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Reaction of Arylnitroso Derivatives: Synthesis of Arylimino 2,5-Dihydrofuran and Arylamino Fulvenes Derivatives

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Abstract

Herein we report the reactivity of N-(2,4-dicyano-1,5-dimethyl-3-arylcyclopenta-2,4-dienyl)-2,2,2-trifluoroacetamides and N,N-dimethyl-4-nitrosoaniline which provide compounds derived from Ehrlich-Sachs condensation, dihydrofuran derivatives and fulvene derivatives by adjusting the reaction conditions.

Keywords

Cyclopentadienes, Nitrsoarenes, Dihydrofuran, Fulvenes

1. Introduction

Densely functionalized cyclopentadienes **1** were recently prepared [1] and exploited as useful building blocks in synthetic chemistry. We have previously reported, in a preliminary account, the preparation of notable compounds using **1** as starter material. These syntheses involved the cycloaddition of **1** with a suitable reagent, followed by rearrangement (**Figure 1**) [2]. As an expansion of this study, we focused on arylnitroso derivatives as potential reagents for cyclopentadiene **1**. Arylnitroso species were shown to give numerous reactions with unsaturated molecules, including cycloadditions and Aldol Michael [3]-[9]. In this context, the formation of 1,2-oxazines would be of wide importance, due to the possibility of further chemical elaboration of this structure to access important scaffolds [10]. Herein we report our studies on the reactivity of N-(2,4-dicyano-1,5-dimethyl-3-phenylcyclopenta-2,4-dienyl)-2,2,2-trifluoroacetamide and p-NO_2, 2,4-di-NO_2, p-OMe phenyl derivatives in presence of nitrosobenzene or *N*,*N*-dimethyl-4-nitrosoaniline. This reaction is showed to give different products in dependence of the experimental conditions applied.

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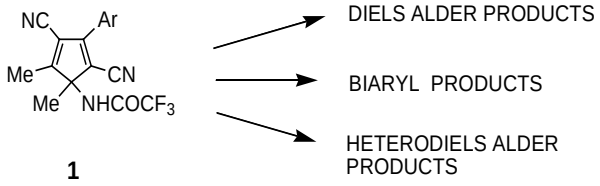


Figure 1. Synthetic target from cyclopentadiene **1**.

2. Experimental

2.1. Chemicals and Instruments

General: Melting point was measured with a Kofler apparatus and was uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded at 400.13 MHz and 100.13 MHz on a Bruker Advance DPX400. Chemical shifts are reported relative to tetramethylsilane at 0.00 ppm. ESI-MS spectra were recorded with a LCQ-DECA Thermo Finnigan instrument. TLC was performed on precoated 4 × 6.7 silica gel 60 F254 plates silica gel on aluminum (Aldrich) with detection by UV light. Column chromatography was carried out on Silica gel (E. Merck, 0.040 - 0.063 mm). Microwave irradiations were conducted using a CEM Discover Synthesis Unit. Elemental analyses were performed on a Perkin Elmer PE 2004 Elemental Analyzer.

2.2. General Method for the Preparation of Compounds 3a-d

A mixture of compounds **1a-d** (0.1 mmol) and N,N-dimethyl-4-nitrosoaniline **2** (0.12 mmol) in CH_2Cl_2 (3 ml) was stirred at room temperature for a week or in Sovirel tube in bath oil at 60˚C for 7 h. Alternatively the same mixture was heated under MW irradiation, (150 W) for 90 minutes. The crude reaction was purified by column chromatography (ethyl acetate/petroleum ether 1/4).

2(5*Z*)-5-((4-*dimethylamino*) *phenylimino*)-2*acetyl*-2-*dihydro*-2-*methyl*-4-*phenylfuran*-3-*carbonitrile* (**3a**)

Red oil (40% yield) ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.80 (s, 3H, Me), 2.29 (s, 3H, Me), 2.98 (s, 6H, NMe_2), 6.70 (d, 2H, J = 8.8 Hz, Ph), 7.47 - 7.53 (m, 5H, Ph), 8.00 - 8.07 (m, 2H, Ph). ^{13}C-NMR ($CDCl_3$): δ (ppm) 21.52, 24.67, 40.43, 92.33, 110.15, 112.03, 113.18, 118.44, 127.16, 129.38, 129.46, 131.29, 133.40, 147.08, 149.05, 152.49, 203.25. MS (ESI): 360 ($M+H^+$); Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69; Found: C, 73.28; H, 5.90; N, 11.73.

2'(5*Z*)-5-((4-*dimethylamino*) *phenylimino*)-2-*acetyl*-2,5-*dihydro*-2-*methyl*-4-(4'-*nitrophenyl*)*furan*-3-*carbo nitrile* (**3b**)

Crystalline red solid (35% yield) (m.p. 146˚C - 147˚C) ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.83 (s, 3H, Me), 2.33 (s, 3H, Me), 2.99 (s, 6H, NMe_2), 6.69 (d, 2H, J = 9.0 Hz, Ph), 7.51 (d, 2H, J = 9.0 Hz, Ph), 8.20 (d, 2H, J = 8.8 Hz, Ph), 8.32 (d, 2H, J = 8.8 Hz, Ph). ^{13}C-NMR ($CDCl_3$): δ (ppm) 21.81, 24.90, 40.26, 92.82, 110.73, 111.04, 111.94, 123.56, 127.47, 130.62, 132.73, 134.03, 144.86, 148.90, 151.21, 151.62, 202.78. MS (ESI): 405 ($M+H^+$); Anal. Calcd for $C_{22}H_{20}N_4O_4$: C, 63.34; H, 4.98; N, 13.85; Found: C, 63.55; H, 4.96; N, 13.89.

2'(5*Z*)-5-((4-*dimethylamino*)*phenylimino*)-2-*acetyl*-2,5-*dihydro*-2–*methyl*-4-(2'-4'-*nitrophenyl*)*furan*-3-*carbo nitrile* (**3c**)

Blu solid (20% yield) (m.p. 149˚C - 151˚C) ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.97 (s, 3H, Me), 2.15 (s, 3H, Me), 3.08 (s, 6H, NMe_2), 6.70 (d, 2H, J = 8.8 Hz, Ph), 7.36 (d, 2H, J = 8.8 Hz, Ph), 7.96 (d, 1H, J = 8.4 Hz, Ph), 8.67 (d, 1H, J_o = 8.4 Hz J_m = 1.6 Hz, Ph), 9.20 (bs, 1H). MS (ESI): 450 ($M+H^+$); Anal. Calcd for $C_{22}H_{20}N_5O_6$: C, 58.80; H, 4.26; N, 15.58; Found: C, 59.00; H, 4.24; N, 21.43.

2'(5*Z*)-5-((4-*dimethylaminophenylimino*)-2-*acetyl*-2,5-*dihydro*-2-*methyl*-4-(4'-*methoxyphenyl*)*furan*-3-*carbon itrile* (**3d**)

Crystalline orange-red solid (50% yield) (m.p. 148˚C - 150˚C) ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.77 (s, 3H, Me), 2.26 (s, 3H, Me), 2.98 (s, 6H, NMe_2), 3.86 (s, 3H, OMe), 6.69 (d, 2H, J = 8.8 Hz, Ph), 6.99 (d, 2H, J = 8.8 Hz, Ph), 7.49 (d, 2H, J = 8.8 Hz, Ph), 8.13 (d, 2H, J = 8.8 Hz, Ph). ^{13}C-NMR ($CDCl_3$): δ (ppm) 21.48, 24.58, 40.50, 55.45, 92.14, 112.15, 113.14, 114.08, 116.07, 120.64, 127.05, 131.33, 133.67, 146.13, 149.04, 153.01, 162.13, 203.34. MS (ESI): 390 ($M+H^+$); Anal. Calcd for $C_{23}H_{23}N_3O_3$: C, 70.93; H, 5.95; N, 10.79; Found: C, 71.16; H, 5.93; N, 10.82.

2.3. General Method for the Preparation of Compounds 4a-d, 5a-d, 6a-d

Compounds **1a-d** (0.1 mmol) and N,N-dimethyl-4-nitroso aniline **2** (0.12 mmol) were heated under MW irradiation at 150˚C for 15 minutes, 150 W solvent free or were heated in Sovirel tube in oil bath at 110˚C, solvent free for 3 h. The crude reaction was purified by column chromatography (ethyl acetate/petroleum ether 1/4).

(5*Z*)-5-((4-(*dimethylamino*)*phenylamino*)*methylene*)-4-*methyl*-2-*phenylcyclopenta*-1,3-*diene*-1,3-*dicarbonitrile* (**4a**)

Crystalline red solid (25% yield) m.p. 255˚C - 258˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.46 (s, 3H, Me), 2.99 (s, 6H, NMe_2), 6.73 (d, 2H, J = 8.6 Hz, Ph), 7.13 (d, 2H, J = 8.6 Hz, Ph), 7.38 (d, 1H, J = 7.5 Hz, Ph), 7.45 (t, 2H, J = 7.5 Hz, Ph), 7.76 (d, 2H, J = 7.5 Hz, Ph), 7.89 (d, 1H, J = 15.0 Hz), 9.30 (d, 1H, J = 15.0 Hz, NH). ^{13}C-NMR ($CDCl_3$): δ (ppm) 11.85, 40.46, 101.51, 112.89, 115.89, 117.22, 119.44, 120.91, 126.96, 127.82, 128.86, 132.50, 142.61, 146.51, 147.34, 149.54. MS (ESI): 353 ($M+H^+$); Anal. Calcd for $C_{23}H_{20}N_4$: C, 78.38; H, 5.72; N, 15.90; Found: C, 78.63; H, 5.70; N, 15.86.

(*Z*)-*N*-((2,4-*dicyano*-5-*methyl*-3-*phenyl*-5-(2,2,2-*trifluoroacetamido*)*cyclopenta*-1,3-*dien*-1-*yl*)*methylene*)-4-(*dimethylamino*)*aniline oxide* (**5a**)

Red-violet solid (20% yield) m.p. 205˚C - 208˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.1 (s, 3H, Me), 3.07 (s, 6H, NMe_2), 6.65 (d, 2H, J = 9.4 Hz, Ph), 7.64 (d, 2H, J = 9.4 Hz, Ph), 7.48 - 7.53 (m, 3H, Ph), 7.72 - 7.75 (m, 2H, Ph), 8.11 (s, 1H), 8.20 (s, 1H, NH). MS-ESI: 480 ($M+H^+$), 502 ($M+Na^+$); Anal. Calcd for $C_{25}H_{20}F_3N_5O_2$: C, 62.63; H, 4.20; N, 14.61. Found: C,62.60; H,4.22; N,14.63.

N-(2-((*E*)-(4-(*dimethylaminophenylimino*)*methyl*)-3,5-*dicyano*-1-*methyl*-4-*phenylcyclopenta*-2,4-*dienyl*)-2,2,2-*trifluoroacetamide* (**6a**)

Blu-violet solid (22% yield) m.p. 215˚C - 218˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.91 (s, 3H, Me), 3.06 (s, 6H, NMe_2), 6.69 (d, 2H, J = 9.0 Hz, Ph), 7.06 (s, 1H, NH), 7.35 (d, 2H, J = 9.0 Hz, Ph), 7.48 - 7.54 (m, 3H, Ph), 7.76 - 8.01 (m, 2H, Ph), 8.65 (s, 1H). MS-ESI: 464 ($M+H^+$); Anal. Calcd for $C_{25}H_{20}F_3N_5O$: C, 64.79; H, 4.35; N, 15.11. Found: C, 65.00; H, 4.33; N, 15.07.

(5*Z*)-5-((4-*dimethylamino*)*phenylamino*)*methylene*)-4-*methyl*-2-(*nitrophenyl*)*cyclopenta*-1,3-*diene*-1,3-*dicarbonitrile* (**4b**)

Red-orange solid (23% yield) m.p. 280˚C - 282˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.48 (s, 3H, Me), 3.01 (s, 6H, NMe_2), 6.72 (d, 2H, J = 9.0 Hz, Ph), 7.15 (d, 2H, J = 9.0 Hz, Ph), 7.91 (d, 2H, J = 8.8 Hz, Ph), 7.97 (d, 1H, J = 15.2 Hz), 8.31 (d, 2H, J = 8.8 Hz, Ph), 9.47 (d, 1H, J = 15.2 Hz, NH). MS-ESI: 396 ($M-H^+$); Anal. Calcd for $C_{23}H_{19}N_5O_2$: C, 69.51; H, 4.82; N, 17.62. Found: C, 69.38; H, 4.83; N, 17.59.

(*Z*)-*N*-((2,4-*dicyano*-5-*methyl*-3-(4-*nitrophenyl*)-5-(2,2,2-*trifluoroacetamido*)*cyclopenta*-1,3-*dien*-1-*yl*)*methylene*)-4-(*dimethylamino*)*aniline oxide* (**5b**)

Blu solid (20% yield) m.p. 169˚C - 171˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.12 (s, 3H, Me), 3.08 (s, 6H, NMe_2), 6.65 (d, 2H, J = 9.4 Hz, Ph), 7.65 (d, 2H, J = 9.4 Hz, Ph), 7.89 (d, 2H, J = 8.6 Hz, Ph), 8. 13 (s, 1H), 8.28 (s, 1H, NH), 8.37 (d, 2H, J = 8.6 Hz, Ph). MS-ESI: 525 ($M+H^+$) Anal. Calcd for $C_{25}H_{19}F_3N_6O_4$: C, 57.25; H, 3.65; N, 16.02. Found: C, 57.43; H, 3.66; N, 16.05.

N-(2-((*E*)-(4-(*dimethylamino*)*phenylimino*)*methyl*-3,5-*dicyano*-1-*methyl*-4-(4-*nitrphenyl*)*cyclopenta*-2,4-*dienyl*)-2,2,2-*trifluoacetamide* (**6b**)

Blu-violet solid (20% yield) m.p. 116˚C - 118˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.93 (s, 3H, Me), 3.08 (s, 6H, NMe_2), 6.70 (d, 2H, J = 9.0 Hz, Ph), 7.37 (d, 2H, J = 9.0 Hz, Ph), 7.94 (d, 2H, J = 8.8 Hz, Ph), 8.39 (d, 2H, J = 8.8 Hz, Ph), 8.64 (s, 1H). MS-ESI: 509 ($M+H^+$); Anal. Calcd for $C_{25}H_{19}F_3N_6O_3$: C, 59.06; H, 3.77; N, 16.53. Found: C, 59.25; H, 3.75; N, 16.57.

(5*Z*)-5-((4-(*dimethylamino*)*phenyamino*)*methylene*)-4-*methyl*-2-(2,4-*dinitrophenyl*)*cyclopenta*-1,3-*diene*-1,3-*dicarbonitrile* (**4c**)

Red-orange solid (28% yield) m.p. 155˚C - 157˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.48 (s, 3H, Me), 2.99 (s, 6H, NMe_2), 5.25 (bs, 1H, NH), 6.73 (d, 2H, J = 8.8 Hz, Ph), 7.19 (d, 2H, J = 8.8 Hz, Ph), 7.71 (d, 1H, J_o = 8.6 Hz, Ph), 8.11 (d, 1H, J = 13.6 Hz,), 8.48 (dd, 1H, J_o = 8.6 Hz, J_m = 1.6 Hz, Ph), 8.85 (d, 1H, J_m = 1.6 Hz, Ph). MS-ESI: 441 ($M-H^+$); Anal. Calcd for $C_{23}H_{18}N_6O_4$: C, 62.44; H, 4.10; N, 19.00. Found: C, 62.64; H, 4.08; N, 19.02.

(*Z*)-*N*-((2,4-*dicyano*-5-*methyl*-3-(2,4-*dinitrophenyl*)-5-(2,2,2-*trifluoroacetamido*)*cyclopenta*-1,3-*dien*-1-*yl*)*methylene*)-4-(*dimethyl amino*)*aniline oxide* (**5c**)

Blu-violet solid (25% yield) m.p. 177˚C - 179˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.16 (s, 3H, Me), 3.07 (s, 6H, NMe_2), 6.65 (d, 2H, J = 9.2 Hz, Ph), 7.64 (d, 2H, J = 9.2 Hz, Ph), 7.97 (d, 1H, J_o = 8.4 Hz, Ph), 8.04 (s, 1H),

8.63 - 8.66 (m, 2H, NH, Ph), 9.17 (d, 1H, J_m = 2.0 Hz, Ph). ^{13}C-NMR ($CDCl_3$): δ (ppm) 19.45, 40.24, 68.60, 111.26, 112.09, 112.18, 114.00, 116.63, 119.29, 121.14, 122.93, 124.545, 129.15, 131.05, 133.71, 136.11, 146.86, 147.17, 149.44, 152.73, 153.92, 156.70. MS-ESI: 592 (M+Na), 568 (M-H$^+$); Anal. Calcd for $C_{25}H_{18}F_3N_7O_6$: C, 52.73; H, 3.19; N, 17.22. Found: C, 52.90; H, 3.21; N, 17.27.

N-(2-((*E*)-(4-(*dimethylamino*)*phenylimino*)*methyl*)-3,5-*dicyano*-1-*methyl*-4-(2,4-*dinitrophenyl*)*cyclopenta*-2,4-*dienyl*)-2,2,2-*trifluoroacetamide* (**6c**)

Blu solid (24% yield) m.p. 110˚C - 112˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.97 (s, 3H, Me), 3.08 (s, 6H, NMe_2), 6.70 (d, 2H, J = 9.0 Hz, Ph), 7.36 (d, 2H, J = 9.0 Hz, Ph), 7.96 (d, 1H, J_o = 8.0 Hz, Ph), 8.56 (s, 1H), 8.67 (dd, 1H, J_o = 8.0 Hz, J_m = 2.0 Hz, Ph), 9.20 (d, 1H, J_m = 2.0 Hz, Ph). ^{13}C-NMR ($CDCl_3$): δ (ppm) 23.04, 29.66, 40.25, 67.96, 111.82, 112.09, 114.07, 120.31, 121.16, 124.83, 129.07, 131.27, 133.72, 137.44, 140.13, 146.91, 149.06, 149.44, 152.13, 158.98, 166.58. MS-E SI: 576 (M+Na), 552 (M-H$^+$); Anal. Calcd for $C_{25}H_{18}F_3N_7O_5$: C, 54.25; H, 3.28; N, 17.72. Found: C, 54.12; H, 3.29; N, 17.66.

(5*Z*)-5-((4-(*dimethylamino*)*phenylamino*)*methylene*)2-(4-*methoxyphenyl*)-4-*methylcyclopenta*-1,3-*diene*-1,3-*di carbonitrile* (**4d**)

Red-orange solid (27% yield) m.p. 215˚C - 218˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.45 (s, 3H, Me), 2.99 (s, 6H, NMe_2), 3.84 (s, 3H, OMe), 6.72 (d, 2H, J = 8.8 Hz, Ph), 6.99 (d, 2H, J = 8.8 Hz, Ph), 7.12 (d, 2H, J = 8.8 Hz, Ph), 7.74 (d, 2H, J = 8.8 Hz, Ph), 7.85 (d, 1H, J = 14.8 Hz), 9.22 (d, 1H, J = 14.8 Hz, NH). MS-ESI: 383 (M+H$^+$); Anal. Calcd for $C_{24}H_{22}N_4O$: C, 75.37; H, 5.80; N, 14.65. Found: C, 75.50; H, 5.78; N, 14.68.

(*Z*)-*N*-((2,4-*dicyano*-5-*methyl*-3-(4-*methoxyphenyl*)-5-(2,2,2-*trifluoroacetamido*)*cyclopenta*-1,3-*dien*-1*yl*)*meth ylene*)-4-(*dimethylamino*)*aniline oxide* (**5d**)

Blu-violet solid (18% yield) m.p. 201˚C - 203˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.09 (s, 3H, Me), 3.06 (s, 6H, NMe_2), 3.85 (s, 3H, OMe), 6.65 (d, 2H, J = 8.8 Hz, Ph), 7.01 (d, 2H, J = 8.8 Hz, Ph), 7.63 (d, 2H, J = 8.8 Hz, Ph), 7.73 (d, 2H, J = 8.8 Hz, Ph), 8.01 (s, 1H), 8.23 (s, 1H, NH). MS-ESI: 510 (M+H$^+$); Anal. Calcd for $C_{26}H_{22}F_3N_5O_3$: C, 61.29; H, 4.35; N, 13.75. Found: C, 61.45; H, 4.36; N, 13.71.

N-(2-((*E*)-(4-(*dimethylamino*)*phenylimino*)*methyl*-3,5-*dicyano*-4-(4-*methoxyhenyl*)-1-*methylcyclopenta*-2,4-*di enyl*)-2,2,2-*trifluoro acetamide* (**6d**)

Blu-violet solid (20% yield) m.p. 235˚C - 240˚C ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.89 (s, 3H, Me), 3.06 (s, 6H, NMe_2), 3.86 (s, 3H, OMe), 6.69 (d, 2H, J = 8.8 Hz, Ph), 7.01 - 7.05 (m, 3H, NH, Ph), 7.35 (d, 2H, J = 9.0 Hz, Ph), 7.79 (d, 2H, J = 9.0 Hz, Ph), 8.64 (s, 1H). MS-ESI: 516 (M+Na); Anal. Calcd for $C_{26}H_{22}F_3N_5O_2$: C, 63.28; H, 4.49; N, 14.19. Found: C, 63.47; H, 4.47; N, 14.22.

2.4. RX Crystallography Data

Single crystals of **3b**, **4a** and **5a** were submitted to X-ray data collection by using a Siemens P4 four-circle or an Oxford-Diffraction Xcalibur Sapphire 3 diffractometer. The structures were solved by direct methods implemented in SHELXS-97 program [11]. The refinements were carried out by full-matrix anisotropic least- squares on F^2 for all reflections for non-H atoms by means of the SHELXL-97 program [11]. Crystallographic data for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1416382 (**3b**), CCDC 995914 (**4a**), CCDC 995915 (**5a**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, CambridgeCB2 1EZ, UK; (fax: + 44 (0) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk).

Crystal data for **3b**: $C_{22}H_{20}N_4O_4$ (CCDC 1416382): M_W = 404.42, triclinic, space group P-1, a = 7.6387 (6) Å, b = 16.6184 (12) Å, c = 17.7794 (13) Å, α = 112.298 (7), β = 94.328 (6), γ = 92.519 (6)˚, V = 2075.9 (3) Å^3, Z = 4, D_c = 1.294 mg/m^3, F (000) = 848, crystal dimension 0.3_0.1_0.1 mm, radiation, MoKα (λ = 0.71073 Å), 9355 intensity data were collected at 293(2) K, employing $\omega/2\theta$ scanning technique, in the range of −10h9, −20k19, −24l23; the structure was solved by a direct method, all non-hydrogen atoms were refined anisotropically from 2585 observed reflections by a full-matrix least-squares technique. R = 0.0467 [I > 2σ(I)] and wR_2 (all data) = 0.1012

Crystal data for **4a**: $C_{23}H_{20}N_4$(CCDC 995914): M_W = 352.43, monoclinic, space group $P2_1/n$, a = 8.3817 (4) Å, b = 12.9420 (7) Å, c = 17.4334 (12) Å, α = 90, β = 98.704 (5), γ = 90˚, V = 1869.3 (1) Å^3, Z = 4, D_c = 1.252 mg/m^3, F (000) = 744, crystal dimension 0.4_0.3_0.1 mm, radiation, MoKα (λ = 0.71073 Å), 4310 intensity data were collected at 293(2) K, employing $\omega/2\theta$ scanning technique, in the range of −10h8, −16k16, −22l15; the structure was solved by a direct method, all non-hydrogen atoms were refined anisotropically from 1344 observed reflections by a full-matrix least-squares technique. R = 0.0426 [I > 2σ(I)] and wR_2 (all data) = 0.0873

Crystal data for **5a**: $C_{25}H_{20}F_3N_5O_2 \cdot C_6D_6$(CCDC 995915): M_W = 479.46, monoclinic, space group $P2_1/a$, a = 11.832 (1) Å, b = 13.5134 (9) Å, c = 14.934 (2) Å, α = 90, β = 95.522 (2), γ = 90˚, V = 2376.7 (4) Å^3, Z = 4, D_c = 1.34 mg/mm^3, F (000) = 992, crystal dimension 0.3_0.15_0.10 mm, radiation, MoK_α (λ = 0.71073 Å), 5426 intensity data were collected at 293(2) K, employing $\omega/2\theta$ scanning technique, in the range of −13h15, −18k18, −18l17; the structure was solved by a direct method, all non-hydrogen were refined anisotropically from 1703 observed reflections by a full-matrix least-squares technique. R = 0.0941 [I > 2σ(I)] and wR_2 (all data) = 0.1829.

3. Result and Discussion

Hence, when dienes **1a-d** (0.1 mmol) were left to react with *N*,*N*-dimethyl-4-nitrosoaniline (0.12 mmol) in CH_2Cl_2 at room temperature for 5 - 7 days a new unexpected compound we observed. This product was also observed when the same reaction mixture was heated at 60˚C for 7 h. The crude reaction mixture was purified by column chromatography (ethyl acetate/petroleum ether 1/4) to give starting material and compounds **3a-d** (**Scheme 1**).

The structure of compound **3b** was established by X-ray analysis (**Figure 2**), whereas allowed MS/ESI and ^{1}H-NMR and ^{13}C-NMR data were sufficient to establish, by comparison, the structures of derivatives **3a, 3c** and **3d**.

The reaction conditions were optimized to provide compounds **3a-d** in highest yields. A solution of **1a-d** (0.1 mmol) and **2** (0.12 mmol) in CH_2Cl_2 was heated under MW (150 W) for 90 minutes. In alternative, heating the same mixture in an oil bath for 7 hours at 60˚C gave desired **3a-d** in similar high yields. We have verified that increasing the temperature did not increase the yield due, which we explained considering the thermolability of the compounds **3a-d**.

In order to understand the effect of the temperature on product distribution, a new set of experiments was also performed. When a mixture of dienes **1a-d** (0.1 mmol) and *N*,*N*-dimethyl-4-nitrosoaniline **2** (0.12 mmol) neat were heating under MW irradiation (150 W) at 150˚C for 15 minutes, the tlc (ethyl acetate/petroleum ether 1/4) and ^{1}H-NMR spectra of the crude reaction mixture indicated complete conversion of the starting material and appearance of compounds **4a-d**, **5a-d** and **6a-d** (**Scheme 2**). The reaction products were isolated by column chromatography (ethyl acetate/petroleum ether 1/4) and further characterised via NMR spectroscopy and X-ray analysis.

RX analysis (**Figure 3**, **Figure 4**) allowed us to assign the structure of compounds **4a** and **5a**.

The Z configuration of compound **4a** was also confirmed by NMR-NOESY experiments, which showed correlation between the 4-methyl group at 2.46 ppm and the CH group at 7.89 ppm. It is to be noted that **4a** did not rearrange to the corresponding *E*-isomer upon UV-VIS irradiation at 440 nm.

The structure of other **4**, **5** and **6** analogues was assigned by comparison of their ^{1}H-NMR data (**Table 1**).

The analysis of the chemical shifts indicated very similar trend of the C-methyl group and the CH-N signals along the three series of compounds.

Also analysis of the MS/ESI data (molecular ion value and ms/ms fragmentation) confirms the assigned structure.

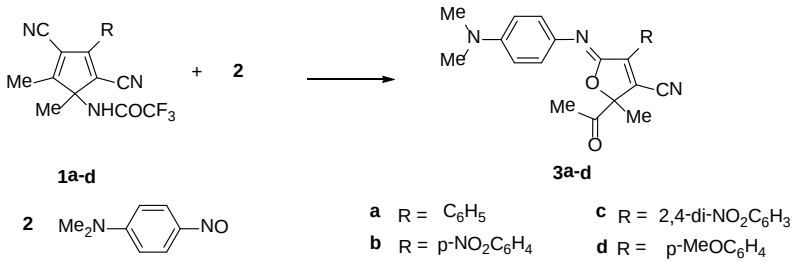
The medium basicity (due the presence of nitrosoamine) is a crucial parameter for the Ehrlich-Sachs reaction. In fact compounds **1a-d** (0.1 mmmol in CH_2Cl_2) does not react with nitrosobenzene (0.12 mmmol) in the absence of base and under MW irradiation (solvent free) gave no conversion to corresponding compounds **4**.

Conversely, in the presence of triethylamine (0.12 mmmol) the corresponding aniline oxide was obtained from compounds **1b,d** (0.1 mmmol in CH_2Cl_2) and nitrosobenzene, (0.12 mmmol), as confirmed by MS/ESI data and ^{1}H-NMR spectra: the chemical shifts of the methyl group (2.15 ppm for NO_2 derivative and 2.11 ppm for OMe derivative) and those of the CH-N proton (8.18 ppm and 8.15 ppm respectively for NO_2 and OMe derivatives) are diagnostic for the assignement of the structure. In addition compounds **5** (and **6** in trace) were obtained from **1** (0.1 mmmol in CH_2Cl_2) and **2** (0.12 mmmol) and trimethylamine (0.12 mmmol) without heating.

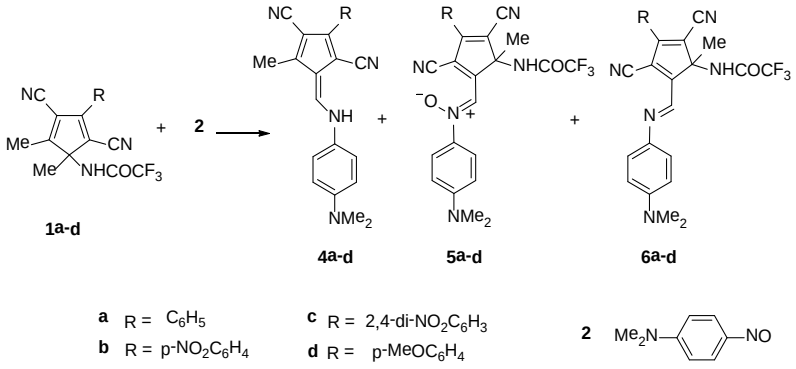
Fulvenes requires higher temperatures: **4a-d** together with **5a-d** were also obtained by heating of **1a-d** (0.1 mmol) and **2** (0.12 mmol) at 100˚C in oil bath, solvent free, for 3 hours.

The formation of **3a-d** may be accounted by the following mechanisms (**Scheme 3**).

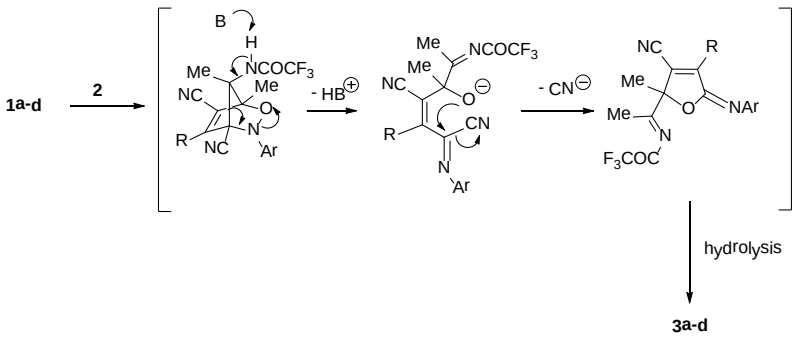
We envisaged that, following an initial hetero Diels-Alder reaction [2], deprotonation of $NHCOCF_3$ group lead to formation of an open intermediate which rearranged to a dihydrofuran. Finally, the hydrolysis (the reaction is made in non-anhydrous conditions) of the trifluoroacetamidate group gave the observed compounds **3a-d**.



Scheme 1. 1a-d (0.1 mmol) and 2 (0.12 mmol) in CH_2Cl_2 (3 ml) at RT for 5 - 7 days or T = 60˚C in bath oil for 7 h, or heating in MW 150 W for 90 minutes.



Scheme 2. 1a-d (0.1 mmol) and 2 (0.12 mmol) in MW at T = 150˚C, 150W for 15' solvent free or heating in oil bath at T = 100˚C for 3 h solvent free.



Scheme 3. Proposed mechanism for the formation of compounds 3a-d.

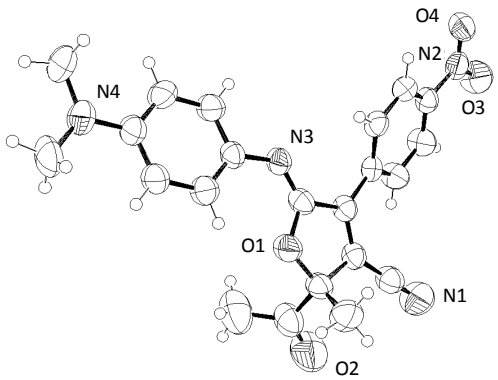


Figure 2. Crystal structure of compound 3b (CCDC1416382). Ellipsoids enclose 50% probability.

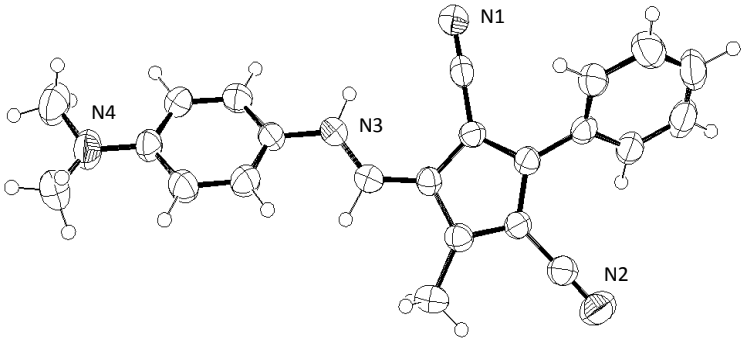


Figure 3. Crystal structure of compound 4a (CCDC995914). Ellipsoids enclose 50% probability.

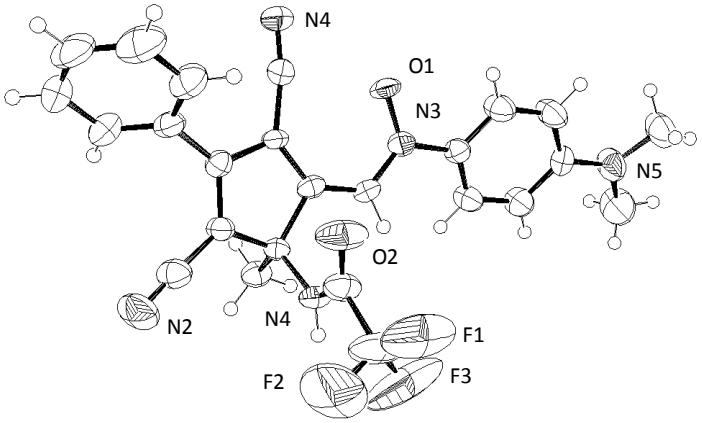


Figure 4. Crystal structure of compound 5a (CCDC995915). Ellipsoids enclose 50% probability.

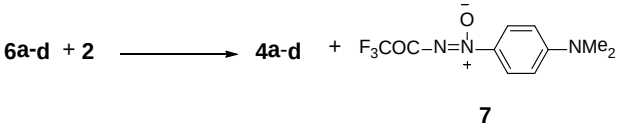
Table 1. Selected proton NMR of compounds **4a-d**, **5a-d** and **6a-d**.

R	4a-d		5a-d		6a-d	
	Me	CH-N	Me	CH-N	Me	CH-N
Phenyl	7.89	2.46	2.11	8.11	1.91	8.65
4-NO_2Phenyl	7.97	2.48	2.12	8.13	1.93	8.64
2,4diNO_2Phenyl	8.11	2.48	2.16	8.04	1.97	8.56
4-OMePhenyl	7.85	2.45	2.09	8.01	1.89	8.64

The formation of the imines **6a-d** and nitrones **5a-d** could be explained by an Ehrlich-Sachs condensation mechanism involving nitroso group and acidic methyl group, followed by partial oxidation to **5** by the excess of reagent [3].

The formation of fulvenes can be hypothesized as deriving from **6a-d** considering that nitrosobenzene, in presence of carbanions with good leaving groups gave N-oxides [3]. In this case, the acidic NH was deprotonated to an N-anion able to carry a nucleophilic attack to the electrophilic nitrosoaniline. In this context, the fulvene behaved as a leaving group generating compounds **4a-d** and trifluoroacetyldiazene-oxide **7** (**Scheme 4**).

We have carried out some mechanistic studies that support this interpretation. For example, heating compounds **6a-d** in the presence of *N*,*N*-dimethyl-4-nitrosoaniline **2**, under neat conditions, provided fulvenes which were characterised by t.l.c. mass spectrometry and ^{1}H-NMR. In addition, the presence of trifluoroacetyl-



Scheme 4. Proposed reaction for the formation of compounds **4a-d**.

diazene-oxide **7** could be evidenced in the crude mixture [12].

4. Conclusion

In conclusion, we have shown that the reaction of compounds **1** and **2** could be in two diverse directions providing either substituted dihydrofuran or fulvenes depending upon conditions applied. The increase in temperature does not lead to the cycloaddition reaction, but a different mechanism occurs. The interest on synthetic methodologies leading to 2,5-dihydrofuran and imino-2,5-dihydrofuran derivatives [13] is very considerable. These structures are subunit of several bioactive natural and synthetic products [14] [15]. Fulvenes have high relevance as synthons [16] [17] and materials [18]-[24]. This report will provide a fast and easy protocol to execute the preparation of the abovementioned heterocycles cores.

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