STEREOSELECTIVE SYNTHESIS OF A NEW PHOTOCHROMIC SPIRO[AZABICYCLO-NAPHTHOXAZINE]

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Abstract: Diastereoselective synthesis of the new 8-ethoxy-2-methylspiro-[*syn*-5,6-benzo-2-azabicyclo[2,2,2] octane-3,3'-[3*H*]-naphtho[2,1-*b*][1,4]oxazine] **3** allows to estimate the influence of steric hindrance on photochromic properties.

Introduction:

Bradsher's cycloaddition is of wide scope: substituted naphthols (1), naphthaldehydes (2), naphthoquinones (3) and synthons for natural products synthesis (4) are readily available by this reaction. We wish to report here a new application for the synthesis of sterically hindered spiro-naphthoxazines. In the field of organic photochromic compounds (5a) spiro[indoline-naphthoxazine] (5b) series presents a good compromise between photochromic properties (colour efficiency, stability of the coloured open form and resistance towards photodegradation) giving rise to fundamental and technological interests.(5,6).

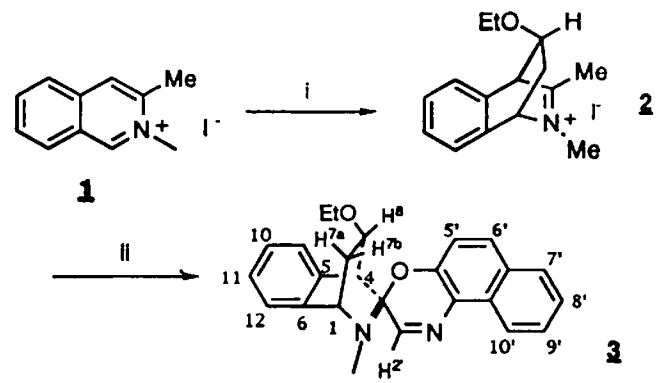
The purpose of the present work was to study the effect of steric hindrance on photochromic properties of spironaphthoxazines. Thus, we have prepared a new class of spirooxazines having a highly strained azabicyclic part linked to the spiro-carbon atom.

Results and discussion:

The first step of the synthesis (scheme 1) consists of a (4^++2) Bradsher's cycloaddition (7,8) between ethylvinylether and 2,3-dimethylisoquinolinium iodide, affording the azabicyclo isoquinolinium salt 2 in 85% yield, regio- and stereo-selectively. Condensation reaction of 2 with 1-nitroso-2-naphthol in trichlorethylene, with a stoechiometric amount of triethylamine leads to the spironaphthoxazine 3 in 30% yield.

Condensation of 1-nitroso-2-naphthol with various asymetric Fischer's bases generally gives an equal ratio of diastereoisomers (5a). Interestingly, in the case of the synthesis of spironaphthoxazine 3, the cyclisation of the oxazine nucleus occurs only on one face of the azacyclic ring, affording a single diastereoisomer.

Diamagnetic anisotropy provides an easy way to determine the configuration of 3 by ^{1}H NMR study. Thus, 2'-H is the only one singlet in the aromatic field of the spectrum and is shielded at δ=6.87ppm due to the anisotropy induced by the 5,6-annelated benzene ring. This chemical shift can only be obtained for the enantiomeric pair [8S,3S] and [8R,3R], as shown in the molecular modelling representations (9) (Figure 1).



Scheme 1 : *Reagents and conditions* :
i- Ethylvinylether, one week, 20°C, CH_3CN.
ii- 1-Nitroso-2-naphthol, NEt_3, 12 h, 50°C, Trichloroethylene.

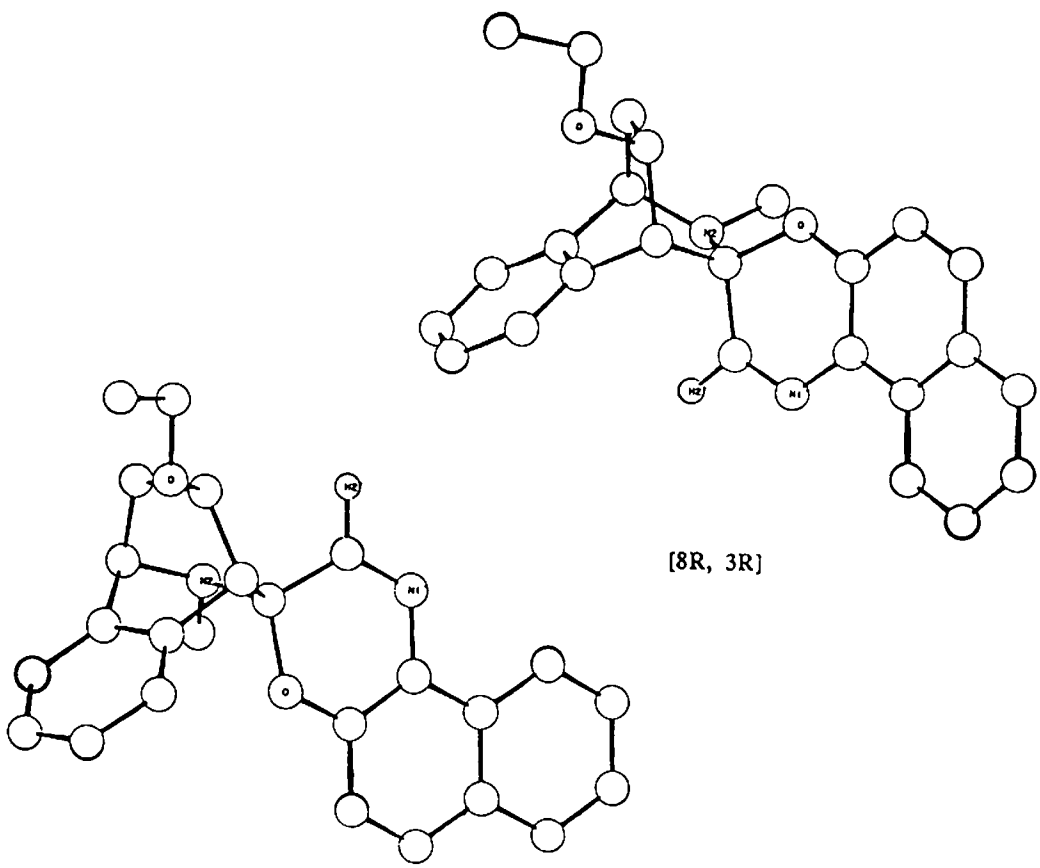
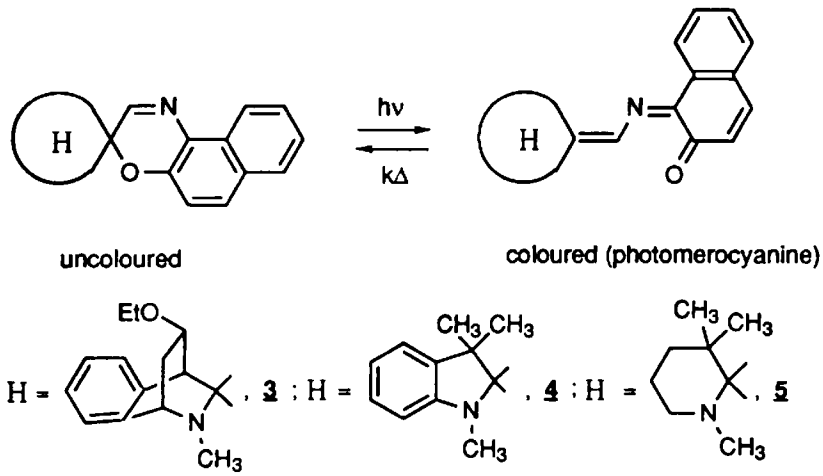


Fig.1: Molecular modelling representations of two diastereoisomers.

The second enantiomeric pair 3*-[8R,3S] and [8S,3R]-appears in ^1H NMR spectrum (about 5%) when a $CDCl_3$ solution of 3 is exposed to day-light, the photochromic equilibrium (scheme 2) inducing an inversion of configuration of the spiro-carbon atom. For this diastereoisomer, H-2' appears downfield at δ=7.55ppm.



Scheme 2 *Photochromic equilibrium*

Photochromic parameters (10) of this new spironaphthoxazine 3 (thermobleaching constant k_Λ= 0.36s^{-1}, maximum wavelengths of the colored form λ_{max}= 535 and 563nm, colourability A_0= 1.3) were determined in toluene (C=2.5 10^{-5}M, 25°C), using a flash photolysis apparatus coupled to a fast-scanning spectrometer (11). Comparison with the values obtained under the same experimental conditions for spiro[indoline-naphthoxazine] 4 (scheme 2) used as reference (11) (k_Δ= 0.54s^{-1}, λ_{max}= 595nm, A_0= 1.0), shows a slight increase of the colourability and, particularly, a high hypsochromic shift of the wavelength of the photomerocyanine (-60 and -32nm). With previously described compound 5 (12) the shift is smaller (λmax=580nm; C=5.10^{-5}M, 25°C, toluene), and can be attributed to the lack of conjugaison. As compound 3 presents nearly the same electronic feature for the azacyclic part, the hypsochromic shift seems thus to be principally provided by steric hindrance, the twisted conformation of the coloured form inducing a change in the electronic delocalization.

Conclusion:

This behaviour is very interesting both for the knowledge of relationships between structure-properties and for practical applications (13) such as organic photochromic glasses (14). The synthesis of substituted and more hindered aza-polycyclo-spironaphthoxazines is underway and will be reported in due course. The study of the stereoselectivity of the spiro-condensation reaction will be extended.

Experimental:

2,3-D*imethyl*-8-*ethoxy*-(syn-5,6-*benzo*-2-*azabicyclo*-(2,2,2)*octane) iodide* **2** - mp 215°C (Litt.(7) 212-215°C); δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.04 (3H, t, OCH_2CH_3, J 7.0Hz); 1.43 (1H, d, 7a-H, J 13.6Hz); 3.01 (3H, s, 3-Me); 3.18 (1H, ddd, 7b-H, J 13.6, 8.4, 3.4Hz); 3.45-3.70 (2H, m, diastereotropic OCH_2-, J 7.0Hz); 3,97 (3H, s, N-Me); 4.69 (1H, ddd, 8-H, J 8.5, 3.0Hz); 5.10 (1H, d, 4-H, J 3.2Hz); 5.80 (1H, s, 1-H); 7.30-7.60 (4H, m, 9-12-H); δ_C (62.5 MHz; $CDCl_3$; Me_4Si) 15.2 (OCH_2CH_3); 24.3 (3-C); 33.6 (7-C); 43.9 (2-C); 54.3 (4-C); 65.0 (OCH2); 67.9 (1-C); 72.2 (8-C); 123.6-134.7 (9 to 12-C).

8-E*thoxy*-2-*methylspiro*-[syn-5,6-*benzo*-2-*azabicyclo [2,2,2] octane*-3,3'-*[3H]-naphtho*[2,1-*b] [1,4] oxazine]* **3.**-To a solution of the salt **2** (0.1 g, 0.28 mmol) in trichlorethylene (10 ml) was added triethylamine (28 mg, 0.28 mmol), after which a solution of 1-nitroso-2-naphthol (48 mg, 0.28 mmol) in trichlorethylene was added dropwise. The reaction mixture was stirred at 50°C for 12 hours under inert atmosphere. Evaporation of the solvent gave an oil which was purified by elution through silica gel using hexane-ethyl acetate (95:5). Recrystallization from heptane gave crystalline material; mp 137°C (Found: C, 78.11; H, 6.16; N, 7.30; $C_{25}H_{24}N_2O_2$ Calc. C, 78.10; H, 6.29; N, 7.29 %): δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.03 (3H, t, OCH_2CH_3, J 7.0Hz); 1.45 (1H, ddd, 7a-H, J 13.6, 2.3Hz); 2.32 (3H, s, N-Me); 2.91 (1H, ddd, 7b-H, J 13.6, 8.6, 3.3Hz); 3.36-3.49 (2H, m, diastereotropic OCH_2-, J 7.0Hz); 3.80 (1H, dd, 1-H, J 3.0Hz); 3.87 (1H, d, 4-H, J 3.1Hz); 4.60 (1H, ddd, 8-H, J 8.8, 2.9Hz); 6.87 (1H, s, 2'-H); 7.21 (1H, d, 5'-H, J 8.9Hz); 7.25-7.35 (4H, m, 9-12-H); 7.39 (1H, dd, 8'-H, J 6.8, 1.1Hz); 7.53 (1H, dd, 9'-H, J 6.8, 1.2Hz); 7.72 (1H, d, 6'-H, 8.9Hz); 7.77 (1H, d, 7'-H, J 8.2Hz); 8.45 (1H, d, 10'-H, J 8.5Hz); δ_C (100 MHz; $CDCl_3$; Me_4Si) 15.3 (OCH_2CH_3); 37.3 (7-C); 38.4 (N-Me); 47.0 (4-C); 59.7 (1-C); 63.7 (OCH_2); 68.7 (8-C) ; 88.4 (3-C); 117.9 (5'-C); 121.8 (10'-C); 124.3 (8'-C); 126.9 (9'-C); 123.1,127.1,127.4, 128.0 (9 to 12-C); 127.8 (7'-C); 129.6 (6'-C); 153.3 (2'-C).

Couple of enantiomers [8R,3S] and [8S,3R] **3*** - δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.21 (1H, d, 7a-H); 2.43 (3H, s, N-Me); 2.72 (1H, ddd, 7b-H); 4.12 (1H, ddd, 8-H); 6.58 (1H, d, 5'-H); 7.55 (1H, s, 2'-H); 8.50 (1H, d, 10'-H). δ_C (100 MHz; $CDCl_3$; Me_4Si) 36.0 (N-Me); 46.0 (4-C); 58.5 (1-C); 70.5 (8-C).

Acknowledgements: We are grateful to Essilor International (France), PPG Industries (USA), and the Conseil Régional Provence-Alpes-Côte d'Azur for financial support. We express our many thanks to Dr. J. Aubard and R. Dubest (Universite Paris VII, France) for the monitoring of spectrokinetic parameters, and to Dr. C. Mioskowski (Universite Louis Pasteur, Strasbourg) for helpful discussions.

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Received August 27, 1994