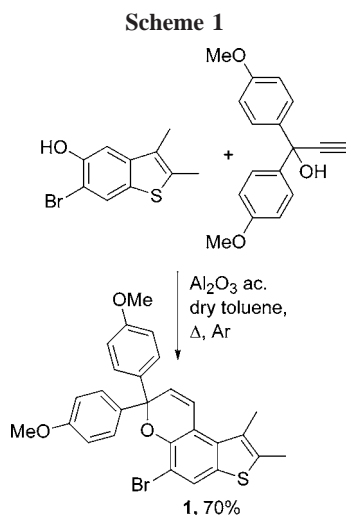


original state (bleaching) predominantly through a thermal process with a reasonable kinetics (relatively fast, 10^{-1} s^{-1}). Furthermore, they should be resistant, allowing the occurrence of many coloring–decoloring cycles. The evaluation of the photochromic behavior of molecules involves the knowledge of some relevant parameters, related to the kinetic and spectral properties, through a kinetic analysis performed under flash photolysis or continuous irradiation. The information obtained by the two methods can be very distinct since the time scales of observation are completely different.

The photochromic behavior of *2H*-1-benzopyrans (*2H*-chromenes) is based on a photoinduced reversible opening of the pyran ring that converts the colorless form (closed form) into a set of isomers with the pyran ring opened (open forms), leading to distinct absorption spectra. Much research has been devoted to this class of compounds, and the heteroannellation represents an interesting approach in promoting improvements in their photochromic properties.⁶

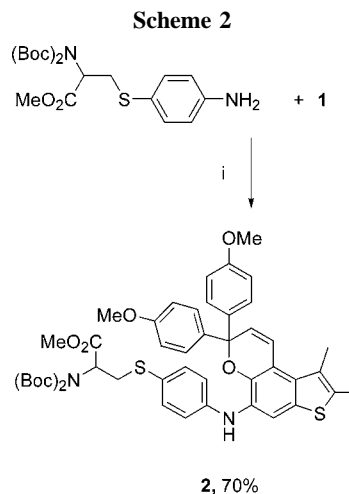
Herein we describe the synthesis of a new photochromic α -amino acid based on a *2H*-chromene annellated with a dimethylthiophene ring on the *f* face, using a C–N palladium-catalyzed cross-coupling and the study of its photochromic behavior under flash photolysis and continuous irradiation.

We began with the synthesis of the precursor bromothiено-*2H*-chromene **1** in good yield, by chromenization reaction of the, also prepared, 6-bromo-5-hydroxy-2,3-dimethylbenzo-*[b]*thiophene with 1,1-bis(4-methoxyphenyl)prop-2-yn-1-ol,⁷ using acidic Al_2O_3 as catalyst and drying agent (Scheme 1).



These conditions were already used by us in the synthesis of methyl-induced linear and angular thieno-*2H*-chromenes.⁸ Compound **1** was then coupled under C–N coupling condi-

tions,⁹ with a Michael adduct bearing an aromatic amino function,¹⁰ to give the thieno-*2H*-chromene amino acid derivative **2** in good yield (Scheme 2).



(i) $\text{Pd}(\text{OAc})_2$ (10 mol %), BINAP (15 mol %), Cs_2CO_3 (1.4 equiv), dry toluene, 100°C , 3 h.

The photochromic properties of compounds **1** and **2** were evaluated by flash photolysis, and due to the good results of compound **2**, it was also studied under continuous irradiation and compared with a reference *2H*-chromene benzoannellated on the *f* face and derivative of the same propargylic alcohol^{11,12} (Table 1).

The activation wavelengths of the closed form of compound **2** in toluene [λ_{max} (ϵ) 280 (35490), 286 (26700); 309 (41300), 327sh (30500), 339 (18500), 375 (10100) nm] correspond to strong bands in the near UV, which is very important, as the activation with less energetic radiation usually improves the sensitiveness to sunlight and also fatigue resistance. The photochromic behavior of compounds **1**, **2**, and reference, under flash photolysis in toluene at room temperature (Table 1), was quantified by *three spectrokinetic parameters*: absorption maxima of the colored forms (λ_{max}); thermal bleaching (ring closure) rate (k_{A}); and “colorability” (A_0). The latter parameter, which has been defined for photochromic compounds,¹³ is directly connected to the molar absorptivity of colored species and to the quantum yield of coloration, and was evaluated by monitoring the absorbance (A_0) at λ_{max} immediately after the flashgun was fired. A_0 is the experimental value corresponding to the following equation:

$$A_0 = \epsilon_{\text{MC}} \times \Phi_{\text{col}} \times k \times C_{\text{CF}} \text{ (for low concentration)}$$

ϵ_{MC} , molar absorptivity of colored forms

Φ_{col} , quantum yield for photocoloration

k , constant including photolysis conditions

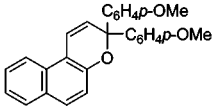
C_{CF} , initial concentration of the colorless form

(6) Van Gemert, B. In *Organic Photochromic and Thermochromic Compounds*; Crano, J. C., Guglielmetti, R., Eds.; Plenum Press: New York, 1999; Vol. 1, Chapter 3, pp 111–140 and references therein.

(7) Gabbutt, C. D.; Heron, B. M.; Instone, A. C.; Thomas, D. A.; Partington, S. M.; Hursthouse, M. B.; Gelbrich, T. *Eur. J. Org. Chem.* **2003**, 1220–1230.

(8) Queiroz, M.-J. R. P.; Plasencia, P. M. S.; Dubest, R.; Aubard, J.; Guglielmetti, R. *Tetrahedron* **2003**, 59, 2567–2573.

Table 1. Photochromic Behavior of Compounds **1**, **2**, and Reference: Maxima Wavelengths of Colored Forms (λ_1 , λ_2 , nm), Color Abilities (A_{01} , A_{02} , and A_{eq}) and Thermal Fading Rate Constants (k_Δ , s $^{-1}$)

chromenes	flash photolysis ^a				continuous irradiation ^b		
	λ_1	A_{01}	λ_2	A_{02}	k_Δ	A_{eq}	k_Δ
1	479	1.3	564	0.54	$k_1 = 2.13$ (95%) $k_2 = 0.23$ (5%)	—	—
2	490	3.9	>650	0.6	$k = 0.21$	0.57	$k = 0.15$
 Reference ¹²	481	1.2	—	—	$k_1 = 0.42$ (95%) $k_2 = 0.07$ (5%)	0.09	$k_1 = 0.25$ (93%) $k_2 = 0.001$ (7%)

^a Flash photolysis conditions (60 J, 50 μ s, 2.5×10^{-5} M in toluene, 25 $^\circ$ C). ^b Continuous irradiation conditions (light flux 40 W m $^{-2}$, 1×10^{-4} M in toluene, 20 $^\circ$ C).

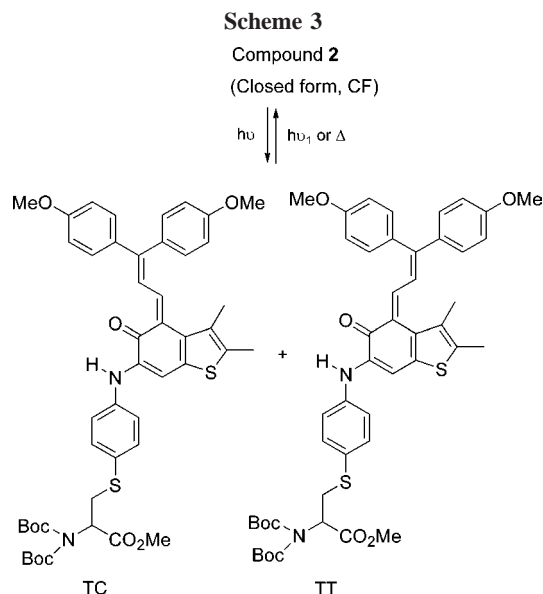
We have already observed that the fusion of a dimethylthiophene^{8,14} on the 2*H*-chromene leads to a two-bands profile on the visible absorption of the open forms not observed on the parent naphthopyrans.^{11,12} The maxima wavelengths of the open forms of compounds **1** and **2** show a two-bands expected profile and a bathochromic shift for the latter in both bands (Table 1).

The amino acid derivative **2** presents much higher colorability (3.9) than compounds **1** (1.3) and reference (1.2) for λ_1 and a thermal bleaching rate in the same range (10^{-1} s $^{-1}$) as that of the reference compound (Table 1). For compound **1**, the much faster thermal bleaching rate ($k_\Delta = 2.13$ s $^{-1}$) makes it unsuitable for application in ophthalmic lenses.

The resistance to fatigue (photodegradation) under continuous irradiation was evaluated for compound **2**, using the “Degraphot” apparatus.¹⁵ It was found that the time required to reach 50% of the initial absorbance value ($A_{0d} = 0.67$) was $t(A_{0d}/2) = 85$ min. This value is relatively low compared to the one obtained in the same experimental conditions for the parent compound of the series (unsubstituted diphenyl-naphthopyran), which is about 500 min.

Under continuous irradiation, compound **2** reaches the photostationary equilibrium ($A_{eq} = 0.57$, CF+TC+TT, Scheme 3) very quickly, and the absorption decreases very rapidly following a monoexponential thermal bleaching kinetics ($k_\Delta = 0.15$ s $^{-1}$), showing a low residual absorption

at the end of the measurements (ca. 0.043). This can be attributed to a very stable isomer of the open form or to



colored degradation products. The last assumption was not considered because degradation was estimated to be less than 1% since after successive coloration/decoloration cycles the colorability was not altered. The complete bleaching was only achieved with visible irradiation (>420 nm) (Figure 1), following a biexponential model [$k_1 = 0.0086$ s $^{-1}$ (92%); $k_2 = 1 \times 10^{-4}$ s $^{-1}$ (8%)], indicating that the residual color could be due to the most stable photoisomer, TT.¹⁶

When the decoloration process was promoted, only with visible light (>420 nm) total bleaching is achieved (Figures

(9) Abreu, A. S.; Silva, N. O.; Ferreira, P. M. T.; Queiroz, M.-J. R. P. *Eur. J. Org. Chem.* **2003**, 1537–1544 and references therein.

(10) Ferreira, P. M. T.; Maia, H.; Monteiro, L. S.; Sacramento, J. J. *Chem. Soc., Perkin Trans. 1* **2001**, 3167–3174.

(11) Van Gemert, B.; Bergomi, D.; Knowles, D. *Mol. Cryst. Liq. Cryst.* **1994**, 246, 67–73.

(12) Frigoli, M. Ph.D. Thesis, Université de la Méditerranée, Luminy, Marseille, France, 2000.

(13) Appriou, P.; Garnier, F.; Guglielmetti, R. *J. Photochem.* **1978**, 8, 145–165.

(14) Queiroz, M.-J. R. P.; Dubest, R.; Aubard, J.; Faure, R.; Guglielmetti, R. *Dyes and Pigments* **2000**, 219–229.

(15) Dubest, R.; Levoir, P.; Meyer, J. J.; Aubard, J.; Baillet, G.; Giusti, G.; Guglielmetti, R. *Rev. Sci. Instrum.* **1993**, 64, 1803–1808.

(16) Delbaere, S.; Micheau, J.-C.; Vermeersch, G. *J. Org. Chem.* **2003**, 68, 8968–8973.

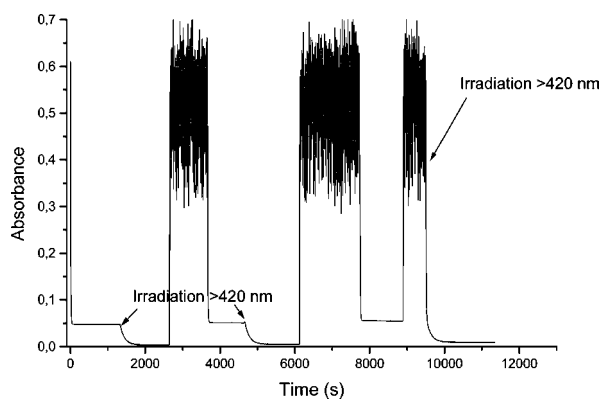


Figure 1. Cycles of coloration/decoloration for compound **2**.

1 and 2). The solution followed a multiexponential model (Figure 2) [$k_1 = 0.12 \text{ s}^{-1}$ (4%); $k_2 = 0.0083 \text{ s}^{-1}$ (77%); $k_3 = 1 \times 10^{-4} \text{ s}^{-1}$ (19%)]. The first kinetic seems to correspond to the very rapid $\text{TC} \rightarrow \text{CF}$ process (similar to the kinetic observed for the thermal decoloration). The second one seems to involve two steps, $\text{TT} \rightarrow \text{TC} \rightarrow \text{CF}$, the rate-determining step being the photoisomerization $\text{TT} \rightarrow \text{TC}$, and the third kinetics may correspond to a mixture of all processes.

We were able to prepare a photochromic α -amino acid derivative that shows very interesting properties regarding especially the high coloration efficiency and the visible spectrum coverage. This is very important to photoinduce transformations in both directions, using light of different wavelengths. The resistance to fatigue is not very high, but stabilizers might make our compound stable enough to be used in ophthalmic lenses.¹⁷

(17) Tanaka, T.; Imura, S.; Kita, Y. U.S. Patent 4,960,678 (1990).

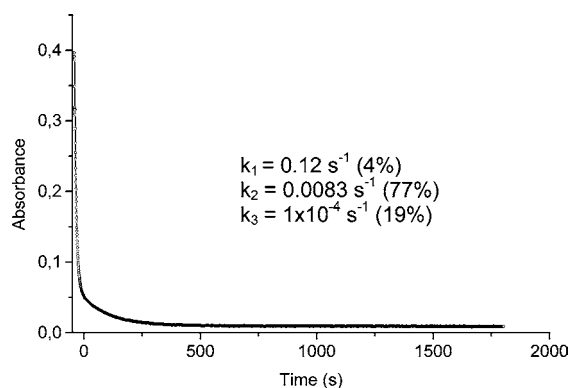


Figure 2. Photochemical bleaching of compound **2** only with visible light (>420 nm).

After deprotection of the photochromic amino acid, it can also be inserted into proteins for structural studies.

To our knowledge, it is the first time that a *2H*-chromene is attached to an α -amino acid side chain.

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Supporting Information Available: Experimental procedures and characterization data of compounds; flash photolysis, continuous irradiation, and photodegradation instrumental conditions. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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