

Reaction of N^1,N^2 -Diarylacetamidines with
(2,4,7-Trinitro-9*H*-fluoren-9-ylidene)propanedinitriles

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Novel spiro[fluorene-9,4'-(1',2',3',4'-tetrahydropyridine)]-5'-carbonitriles **6a-c** have been obtained from the reaction of N^1,N^2 -diarylacetamidines **1a-c** with (2,4,7-trinitro-9*H*-fluoren-9-ylidene)propanedinitrile (**2**) in ethyl acetate solutions at ambient temperature for **6a,b** or under reflux for **6c**, respectively.

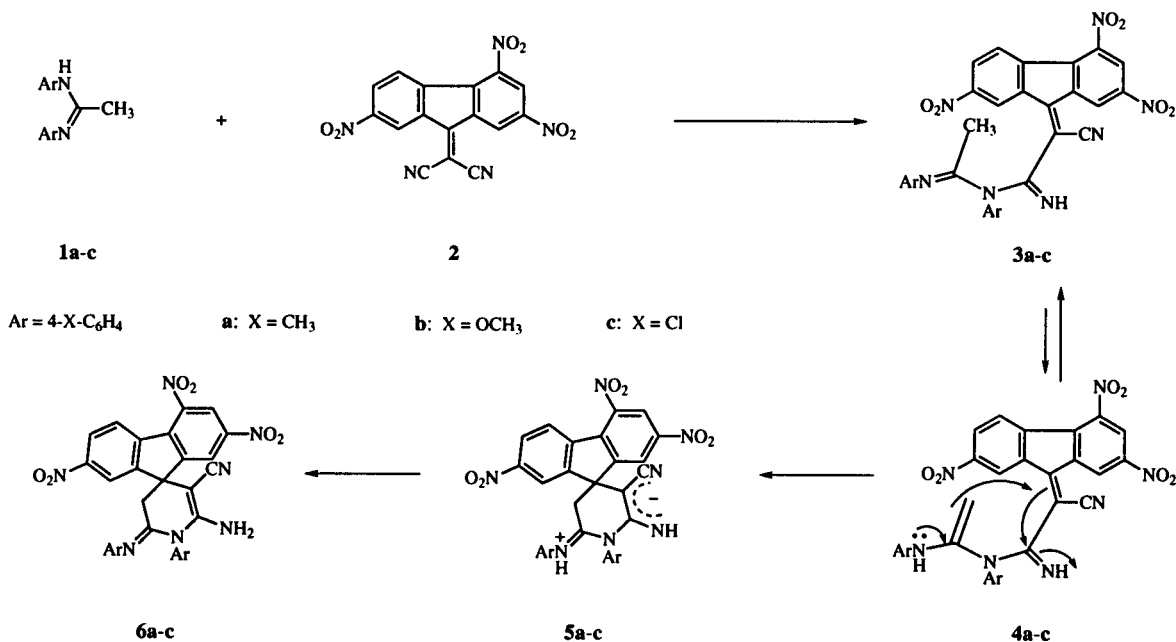
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The reaction of N^1,N^2 -diarylformamidines and -acetamidines with π -acceptors, like 2,3,5,6-tetrachlorobenzoquinone, 2,3-dichloro-1,4-naphthoquinone, and 2-(dicyanomethylene)indane-1,3-dione gave rise to several new heterocyclic compounds [1,2]. With 2-(2-oxo-2,3-dihydro-1*H*-indol-2-ylidene)propanedinitrile, two novel 2-oxospiro[(2,3-dihydro-1*H*-indole)-3,4'-(1',2',3',4'-tetrahydropyridine)]-5'-carbonitriles could be obtained by reaction of the former with two N^1,N^2 -diarylacetamidines [2]. The same biologically important spiro skeleton has independently been synthesized [3] from other starting materials. In this work we report another access to this spirocyclic system *via* the reaction of (2,4,7-trinitro-9*H*-fluoren-9-ylidene)propanedinitrile (**2**) with N^1,N^2 -diarylacetamidines **1a-c**.

It had been reported earlier, that **2** and other 9-dicyanomethylenenitrofluorene derivatives react with secondary amines with subsequent *substitution* of cyano groups by amino groups to afford nitro-substituted 9-aminomethylenefluorene compounds [4]. In contrast, we have found an addition of N^2 of the amidine to one of the cyano groups, followed by intramolecular conjugate addition of the methylene-active α -carbon atom of the acetamide moiety to C-9 of the fluorene.

Ethyl acetate solutions of **2**, when added to solutions of acetamidines **1a,b** in the same solvent and left standing overnight at room temperature, gave the novel spiro[(9*H*-fluorene)-9,4'-(1',2',3',4'-tetrahydropyridine)]-5'-carbonitriles **6a,b** in 56 and 63% yields, respectively. Compound **1c**, on the other hand, required 4 hours of reflux of the combined solutions to give 59% yield of **6c**.

Scheme 1



The structural assignment of **6a-c** is based on the following data: ^{13}C -DEPT-spectra exhibited one negative signal each between 34.4 and 34.6 ppm confirming the presence of a CH_2 group, ^{13}C signals between 48.4 and 48.8 ppm were assigned to the spiro carbon atoms and those between 118.5 and 119.5 to the cyano group. It should be mentioned that the position of the signals of the olefinic C-atoms bearing the cyano groups, *i.e.* C-3 in **6a-c**, show up at relatively high field (between 54.8 and 55.2 ppm). Precedence for this unexpected upfield shift of the $\beta\text{-sp}^2$ carbon atom attached to the nitrile group in a 3-aminopropenenitrile has been previously reported [5,6]. The ^1H nmr spectra revealed AB patterns with δ_{A} in the range of 3.09-3.13, δ_{B} in the range of 3.19-3.25 ppm, and $|\Delta J|$ between 14.80 and 14.89 Hz, which indicates that the methylene protons are diastereotopic, in addition to signals between 6.11 and 6.39 for NH_2 protons. The ir spectra showed characteristic absorptions for the amino group between 3463 and 3317 and between 2184 and 2178 for CN (for more details see the Experimental).

Formation of these spiro compounds **6a-c** may be rationalized by a nucleophilic attack of N^2 of **1a-c** on one CN group of **2** giving rise to **3a-c** being in equilibrium with **4a-c**. The terminal methylene carbon atoms of the tautomers **4a-c** exhibit their nucleophilic character by attacking C-9 and thereby products **6a-c** are formed.

Since acetamidines may react like secondary amines with **2** [1], one might at first glance expect that one of the cyano groups is replaced by N^2 . But due to their ambident nature acetamidines behave like ketene amins or enamines [7] in a Michael type addition towards the ylidene malononitrile derivatives. Therefore acetamidines as **1a-c** allow for the synthesis of new spiro pyridine derivatives by their reaction with the title dicyanomethylene compound **2**. Structurally related spiro pyrans [8,9] have also been reported.

EXPERIMENTAL

The uncorrected melting points were determined on a Reichert Thermovar hot stage microscope. Elemental analyses were obtained on a Carlo Erba 1106 CHN analyzer, while the ir (potassium bromide) were recorded on a Perkin Elmer 983 spectrophotometer. The 300 MHz ^1H and 75 MHz ^{13}C nmr spectra were observed on a Bruker WM 300 instrument with tetramethylsilane as the internal standard using dimethylsulfoxide- d_6 as solvent. The ^{13}C signals were assigned on the basis of DEPT 135/90 spectra. The mass spectra (70 eV, electron impact mode) were recorded on an AMD 604 instrument. Preparative layer chromatography (plc) used air dried 1.0 mm thick layers of slurry applied silica gel Merck PF₂₅₄ on 48 cm wide and 20 cm high glass plates and toluene-ethyl acetate (10:1) as developing solvent. Zones were detected by their color or by quenching of indicator fluorescence upon exposure to 254 nm light and eluted with acetone or ethyl acetate.

Starting Materials.

(2,4,7-Trinitro-9H-fluorene-9-ylidene)propanedinitrile (**2**), previously referred to as 9-dicyanomethylene-2,4,7-trinitrofluorene, was used as received from Acros Chimica. N^1, N^2 -Diarylacetamidines **1a-c** were prepared according to literature procedures [10].

Reaction of Acetamidines **1a-c** with **2**.

A solution of **2** (0.5 mmole) in 5 ml of dry ethyl acetate is added dropwise to a solution of the acetamidine **1a-c** (0.5 mmole) in 5 ml of dry ethyl acetate at room temperature. In the case of **1a,b**, the solution is kept at room temperature overnight, while in the case of **1c** the solution is heated at reflux for 4 hours. The reaction mixture assumed a deep green color and was concentrated *in vacuo* and subjected to plc. The main zones in every case contained compounds **6a**, **6b**, and **6c**, respectively.

6'-Amino-1'-(4-methylphenyl)-2'-(4-methylphenylimino)-2,4,7-trinitrospiro[fluorene-9,4'-(1',2',3',4'-tetrahydropyridine)]-5'-carbonitrile (**6a**).

This compound was obtained (170 mg, 56%) as orange crystals (ethanol) mp 320°; ir: ν 3463, 3317 (NH_2), 2185 (CN), and 1344 (NO_2) cm^{-1} ; ^1H nmr: δ 2.05 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), AB-system (δ_{A} 3.09, δ_{B} 3.19, $|\Delta J|$ 14.80 Hz, CH_2), 6.11 (s, 2H, NH_2), 6.21, 6.83, 7.38, 7.45, 8.10, 8.38, 8.40, 8.54, 8.79 and 8.84 (all m, 13H, aryl); ^{13}C nmr: δ 20.3 and 21.0 (CH_3), 34.6 (C-3'), 48.7 (C-9 = C-4'), 55.1 (C-5'), 118.9, 120.1, 123.0, 124.7, 127.0, 129.4, 129.5 and 130.7 (all aryl CH), 119.2 (CN), 131.9 and 134.3 (aryl CCH_3), 134.6 and 138.4 (aryl C-N), 138.5 (C-4a), 145 (C-8a), 145.2 (C-9a), 147.9 (C-4b); 149.0, 153.3, and 153.7 (C-2, C-4, C-7), 155.3 (C-6') and 156.7 (C-2'); ms: m/z 601 (M^+), 584, 496, 363, 238, 132, 107, 91, 44.

Anal. Calcd. for $\text{C}_{32}\text{H}_{23}\text{N}_7\text{O}_6$: C, 63.89; H, 3.85; N, 16.30. Found: C, 63.82; H, 3.94; N, 16.14.

6'-Amino-1'-(4-methoxyphenyl)-2'-(4-methoxyphenylimino)-2,4,7-trinitrospiro[fluorene-9,4'-(1',2',3',4'-tetrahydropyridine)]-5'-carbonitrile (**6b**).

This compound was obtained (200 mg, 63%) as orange crystals (dioxane), mp 330-332°; ir: ν 3437, 3342 (NH_2), 2178 (CN), 1344 (NO_2) cm^{-1} ; ^1H nmr: AB-system (δ_{A} 3.13, δ_{B} 3.25, $|\Delta J|$ 14.80 Hz, CH_2), 3.52 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 6.14 (s, 2H, NH_2), 6.27, 6.60, 7.19, 7.41, 8.10, 8.39, 8.41, 8.53, 8.78 and 8.84 (all m, 13H, aryl), ^{13}C nmr: δ 34.5 (C-3'), 48.8 (C-9 = C-4'), 54.9 (C-5'), 55.1 and 55.6 (OCH_3), 114.3, 115.4, 118.9, 120.9, 121.3, 123.0, 124.7, 127.1, and 130.8 (all aryl CH), 119.5 (CN), 129.4 and 134.7 (aryl C-N), 138.3 (C-4a), 140.9 (C-8a), 145.1 (C-9a), 147.9 (C-4b), 149.1, 153.8 and 153.8 (C-2, C-4, C-7), 155.3 and 155.5 (aryl C- OCH_3), 157 (C-6') and 159.5 (C-2'); ms: m/z 633 (M^+), 512, 453, 363, 332, 270, 148, 123, 77.

Anal. Calcd. for $\text{C}_{32}\text{H}_{23}\text{N}_7\text{O}_8$: C, 60.66; H, 3.66; N, 15.48. Found: C, 60.60; H, 3.79; N, 15.42.

6'-Amino-1'-(4-chlorophenyl)-2'-(4-chlorophenylimino)-2,4,7-trinitrospiro[fluorene-9,4'-(1',2',3',4'-tetrahydropyridine)]-5'-carbonitrile (**6c**).

This compound was obtained (190 mg, 59%) as orange crystals (dioxane); mp 220-222°; ir: ν 3477 and 3375 (NH_2), 2184 (CN), 1344 (NO_2) cm^{-1} ; ^1H nmr: AB-system (δ_{A} 3.13, δ_{B} 3.25, $|\Delta J|$ 14.89 Hz, CH_2), 6.39 (s, 2H, NH_2), 6.38, 7.09, 7.54, 7.70, 8.10, 8.41, 8.49, 8.74 and 8.85 (all m, 13H, aryl); ^{13}C nmr: δ

34.4 (C-3'), 48.4 (C-9 = C4'), 55.2 (C-5'), 118.6, 120.6, 121.8, 122.6, 124.5, 126.7, 128.7, 129.9 and 131.4 (all aryl CH), 118.9 (CN), 127.0 and 133.4 (aryl CCl), 134.4 and 135.7 (aryl C-N), 138.3 (C-4a), 144.7 (C-8a), 146.3 (C-9a), 147.6 (C-4b), 148.8, 153.2, and 153.9 (C-2, C-4, C-7), 154.9 (C-6'), 156.2 (C-2'); ms: *m/z* 642 (M⁺), 516, 424, 363, 333, 278, 152, 127, 111, 75.

Anal. Calcd. for C₃₀H₁₇Cl₂N₇O₆: C, 56.08; H, 2.67; N, 15.26. Found: C, 56.08; H, 2.77; N, 14.96.

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