# NEW HELICAL MOLECULES VIA 1,3-DIPOLAR CYCLOADDITIONS

Dan G. DUMITRESCU[1], Florea DUMITRAŞCU[2], Florin BADEA[3]

*Au fost obţinuţi doi compuşi elicoidali noi folosind o procedură nouă, constând în cicloadiţia 1,3-dipolară dintre dicianometilide de izochinolină şi ftalazină şi 1,2-naftochinonă ca dipolarofil. Cicloaducţii au fost obţinuţi cu randamente ridicate şi au fost caracterizaţi prin spectroscopie RMN şi IR.*

*Two new helical molecules were prepared using a new protocol consisting of the 1,3-dipolar cycloaddition of isoquinoline and phthalazine dicyanomethylides and 1,2-naphthoquinone as dipolarophile. The corresponding cycloadducts were obtained in good yields and structural confirmation was provided by NMR and IR spectroscopy.*

**Keywords:** azahelicenes, N-ylides, pyrroloazines

## 1. Introduction

Helical chirality was first put in evidence by Newman in 1955 in carbohelicenes obtained by the photocyclization of stilbene like derivatives.[1] Although in the following decades other synthetic methods were developed by numerous groups, helical molecules remain an elusive target for the synthetic chemist.

Their optical properties such as unusually high extinction values and thin film conductivity contributed to the current continuing interest in such compounds.[2-4] In order to expand the synthetic possibilities and potential applications of helicenes, one or more carbon atoms can be replaced with sulfur or nitrogen atoms, leading to thio and azahelicenes. Furthermore, helical chirality was documented in heterocycles containing less than the 5 ring minimum observed in carbohelicenes. In such cases, helicity appears due to bulky substituents in key *ortho* positions on the scaffold.[5-13]

Azahelicenes in particular received increasing interesting in the past two decades, with numerous synthetic approaches reported in literature.[5,6] One of the most facile methods available for obtaining nitrogen heterocycles possessing

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[1] PhD student, Department of Organic Chemistry, University POLITEHNICA of Bucharest, Center for Organic Chemistry "C.D. Nenitzescu", Romania, e-mail: dan.dumitrescu@gmail.com

[2] Eng., Center for Organic Chemistry "C.D. Nenitzescu", Romania

[3] Prof., Department of Organic Chemistry, University POLITEHNICA of Bucharest, Romania, e-mail: fdbadea@yahoo.com

helical chirality are *N*-ylide 1,3-dipolar cycloadditions, which offer the advantages of few reaction steps, moderate to high yields and relatively simple work-up and experimental setup.[14-19] Our previous work in this field lead us to investigate the reaction between the stable isoquinoline and phthalazine dicyanomethylides and 1,2-naphthoquinone as dipolarophile.[5,7] Herein we report the synthesis and spectral characterization of two new helical heterocycles.

## 3. Experimental

Melting points were determined on a Boëtius hot plate. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for $^1$H and 75 MHz for $^{13}$C. Supplementary evidence was given by HETCOR and COSY experiments. The IR spectra (ATR) were recorded on a Vertex 70 Brucker instrument. Elemental analyses were determined on COSTECH Instruments EAS32 (Centre for Organic Chemistry, Spl. Independentei 202B, Bucharest 060023, Romania). Satisfactory microanalyses for all new compounds were obtained. All precursors were purchased from Sigma-Aldrich and were used without further purification.

**General procedure for compounds 2**

Dicyanomethylides **2** were obtained according to literature protocols and used without any further purification.[20,21]

**General procedure for compounds 3**

2 Mmol (0.37g) of the corresponding dicyanomethylide and 1,2-naphthoquinone (2 mmol, 0.32g) were suspended in acetonitrile (15 mL). The mixture was stirred at room temperature for 24h. The resulting precipitate was filtered off and washed with acetonitrile. The crude products was recrystallized from concentrated sulfuric acid.

**5,6-Dioxo-5,6-dihydro-12,12a-diaza-dibenzo[a,g]fluorene-13-carbonitrile (3a).** Beige powder with m.p. 359-360 $^0$C, yield 81%. Anal. Calc. for $C_{20}H_9N_3O_2$: C, 74.30; H, 2.81; N, 13.00. Found: C, 74.39; H, 2.75; N, 13.04. FT-IR($cm^{-1}$): 3076; 2186; 1654; 1653; 1500; 1469. $^1$H-NMR (300 MHz, $CDCl_3$+TFA) δ: 9.88 (d, 1H, *J*=8.6 Hz, H-7); 8.22 (d, 1H, *J*=8.1 Hz, H-4); 8.13-8.10 (m, 2H, H-1, H-10); 7.81-7.67 (m, 3H, H-8, H-9, H-11); 7.53-7.44 (m, 2H, H-2, H-3). $^{13}$C-NMR (75 MHz, $CDCl_3$+TFA) δ: 145.9 (Cq); 140.3 (Cq); 137.1 (CH); 133.0 (Cq); 132.9 (CH); 131.9 (Cq); 131.6 (CH); 130.8 (CH); 130.3 (Cq); 130.0 (CH); 128.9 (CH); 125.3 (CH); 124.4 (Cq); 122.0 (CH); 119.9 (CH); 112.3 (CN); 102.5 (Cq); 97.1 (Cq).

5,6-Dioxo-5,6-dihydro-12a-aza-dibenzo[a,g]fluorene-13-carbonitrile (3b). **Beige powder with m.p. 353-355 $^0$C, yield 81%. Anal. Calc. for $C_{21}H_{10}N_2O_2$: C, 78.25; H, 3.13; N, 8.69. Found: C, 78.20; H, 3.14; N, 8.72. FT-IR ($cm^{-1}$): 3075; 2185; 1653; 1651; 1500; 1469. $^1$H-NMR (300 MHz, $CDCl_3$+TFA) δ: 9.64**

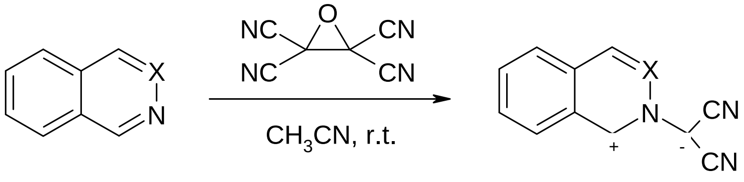
**(d, 1H, *J*=6.9 Hz, H-5); 8.22 (d, 1H, *J*=8.0 Hz, H-4); 8.18-8.12 (m, 2H, H-1, H-10); 7.84-7.7.67 (m, 3H, H-8, H-9, H-12); 7.59-7.46 (m, 3H, H-2, H-3, H-11). $^{13}$C-NMR (75 MHz, CDCl$_3$+TFA) δ: 145.9 (Cq); 140.3 (Cq); 137.0 (CH); 135.2 (Cq); 132.8 (CH); 131.8 (Cq); 131.5 (CH); 130.8 (CH); 130.3 (Cq); 130.0 (CH); 128.9 (CH); 127.8 (CH); 125.2 (CH); 124.5 (Cq); 122.0 (CH); 119.8 (CH); 112.3 (CN); 97.1 (Cq).**

## 3. Results and discussion

### 3.1. Synthesis and structural assignment

Generally, *N*-ylides are unstable compounds and are generated *in situ*. However, dicyanomethylides belong to the class of stable, disubstituted *N*-ylides. As such, they were used as benchmarks to establish the reactivity of several dipolarophiles and solvents effects in 1,3-dipolar cycloadditions.[20, 21]

These compounds are easily available in almost quantitative yields by mixing the corresponding heterocycle and tetracyanoethyleneoxide (TCNEO) in acetonitrile at room temperature. (Scheme 1)

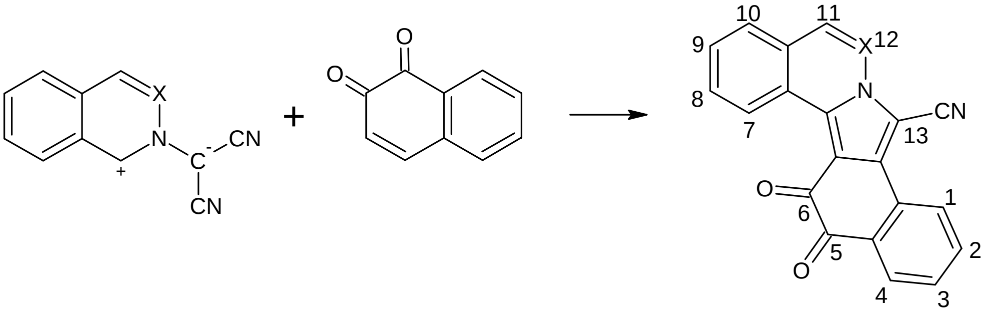


**1a,b** **2a,b**

**a**: X=N; **b**: X=CH

**Scheme 1.** Synthesis of the intermediaries **2a,b**.

Cycloadducts **3a,b** were obtained in excellent yields of 81-83% by stirring dicyanomethylides **2a,b** with 1,2-naphthoquinone in acetonitrile. (Scheme 2)



**2a,b** **a**: X=N; **b**: X=CH **3a,b**

**Scheme 2.** Synthesis of compounds **3a,b.**

Structural confirmation was provided by NMR and IR spectroscopy. As the NMR spectra were performed in $CDCl_3$+TFA mixture, H-7 is the most deshielded, around 9.70 ppm, due to the protonation of the ketone groups in positions 5 and 6. This effect is also observable in the $^{13}$C-NMR spectra, where the two ketone groups are not visible. However, their presence is strongly visible in the FT-IR spectra, with the signals at 1654 and 1651 cm$^{-1}$. The cyano moiety is appears as expected at 112 ppm in the $^{13}$C-NMR spectra and at 2186 cm$^{-1}$ in the FT-IR spectra.

### 3.2. Molecular Modelling

In order to estimate whether the new heterocyclic compounds have helical chirality, molecular computations were carried out. The GAMESS computation package [22] was used at the B3-LYP/6-311G level of theory. The initial geometric guess was determined using the Avogadro UFF molecular mechanics package. [23]

For helicity to occur, 5 *ortho* condensed rings are required. This sterical constraint can also be observed in 3 and 4 *ortho* condensed ring systems, provided that bulky substituents exist in key positions.

In the case of the compounds studied herein the sterical crowding is provided by the ketone group from the 1,2-naphthoquinone residue. By comparing with similar compounds from literature, we expected a small to moderate helical distortion in both compounds. However, a significant difference was observed between the two compounds. This is unexpected, as the molecular scaffold is virtually the same. For clarity purposes, the M isomer was depicted for **3a** and P isomer for **3b**.

In the case of compound **3b**, the rings, numbered A-E, recede successively from plane A to plane E, leading to a helical ring system. The conformation of compound **3a** is different, with the rings adopting a zig-zag conformation (Table 1).

It is interesting to note that this high difference between the geometries is caused by the length of the bond between atoms 7 and 8, a C=C bond of 1.389 Å in the case of **3b** and a C=N bond of 1.298 Å in the case of **3a**. To our knowledge this is a first example of 'helical tuning' not caused by the bay region substituents.

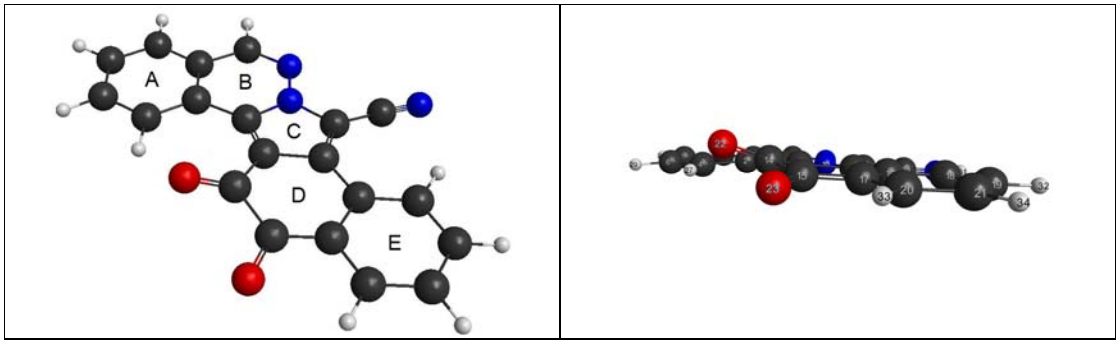


Fig. 1. Front and side view of compound **3a (M isomer)**. Rings are numbered A-E.

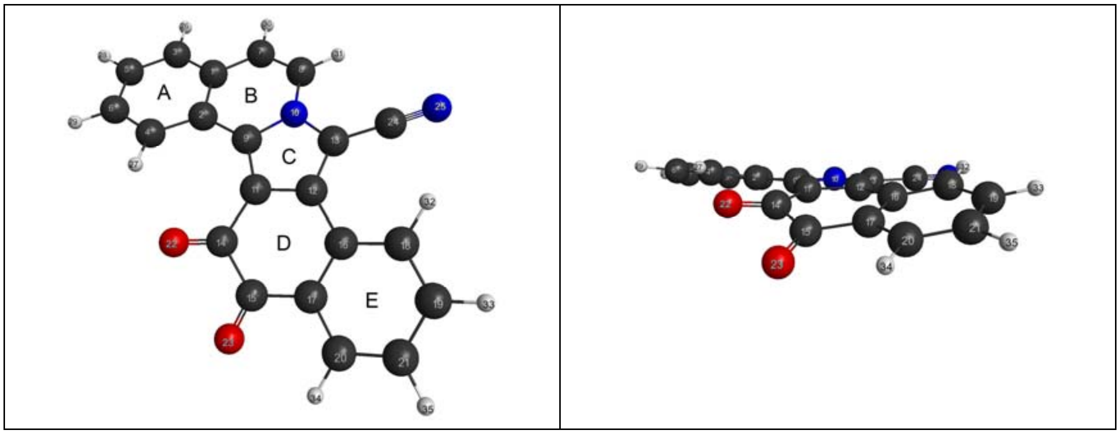


Fig. 2. Front and side view of compound **3b (P isomer)**. Rings are numbered A-E.

*Table 1.*

**Angle between planes in compouns 3a,b**

| Compound/Angle between planes | A^B | B^C | C^D | D^E |
|---|---|---|---|---|
| **3a** | 0.03 | 0.59 | 2.90 | 5.70 |
| **3b** | 6.61 | 2.64 | 5.65 | 12.30 |

## 4. Conclusions

Two new helical heterocycles were synthesized by the 1,3-dipolar cycloaddition of the corresponding dicyanomethylide with 1,2-naphthoquinone as dipolarophile. The regioselectivity of the reaction and structural assignment were ascertained using $^1$H-NMR and $^{13}$C-NMR spectroscopy. Elemental analysis confirmed the proposed structure. Structural considerations were made using molecular modelling. To our knowledge this is the first case where helical distortion can be influenced by ‘tuning’ the molecule outside the bay region.

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