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SYNTHESIS OF SPIRO-PYRAZOLINES: REACTION OF 1,3-DIPHENYLNITRILIMINE WITH FULVENES

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Abstract—A one-step synthesis of a new series of spiro-pyrazolines has been accomplished by the 1,3-dipolar cycloaddition of 1,3-diphenylnitrilimine with various fulvenes (2,3,4,5-tetraphenyl fulvene (**1**) and its analogues (**2**, **3**), 9-benzalfluorene (**7**) and its analogues (**8**, **9**) and 6,6-diphenylfluvene (**13**)). With the exception of **13** all other fulvenes undergo 1,3-dipolar cycloaddition across the exocyclic double bond to give the hitherto unreported spiro-pyrazoline derivatives (**1–6**, **10–12**). In the case of **13**, however, the addition of 1,3-dipole takes place at the site of endo-cyclic double bond, leading to the formation of a pyrazoline derivative (**14**).

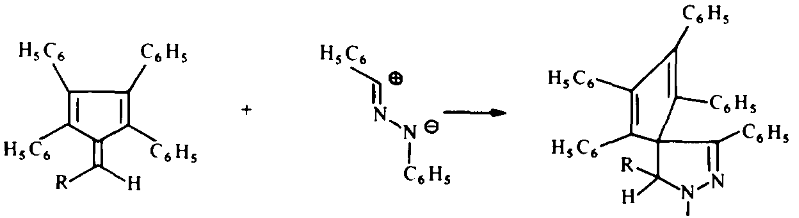
The concept of 1,3-dipolar cycloaddition has been well utilised in the synthesis of a number of heterocyclic compounds by a one-step process.[1,2] Diphenylnitrilimine (DPNI, generated by the dehydrohalogenation of N-chlorobenzylidine-N-phenylhydrazine) which forms a class of 1,3-dipole, acts as a versatile 1,3-dipolar intermediate. As an active dipolarophile it offers a vast scope in the synthesis of 6-membered heterocycles by 1,3-dipolar cycloaddition reaction.[3] It has been well exploited in preparing such compounds by its interaction with alkenes, alkynes, carbonyl compounds and azomethines.[4]

Fulvenes form an interesting class of substrates, in respect of their dual role as an alkene and as well as diene in dipolar cycloaddition reaction.[5] Thus, diazomethane is known to add across the exocyclic or the endocyclic double bond of the fulvene molecule to give the corresponding 1:1 adducts.[6,7] Similar reaction has been described[8] in respect of fulvene and benzonitrile oxide.

RESULTS AND DISCUSSION

In an attempt to extend the scope of 1,3-dipolar cyclo-addition reaction in the synthesis of novel five membered heterocycles, a systematic study of 1,3-dipolar cycloaddition reaction of DPNI with fulvenes was undertaken. These include 2,3,4,5-tetraphenylfulvene (**1**), 9-benzalfluorene (**7**) and their respective analogues (**2**, **3**, **8**, **9**) and 6,6-diphenylfulvene (**13**). Thus **1–3** undergo a facile reaction with DPNI and the reaction time was found to vary depending upon the substituent present in the 6th position of the fulvene (Scheme 1). In the case of **3**, the reaction, however, did not proceed to completion, presumably due to the steric resistance offered by the phenyl group at C_6 of the fulvene molecule. In these reactions, the 1,3-dipolar species was found to add across the exocyclic bond of the fulvenes, leading to the formation of hithero unreported spiropyrazolines, viz 1,3,6,7,8,9-hexaphenyl-2,3-diazaspiro (4.4) nona -1,6,8-triene (**4**), 1,3,6,7,8,9-hexaphenyl-5-methyl-2,3-diazaspiro (4.4) nona-1,6,8-triene (**5**) and 1,3,5,6,7,8,9-heptaphenyl-2,3-diazaspiro (4.4) nona-1,6,8-triene (**6**) respectively.

The structures of the products were fully characterised on the basis of their spectroscopic data. Thus compounds **4**, **5**, **6**, showed UV absorption at 340, 340 and 356 nm respectively which are characteristic of pyrazoline structure. The PMR spectrum of these compounds (**4–6**) exhibited peaks at τ values 6.3 (s, 2H) for methylene protons in **4**, 8.4 (d, 3H, J = 8 Hz), 5.8 (q, 1H, J = 8 Hz) for methyl and methine protons in **5**, 5.1 (s, 1H) for benzylic proton in **6** which are in close agreement with the values reported in literature[9] for a pyrazoline structure. The chemical shift of these protons will be shifted upfield[9] had the addition of



1 R = H
2 R = CH_3
3 R = C_6H_5

4 R = H
5 R = CH_3
6 R = C_6H_5

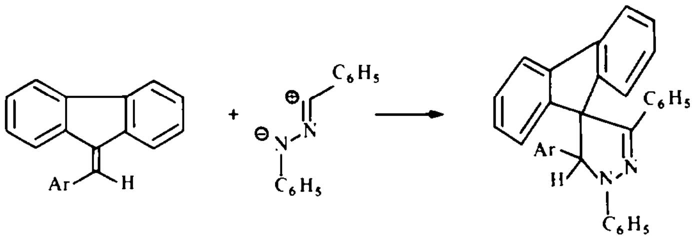
Scheme 1.

Table 1. Reaction of 1,3-diphenylnitrilimine with fulvenes

Starting material (fulvene)	Product (pyra-zoline)	Reaction time (h)	Yield (%)	m.p. (°C)	UV λ_{max}^{MeOH} nm (log ε)	IR cm^{-1} (KBr)	NMR (τ) CDCl$_3$	Mass spectral data (rel. int.) (m/e)
1	**4**	22	90	191–193	340(4.34) 242(4.67)	3060(C–H) 2910, 2860 (CH$_2$) 1595 (C=N) 1565 (C=C)	2.4–3.1 (m, 30H) 6.3 (s, 2H)	576 (M$^+$, 100), 499 (25.6), 397 (17.3), 382 (15.9), 315 (11.8), 302 (43.7), 249 (23.7), 194 (40.6), 104 (6.7), 91 (78.7).
2	**5**	16	87	238–239	340(4.39) 240(4.51)	2930, 2860 (CH$_3$) 1595 (C=N) 1550 (C=C)	2.4–3.1 (m, 30H) 5.8 (q, 1H), 8.4 (d, 3H)	590 (M$^+$, 100), 575 (77.5), 513 (24.2), 471 (14.4), 396 (15.5), 381 (20.1), 302 (53.1), 194 (30.9), 104 (18.6), 91 (47.9).
3	**6**	48	67	135–136	354(4.39) 245(4.56)	3060 (C–H) 1600 (C=N) 1560 (C=C)	2.0–2.83 (m, 35H) 5.1 (s, 1H)	652 (M$^+$, 20.6), 575 (9.9), 296 (14.3), 194 (15.0), 91 (9.7), 77 (38.5), 78 (100).

7	**10**	35	79	175–176	352(3.91) 270(4.04) 222(4.2)	3060 (C–H) 1598 (C=N) 1575 (C=C)	2.3–3.7 (m, 23H) 5.2 (s, 1H)	
8	**11**	30	79	208–210	357(4.77) 270(4.87) 230(4.7)	3060 (C–H) 2920 (C–H) 1590 (C=N) 1560 (C–C)	2.3–3.6 (m, 22H) 5.2 (s, 1H)	482 (M$^+$, 100), 303 (22.7), 281 (15.6), 255 (46.7), 194 (12.4), 178 (57.4), 91 (66.3).
9	**12**	40	70	179–180	352(4.15) 268(4.10) 226(4.56)	3060 (C–H) 2970, 2920 (CH_3) 1595 (C=N) 1558 (C=C)	2.3–3.6 (m, 22H) 5.22 (s, 1H) 7.85 (s, 3H)	462 (M$^+$, 100), 371 (4.8), 255 (45.7), 207 (11.6), 194 (13.0), 165 (13.5), 91 (60.8), 77 (10.0).
13	**14**	40	80	192–193	335(4.65) 289(4.86) 235(4.88)	3060 (C–H) 1598 (C=N) 1560 (C=C)	5.35 (sx, J = 9 Hz) 4.4 (d, 1H, J = 9 Hz) 3.8 (q, 1H, J = 5 Hz) 3.4 (1H).	424 (M$^+$, 99.6), 347 (38.3), 233 (12.3), 194 (23.6), 104 (5.4), 91 (100), 77 (21.8).

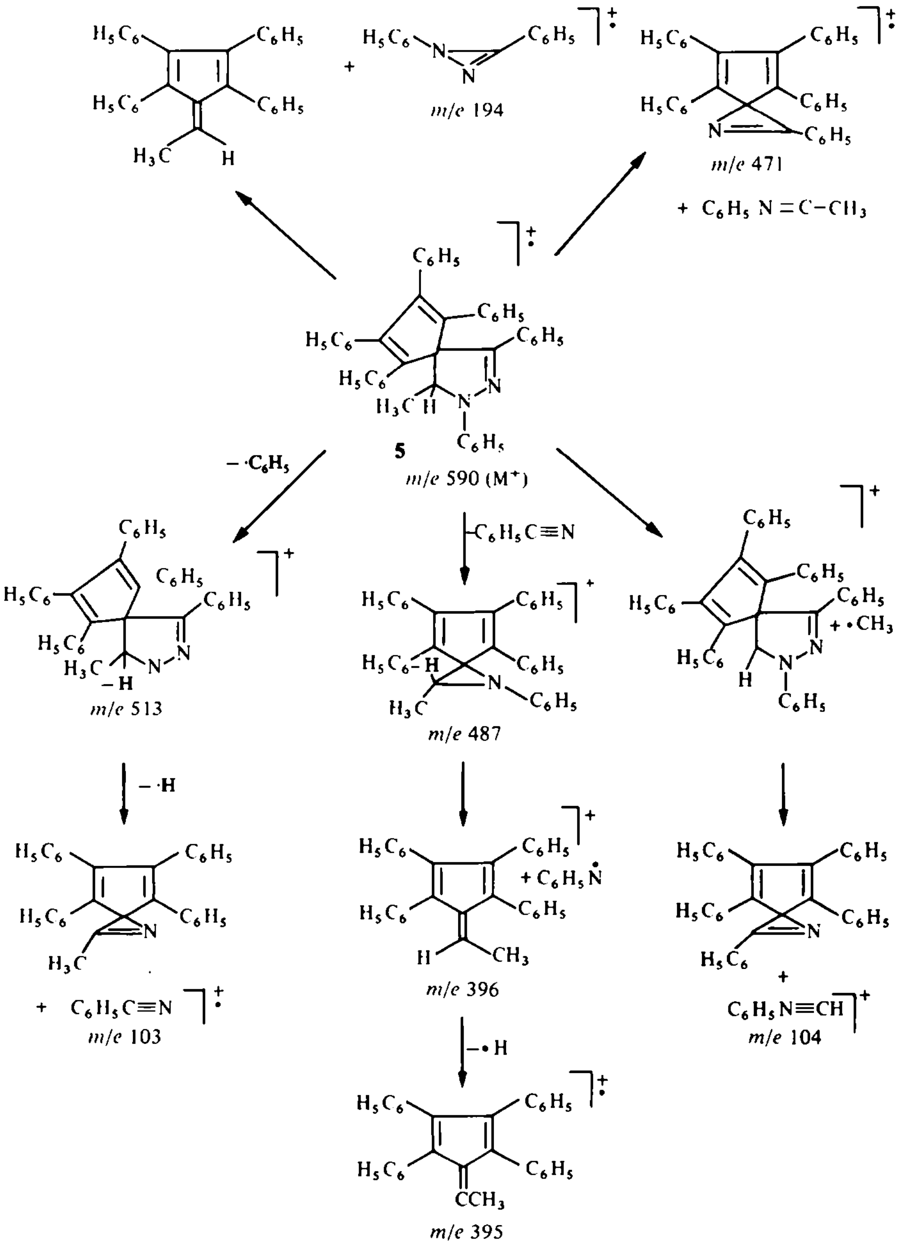
All the compounds gave satisfactory elemental analysis.



7 Ar = C_6H_5
8 Ar = p-ClC_6H_4
9 Ar = p-MeC_6H_4

10 Ar = C_6H_5
11 Ar = p-ClC_6H_4
12 Ar = p-MeC_6H_4

Scheme 2.



Scheme 3.

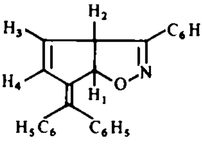
DPNI to the exocyclic double bond taken place in the opposite direction. This rules out the possibility of the formation of other regioisomer.

Likewise DPNI was found to undergo a neat reaction with dibenzofulvenes (**7–9**) to yield the novel spiropyrazolines (**10–12**) (Scheme 2). These compounds exhibited uv absorption around 355, 270 and 220 nm in which 355 nm peak is characteristic of pyrazoline structure. All these compounds showed a strong absorption around 1595 (C=N) in IR spectrum, and a sharp singlet (5.2) in PMR spectrum, due to benzylic methine protons which is in close agreement with the values reported in the literature.[9] The above data taken in conjunction with the mass spectral data confirm the structure of these compounds.

In contrast, the reaction of 6,6-diphenylfulvene (**13**) with DPNI took an entirely different course. The only product isolated (in 80% yield) corresponds to 1 : 1 adduct, based on the analytical and mass spectral data. In this case the reaction may lead to the formation of either (4 + 3) or (3 + 2) adduct (**16** or **17** or **14**) (Scheme 4). Structure **15** is expected if the addition of DPNI were to take place in the opposite direction. The UV spectrum of the product exhibited three maxima viz 355, 289 and 235 nm. The peak at 355 nm indicates the presence of pyrazoline moiety, while the peak at 289 points to the existence of heteroannular diene system.[10] (*cf.* λ_{max} 290 nm for **18**). On the other hand the compound **19** with an isolated double bond has UV absorption at 252 and 242 nm. In view of these facts the possibility of assigning either **16** or **17** as the structure for the adduct is ruled out.

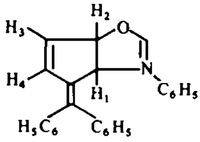
To distinguish between the two regioisomers **14** and **15** we have compared the NMR values of the adduct with those obtained by the cycloaddition reaction of benzonitrile oxide (BNO) with 6,6-diphenylfulvene, reported in Ref. 8. There is a similarity between DPNI and BNO in that the former contains one nitrogen in the place of oxygen in BNO. The following are the observed peaks (in τ value) for our compound in PMR spectrum: H_a, 4.4 (d, J = 9 Hz); H_b, 5.35 (sx, J = 9 Hz); H_c, 3.8 (q, J = 5 Hz); H_d, 3.4 (1H).

These values are in close agreement with the values reported for (the 1 : 1 adduct) **20** than for **21** for which the PMR values are given below. Hence we confirm that DPNI undergo addition in one way only to give exclusively **15**.



20

H_1, 4.66 (d, J = 8 Hz)
H_2, 5.43 (sx, J = 8 Hz)
H_3, 3.94 (q, J = 5.3 Hz)
H_4, 3 61 (q, J = 5.3 Hz)

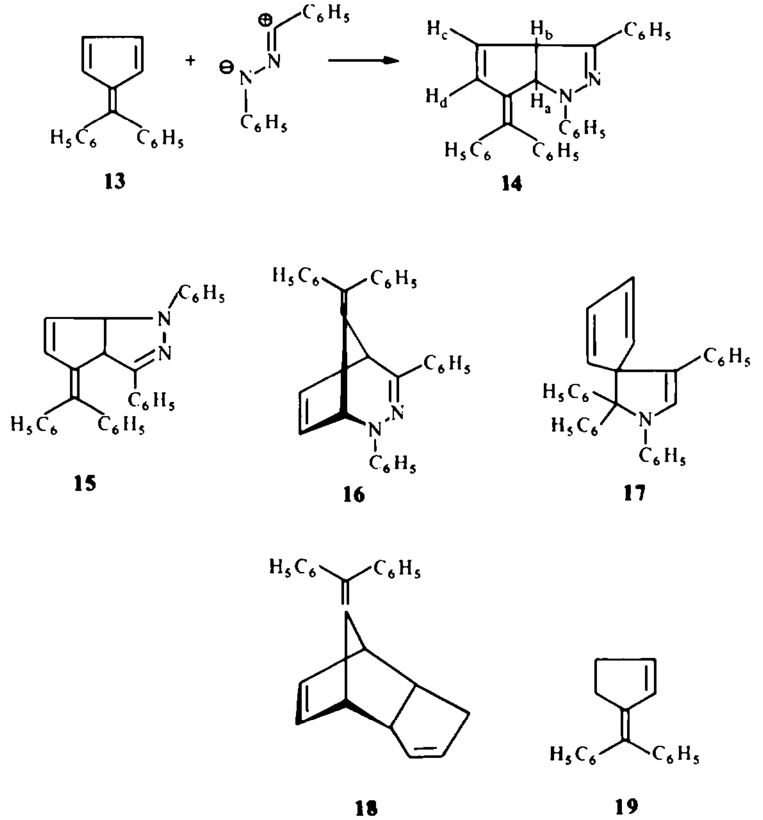


21

H_1, 4.62 (d, J = 8 Hz)
H_2, 4 10 (q, J = 8 Hz)
H_3, 3.88 (q, J = 5.6 Hz)
H_4, 3.42 (d, J = 5.6 Hz)

EXPERIMENTAL

The melting points were taken on Fisher-Johns m.p. apparatus and are uncorrected. Perkin-Elmer-580 infrared spectrophotometer, Cary-17D UV spectrophotometer and Varian 90 MHz spectrometer were used for spectral determinations. The mass spectra were recorded by using Jeol-300D mass spectrometer.



Scheme 4.

Benz-N-phenylhydrazidoyl chloride,[4] tetraphenylfulvenes,[12] dibenzolfulvenes[12] and 6,6-diphenylfulvenes were prepared according to the procedures described in Ref. 12.

Reaction of fulvenes with 1,3-*diphenylnitrilimines*

Triethylamine (0.3 ml) was added to a magnetically stirred solution of the fulvene (1 mmol) and N-phenylbenzhydrazidoyl chloride (0.230 g) in dry benzene (10 ml). The completion of the reaction was monitored by TLC. From the reaction mixture the solid triethylamine hydrochloride was removed by filtration. The evaporation of the solvent from the filtrate, under diminished pressure, yielded a solid. Silica gel chromatography of the solid using petroleum ether (60–80°) as an eluting solvent, furnished the pure product. The pyrazolines where then crystallized from methanol, in yellow needles. Table 1 summarizes the reaction time, yield, melting point and spectral data for the pyrazolines prepared in the present investigation.

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