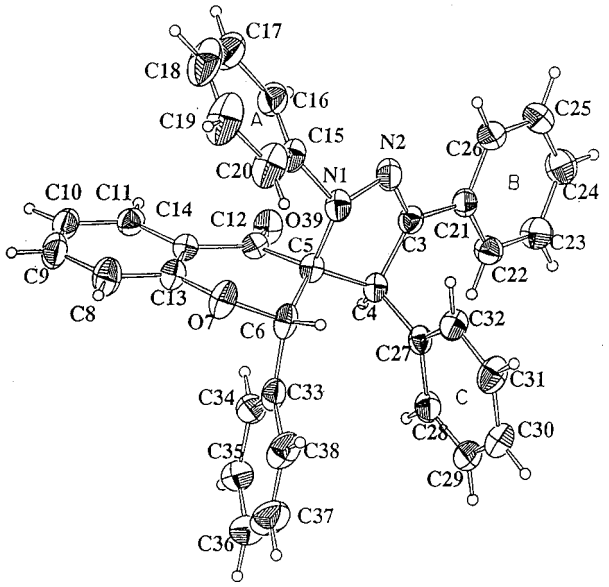

Fig. 1 ORTEP diagram of compound 3a.[10]

Identical results were observed with the other 3-arylmethyleneflavan-4-one derivatives irrespective of the nature of substituents present on the aryl moiety.

In conclusion, the 1,3-dipolar cycloaddition reactions of DPNI to the exocyclic olefins described in this paper offer a ready access to a new class of spiropyrazolines. The observed regiochemistry is consistent with that of DPNI cycloaddition reactions to various other olefins.[8]

Experimental

The starting materials, 3-arylmethyleneflavan-4-ones **1a–e**[11] and *N*-phenylbenzhydrazidoyl chloride **2**[12], were prepared according to the literature procedures.

Reaction of 3-arylmethyleneflavan-4-ones with DPNI: general procedure. To a solution of 3-arylmethyleneflavan-4-one (3 mmol) and N-phenylbenzhydrazidoyl chloride (3 mmol) in dry chloroform, triethylamine (3.3 mmol) was added. The reaction mixture was stirred at r.t. until the disappearance of the starting material, as monitored by TLC, was observed. After the reaction was over, the mixture was filtered to remove the triethylamine hydrochloride, and the solvent was evaporated under a vacuum. The resulting crude product was purified by column chromatography (hexane/ethyl acetate, 9:1) and recrystallised (CHCl3/methanol, 2:1). The reaction time, physical constants and spectral details for **3a–e** are reported in Tables 1 and 2.

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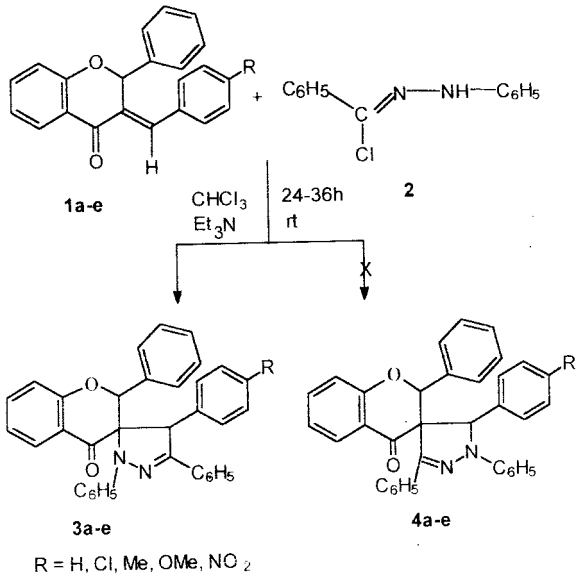
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Spiropyrazolines **3a-e** prepared

Product	Reaction time/h	Yield /%	M.p. /°C	IR (KBr) cm^{-1} $\nu_{C=O}$	MS (70eV *m/z*) (M^+)	Molecular formula	Analysis: calcd/found		
							C	H	N
3a	18	88	144–146	1699	506	$C_{35}H_{26}N_2O_2$	82.97 82.94	5.18 5.19	5.53 5.49
3b	16	90	136–138	1695	540/2	$C_{35}H_{25}ClN_2O_2$	77.75 77.71	4.66 4.60	5.18 5.07
3c	24	79	168–170	1699		$C_{36}H_{28}N_2O_2$	83.04 83.16	5.42 5.21	5.38 5.36
3d	28	81	184–186	1698	536	$C_{36}H_{28}N_2O_3$	80.56 80.69	5.26 4.99	5.22 5.10
3e	20	87	176–178	1697	551	$C_{35}H_{25}N_3O_4$	76.20 76.22	4.57 4.49	7.62 7.59

Table 2 ^1H and ^{13}C NMR data for spiropyrazolines **3a–e**

Product	^1H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) ppm
3a	4.96 (s, 1H), 5.81 (s, 1H), 6.67–7.68 (m, 23H), 8.02 (dd, 1H, J = 7.9, 1.2)	60.36, 71.14, 74.02, 117.25, 118.45, 119.42, 119.65, 121.95, 122.17, 122.64, 126.51, 126.74, 127.53, 128.04, 128.89, 129.42, 130.94, 133.80, 135.65, 137.06, 137.64, 144.09, 149.11, 160.84, 189.21
3b	5.00 (s, 1H), 5.90 (s, 1H), 6.79–7.77 (m, 22H), 7.91 (dd, 1H, *J* = 7.8, 1.3)	60.41, 69.04, 74.64, 117.26, 118.51, 119.49, 119.72, 121.91, 122.19, 122.74, 126.61, 126.71, 127.59, 128.21, 128.91, 129.46, 130.84, 133.46, 135.91, 137.61, 137.42, 145.10, 148.94, 160.44, 189.24
3c	2.34 (s, 3H), 4.94 (s, 1H), 5.87 (s, 1H), 6.74–7.69 (m, 22H), 7.89(dd, 1H, *J* = 7.9, 1.2)	21.77, 60.46, 69.71, 74.24, 117.34, 118.54, 119.20, 119.84, 121.84, 122.24, 122.81, 126.49, 126.84, 127.64, 128.24, 128.88, 129.44, 130.64, 133.94, 135.67, 137.64, 137.91, 145.42, 149.09, 160.49, 189.77
3d	3.82 (s, 3H), 4.95 (s, 1H), 5.86 (s, 1H), 6.68–7.59 (m, 22H), 8.02 (dd, 1H, *J* = 7.8, 1.2)	56.21, 61.04, 69.64, 73.99, 117.34, 118.81, 119.31, 119.54, 121.89, 122.18, 122.48, 126.49, 126.81, 127.64, 128.01, 128.64, 128.91, 129.14, 130.49, 133.81,135.61, 137.61, 137.74, 144.12, 149.04, 160.85, 189.31
3e	4.99 (s, 1H), 5.84 (s, 1H), 6.61–7.55 (m, 20H), 7.91 (dd, 1H, *J*=7.6,1.3), 8.17 (d, 2H, J=7.6)	59.94, 70.54, 73.64, 117.84, 118.49, 119.74, 119.84, 121.94, 122.64, 122.79, 126.14, 126.86, 127.11, 128.43, 128.61, 128.96, 129.16, 129.61, 130.58, 137.14, 141.64, 143.64, 145.04, 148.01, 160.53, 188.64



Scheme 1

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