



**HAL**  
open science

# N-Thiocyanato-2,10-camphorsultam Derivatives: Design and Applications of Original Electrophilic Thiocyanating Reagents

Mélissa Gao, Martin Vuagnat, Philippe Jubault, Tatiana Besset

► **To cite this version:**

Mélissa Gao, Martin Vuagnat, Philippe Jubault, Tatiana Besset. N-Thiocyanato-2,10-camphorsultam Derivatives: Design and Applications of Original Electrophilic Thiocyanating Reagents. *European Journal of Organic Chemistry*, 2021, 2022 (1), pp.e202101255. 10.1002/ejoc.202101255. hal-03744635

**HAL Id: hal-03744635**

**<https://hal.science/hal-03744635>**

Submitted on 16 Nov 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# *N*-Thiocyanato-2,10-Camphorsultam Derivatives: Design and Applications of Original Electrophilic Thiocyanating Reagents

Mélicha Gao,<sup>[a]</sup> Martin Vuagnat,<sup>[a]</sup> Philippe Jubault,<sup>[a]</sup> Tatiana Besset\*<sup>[a]</sup>

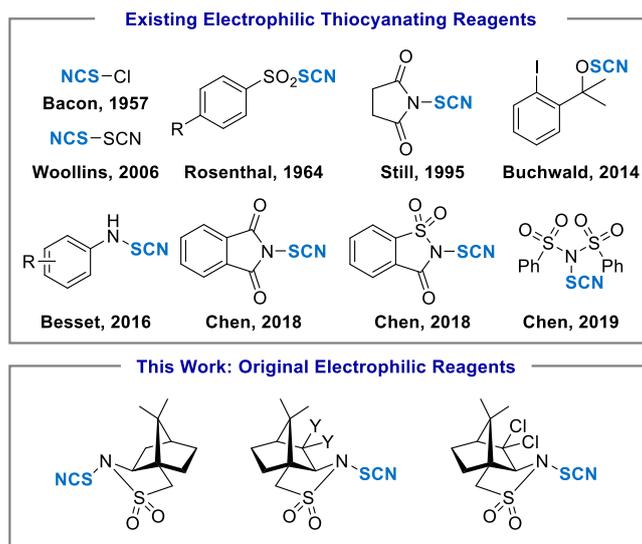
Normandie Univ, INSA Rouen, UNIROUEN, CNRS, COBRA (UMR 6014), 76000 Rouen, France.

E-mail: [tatiana.besset@insa-rouen.fr](mailto:tatiana.besset@insa-rouen.fr); <https://www.bessetgroup.cnrs.fr/>

**Abstract:** The synthesis of bench-stable electrophilic thiocyanating reagents was depicted in two steps from readily available starting materials in good yields. These newly-designed electrophilic reagents were successfully applied for the thiocyanation of different nucleophiles under mild and transition metal-free conditions. Preliminary experiments for the asymmetric C3-thiocyanation of an oxindole derivative were also conducted leading to the expected product with no induction of chirality, although opening possibilities for accessing chiral compounds.

## Introduction

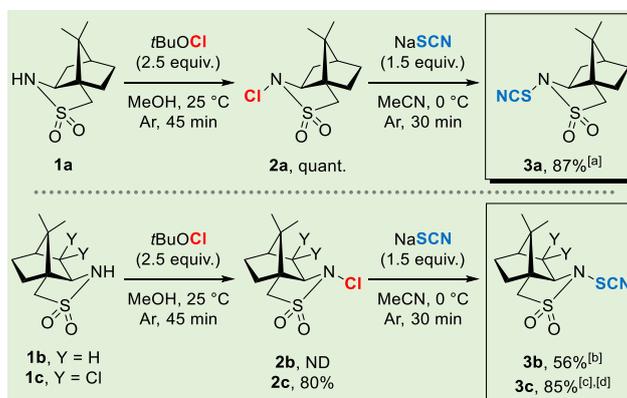
Found in agrochemicals, pharmaceuticals and materials,<sup>[1]</sup> organothiocyanates are playing a pivotal role in chemistry.<sup>[2]</sup> In addition, they are often used as key intermediates for the synthesis of complex molecules.<sup>[3]</sup> Two main approaches are usually employed to access these compounds of interest, relying either on the cyanation of sulfur-containing molecules<sup>[4]</sup> or the direct thiocyanation of derivatives.<sup>[5]</sup> In the latter case, a new trend has emerged over the last years with the design of electrophilic sources (Figure 1).<sup>[6]</sup> Aiming at developing 1) a bench-stable reagent with 2) a short, robust and efficient synthesis, which 3) might potentially act as a chiral source of SCN, we imagine a new class of electrophilic reagents to further explore the chemical space of thiocyanating molecules. Inspired by the recent advances made in the use of 2,10-camphorsultam based on reagents for the asymmetric fluorination,<sup>[7a-c]</sup> trifluoromethylthiolation<sup>[7d]</sup> and difluoromethylthiolation,<sup>[7e]</sup> we envisioned the preparation of enantiopure *N*-thiocyanato-2,10-camphorsultam. This will constitute the first chiral SCN-containing reagent. Herein, the synthesis of an original family of thiocyanating reagents was achieved and the potential of these (chiral) electrophilic reagents was evaluated with different nucleophiles.



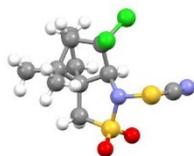
**Figure 1.** Overview of electrophilic thiocyanating reagents and this work.

## Results and Discussion

At the beginning of the study, the optically pure *N*-thiocyanato-2,10-camphorsultam **3a** was straightforwardly synthesized in a two-steps process/no purification starting from the commercially available (1*R*)-(+)-2,10-camphorsultam, *t*BuOH and NaCl being the main waste of the synthesis (Scheme 1). First, the chlorinated reagent **2a** was prepared in the presence of *t*BuOCl in 98% yield.<sup>[8]</sup> Then, **2a** was treated with the inexpensive NaSCN at 0 °C to afford the expected reagent **3a** in 73% yield.<sup>[9]</sup> The reagent **3a** is bench stable, can be stored at room temperature under argon for at least three months. This inexpensive, efficient and easy-to-handle synthesis was then applied to the preparation of *N*-thiocyanato-(1*S*)-(–)-2,10-camphorsultam **3b** and its dichlorinated analog **3c** starting from the naturally occurring (1*S*)-(–)-2,10-camphorsultam **1b** and the chlorinated derivative **1c**. Worth to mention that for the synthesis of **3c**, slightly modified reaction conditions were used, AgSCN being needed for the thiocyanation step. The structure of the compound **3c** was ascertained by single crystal X-ray diffraction analysis (CCDC 2107860, Figure 2).

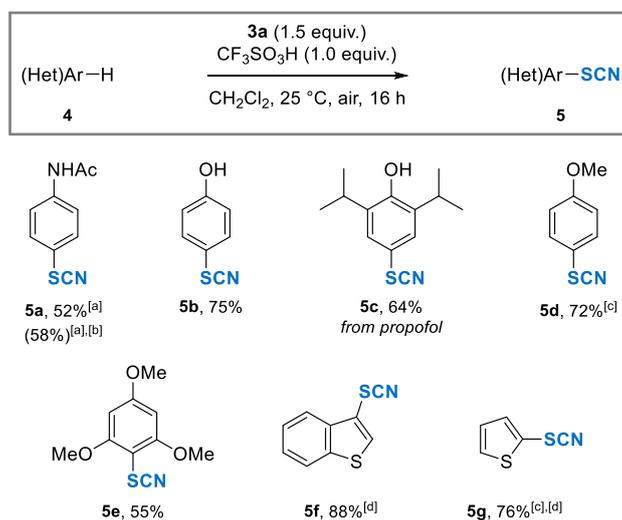


**Scheme 1.** Synthesis of a new class of electrophilic thiocyanating reagents **3a-c**. Isolated yields were provided. See supporting information for more details. [a] 10 mmol scale of **1a**. [b] 1 mmol of **1b**. [c] Reaction carried out on 2.35 mmol scale of **2c**. [d] Using AgSCN (1.5 equiv.), CH<sub>2</sub>Cl<sub>2</sub>, 25 °C, Ar, 8h. **3c** was obtained with 7% of **1c**. ND: Not Determined. Quant. = quantitative.



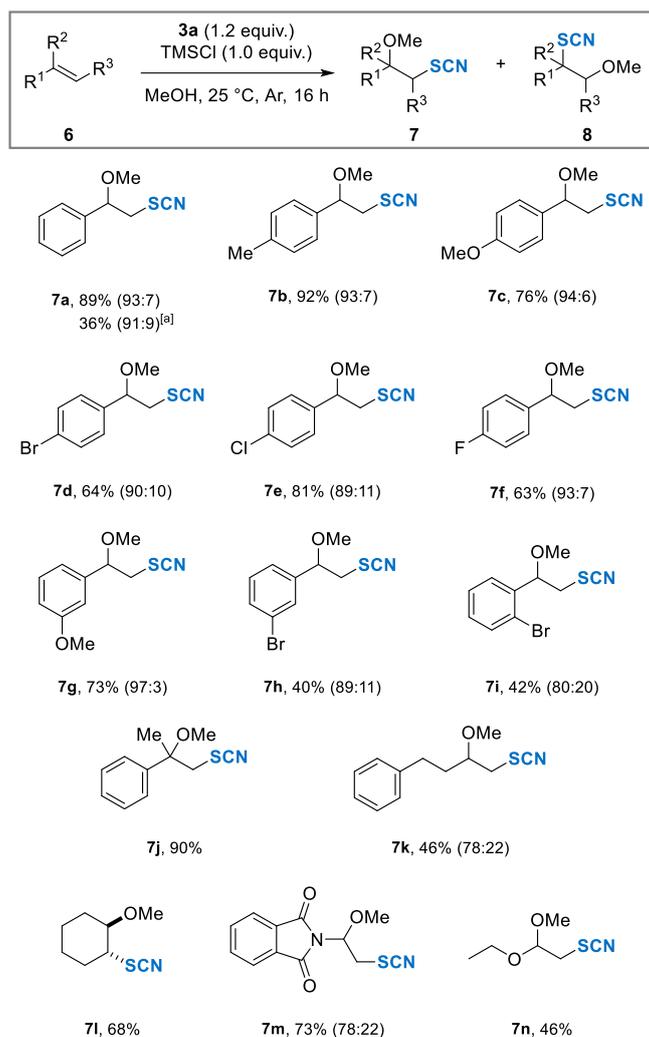
**Figure 2.** X-Ray structure of (1S)-(-)-N-thiocyanato-2,10-camphorsultam **3c** (CCDC 2107860).

With the reagent **3a** in hand, we first studied the electrophilic thiocyanation reaction of electron-rich (hetero)arenes (Scheme 2). In the presence of  $\text{CF}_3\text{SO}_3\text{H}$  in dichloromethane, the selective *para* thiocyanation<sup>[4c]</sup> of the aniline **4a** was achieved and the expected acetylated product was isolated in 52% yield over two steps.<sup>[10]</sup> Interestingly, using **3c** as the SCN source, a similar result was obtained (58% *vs* 52%). The regioselective thiocyanation reaction on the phenol **4b**, the propofol **4c**, a potent anesthetic, as well as anisole derivatives **4d-4e** went smoothly. Hence, the corresponding products **5b-5e** were isolated in good to high yields (up to 75%). Using slightly modified reaction conditions, the selective thiocyanation of benzothiophene **4f** and thiophene **4g** was possible, offering an access to the SCN-containing heterocyclic compounds of interest.



**Scheme 2.** Thiocyanation of electron-rich (hetero)arenes. Reaction conditions: **4** (0.2 mmol, 1.0 equiv.), **3a** (1.5 equiv.),  $\text{CF}_3\text{SO}_3\text{H}$  (1.0 equiv.),  $\text{CH}_2\text{Cl}_2$  (0.2 M), 25 °C, air, 16 h. [a] **5a** was obtained after thiocyanation then acylation reactions. [b] **3c** was used instead of **3a**. [c] The product was isolated with inseparable impurities. [d] **3a** (1.5 equiv.), MeCN (0.2 M), 60 °C.

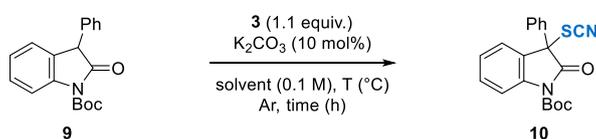
To further showcase the electrophilic potential of the source **3a**, the difunctionalization of alkenes<sup>[11]</sup> was investigated (Scheme 3). First, in the presence of TMSCl under air at room temperature and using MeOH as the solvent, the concomitant formation of a  $\text{C}(\text{sp}^3)\text{-OMe}$  and  $\text{C}(\text{sp}^3)\text{-SCN}$ <sup>[12]</sup> on the styrene **6a** was successfully achieved and the reaction showed a good regioselectivity (93:7 ratio of **7a**:**8a**) in favor of the Markovnikov product **7a** as confirmed by 2D NMR.<sup>[13]</sup> Pleasingly, a similar regioselectivity was obtained using **3c**, albeit **7a** was isolated in a lower yield. Styrene derivatives with an electron-donating group (**6b-6c**) as well as halogens (**6d-6f**) at the *para* position were functionalized in good to high yields with a high regioselectivity (up to 94:6). *meta*-Substituted derivatives (**6g** and **6h**) were also tested and the expected products were isolated in 73% yield and 40% yield, respectively with a good regioselectivity. The 2-bromostyrene **6i** was also a suitable substrate in this transformation. Pleasingly, the methodology was successfully applied to  $\alpha$ -methylstyrene **6j**, affording **7j** in 90% yield.<sup>[12e],[14]</sup> 4-Phenylbut-1-ene **6k** afforded the corresponding compounds **7k/8k** in 46% yield and a lower regioselectivity (78:22). In addition, the difunctionalization of a disubstituted alkene (cyclohexene **6l**) was smoothly conducted to provide **7l** in 68% yield. Finally, the thiocyanation reaction was also possible on the vinylphthalimide **6m** and the ethyl vinyl ether **6n**.



**Scheme 3.** Difunctionalization of alkenes. Reaction conditions: **6** (0.2 mmol, 1.0 equiv.), **3a** (1.2 equiv.), MeOH (0.2 M), 25 °C, Ar, 16 h. Only the major isomer was depicted. Isolated yields were given. Ratios of compounds **7** and **8** in parentheses were determined by <sup>1</sup>H NMR on the crude reaction mixture. [a] **3c** was used instead of **3a**.

Then, these chiral electrophilic sources were used for the asymmetric thiocyanation<sup>[15]</sup> of the *N*-Boc-3-phenyloxindole **9**. First, using a catalytic amount of K<sub>2</sub>CO<sub>3</sub> at room temperature, the expected C3-thiocyanated product was isolated in 83% yield as a racemic mixture. Switching K<sub>2</sub>CO<sub>3</sub> for Cs<sub>2</sub>CO<sub>3</sub>, the compound **10** was isolated in a lower yield. Then several parameters were studied to favor the formation of the enantioenriched product **10**. When the reaction was carried out at lower temperatures (Table 1, entries 3 and 4), no induction was observed. Similar results were obtained by replacing Et<sub>2</sub>O with THF or MeCN (Table 1, entries 5 and 6). We then studied the reaction using the other enantiomer of the source (**3b**) instead of **3a** (Table 1, entry 7) but no improvement was observed. At that stage, we reasoned that using the more sterically hindered thiocyanating reagent **3c** will be beneficial to promote an enantioinduction (Table 1, entries 7 and 8). Hence, the reaction was carried out in Et<sub>2</sub>O at -30 °C or -40 °C, but unfortunately the racemic product was only obtained.

**Table 1.** Optimization studies of C3 thiocyanation of *N*-Boc-3-phenyloxindole.<sup>[a]</sup>



Entry <sup>[a]</sup>	<b>3</b>	solvent	T (°C)	time (h)	Yield (%)	ee (%)
1	<b>3a</b>	Et <sub>2</sub> O	25	16	83	0
2 <sup>[b]</sup>	<b>3a</b>	Et <sub>2</sub> O	25	16	42	0
3	<b>3a</b>	Et <sub>2</sub> O	-20	16	41	0
4	<b>3a</b>	Et <sub>2</sub> O	-30	28	45	0
5	<b>3a</b>	THF	-30	28	9	0
6	<b>3a</b>	MeCN	-30	28	21	0
7	<b>3b</b>	Et <sub>2</sub> O	-30	64	43	0
8	<b>3c</b>	Et <sub>2</sub> O	-30	36	61	0
9	<b>3c</b>	Et <sub>2</sub> O	-40	16	51	0

[a] Reaction conditions: **9** (0.1 mmol, 1.0 equiv.), **3** (1.1 equiv.), K<sub>2</sub>CO<sub>3</sub> (10 mol%), solvent (1.0 mL), T (°C) under argon for time (h). Isolated yields were provided. [b] Cs<sub>2</sub>CO<sub>3</sub> was used instead of K<sub>2</sub>CO<sub>3</sub>.

## Conclusion

In summary, original and optically pure electrophilic thiocyanating reagents **3a-b** and a more sterically hindered reagent **3c** were designed and straightforwardly synthesized in a two-steps protocol from readily available starting materials. The SCN-containing sources turned out to be bench stable, not light sensitive as well as air and moisture tolerant. **3a** was even prepared in 87% yield on 10 mmol scale. It was then successfully applied for the electrophilic thiocyanation of electron-rich (hetero)arenes and for the difunctionalization of alkenes with the concomitant formation of C(sp<sup>3</sup>)-SCN and C(sp<sup>3</sup>)-OMe bonds in good yields and with excellent regioselectivity. Taking benefit from these chiral reagents, preliminary tests were conducted for the asymmetric C3-thiocyanation reaction of the N-Boc-3-phenyloxindole, although so far no enantioenriched product was obtained. With this newly-designed class of electrophilic and robust reagents, the construction of C(sp<sup>2</sup>)-SCN and C(sp<sup>3</sup>)-SCN bonds was efficiently achieved. We strongly believe that these chiral reagents will have an interesting potential to access enantioenriched thiocyanated molecules.

## Experimental section

All reactions were carried out using oven-dried glassware and magnetic stirring under argon unless otherwise stated. Reaction temperatures are reported as the temperature of the bath surrounding the vessel. Analytical thin layer chromatography was performed on silica gel aluminum plates with F-254 indicator and visualized by UV light (254 nm) and/or chemical staining with a KMnO<sub>4</sub> solution or a phosphomolybdic acid solution. Flash column chromatography was performed using 0.040 – 0.063 mm silica gel or a puriFlash® 5.020 flash purification system or Merck PTLC on silica gel 60 F254, 2 mm. <sup>1</sup>H NMR spectra were recorded on a Bruker DXP 300 MHz spectrometer at 300.1 MHz, <sup>13</sup>C NMR spectra at 75.5 MHz and <sup>19</sup>F NMR spectra at 282.4 MHz. Chemical shifts (δ) are quoted in ppm relative to CDCl<sub>3</sub> (1H). Coupling constants (J) are quoted in Hz. The following abbreviations were used to show the multiplicities: s: singlet, d: doublet, t: triplet, hept: heptuplet, m: multiplet. The residual solvent signals were used as references (CDCl<sub>3</sub>: δ<sub>H</sub> = 7.26 ppm, δ<sub>C</sub> = 77.00 ppm or relative to external CFC13, δ<sub>F</sub> = 0 ppm). High-resolution mass spectrometry (HRMS) was carried out on an electrospray ionization mass spectrometer with a micro-TOF analyzer. IR spectra were recorded on a PerkinElmer Spectrum

100, the wave numbers ( $\bar{\nu}$ ) of recorded IR-signals (ATR) are quoted in  $\text{cm}^{-1}$ . Optical rotations were recorded on a PerkinElmer Polarimeter 341 at 20 °C in chloroform. Melting points were reported for new compounds, recorded on a Heizbank System Köfler WME and were uncorrected. HPLC were performed on a ThermoFisher UHPLC system Ultimate RSLC with a PDA detector with columns with chiral stationary phase from Daicel (250 mm x 4.6 mm, 5  $\mu\text{m}$  particle size) at 20 °C.

Procedure for the synthesis of *N*-thiocyanato-(1*R*)-(+)-2,10-Camphorsultam 3a.

In an oven dried round-bottom flask, covered with aluminum foil under argon was added (1*R*)-(+)-2,10-camphorsultam 1a (2.15 g, 10 mmol, 1 equiv.) in anhydrous methanol (25 mL, 0.4 M), then the freshly prepared tBuOCl (1.7 mL, 15 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred for 45 min at room temperature under argon. Solvents were evaporated and the mixture was filtered through a pad of Celite® to afford quantitatively 2a, which was directly engaged in the next step.

In an oven dried round-bottom flask (250 mL) covered with aluminum foil under argon was solubilized 2a (2.35 g, 1 equiv.) in MeCN (100 mL, 0.1 M). The solution was cooled to 0 °C. Then, NaSCN (1.22 g, 15 mmol, 1.5 equiv.) was added in one portion. The reaction mixture was stirred under argon and dark and monitored by TLC. After complete conversion (30 min), the mixture was filtered through a pad of Celite® to obtain the pure product 3a.

Procedure for the synthesis of *N*-thiocyanato-(1*R*)-(+)-2,10-Camphorsultam 3b.

In an oven dried round-bottom flask, covered with aluminum foil under argon was added (1*S*)-(–)-2,10-camphorsultam 1b (215.3 mg, 1 mmol, 1 equiv.) in anhydrous methanol (5 mL, 0.4 M), then the freshly prepared tBuOCl (170  $\mu\text{L}$ , 1.5 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred for 45 min at room temperature under argon. Solvents were evaporated to afford 2b and the product was directly engaged in the next step without further purification. 2b was obtained after filtration through a pad of Celite® and was engaged directly in the next step without further purification.

In an oven dried round-bottom flask (250 mL) covered with aluminum foil under argon was added 2b (0.2 mmol, 1 equiv.) in MeCN (0.1 M). The solution was cooled to 0 °C. Then, NaSCN (122.6 mg, 1.50 mmol, 1.5 equiv.) was added in one portion. The reaction mixture was stirred under argon and dark and monitored by TLC. After complete conversion (30 min), the mixture was filtered through a pad of Celite® to obtain the desired product 3b.

Procedure for the synthesis of (7,7)-Dichloro-*N*-Chloro-(1*S*)-(–)-2,10-Camphorsultam 3c.

In an oven dried round-bottom flask, covered with aluminum foil under argon was added (1*S*)-(–)-7,7-dichloro-2,10-camphorsultam 1c (667.9 mg, 2.35 mmol, 1 equiv.) in anhydrous methanol (6 mL, 0.4 M), then the freshly prepared tBuOCl (400  $\mu\text{L}$ , 3.53 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred for 45 min at room temperature under argon. Solvents were evaporated under vacuum and 2c was obtained after filtration through a pad of Celite®.

In an oven dried round-bottom flask (250 mL) covered with aluminum foil under argon was added 2c (748.0 mg, 2.35 mmol, 1 equiv.) added  $\text{CH}_2\text{Cl}_2$  (24 mL, 0.1 M). Then, AgSCN (586.0 mg, 3.53 mmol, 1.5 equiv.) was added in one portion. The reaction mixture was stirred at 25 °C under argon and dark and monitored by TLC. After complete conversion (8 h), the reaction mixture was filtered through a pad of Celite® to obtain the desired product 3c.

General procedure for thiocyanation reaction on electron-rich (hetero)arenes 4.

In an oven dried tube under argon were solubilized 3a (81.7 mg, 0.3 mmol, 1.5 equiv.) and the solid 4 (0.2 mmol, 1 equiv.) in dichloromethane (1 mL, 0.2 M). CF<sub>3</sub>SO<sub>3</sub>H (18 µL, 0.2 mmol, 1 equiv.) was added dropwise to the mixture. In case 4 was an oil, it was added after the solvent. Then, the reaction mixture was stirred for 16 h at 25 °C under air. Solvents were evaporated under vacuum. The crude mixture was purified by chromatography on silica gel to afford the desired product. Note that in case of 5a, an acetylation step was required,[5] following the procedure below: in an oven dried tube under argon, 5a (0.2 mmol, 1 equiv.) was dissolved in dichloromethane (0.5 mL). Then triethylamine (30 µL, 0.22 mmol, 1.1 equiv.) was added to the solution. The reaction mixture was cooled down to 0 °C. AcCl (14 µL, 0.2 mmol, 1 equiv.) was added dropwise. The reaction mixture was warmed to 25 °C and stirred for 16 h. The aqueous phase was extracted with dichloromethane (3 × 5 mL) then the organic phase was washed with NaHCO<sub>3</sub> (3 × 2 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum.

General procedure for the difunctionalization of alkenes 6.

In an oven dried tube under argon, 3a (65.4 mg, 0.24 mmol, 1.2 equiv.) was dissolved in MeOH (1 mL, 0.2 M). TMSCl (25 µL, 0.2 mmol, 1 equiv.) was added to the solution. Alkene 6 (0.2 mmol, 1 equiv.) was added before the solvent if it is a solid, after the solvent if it is a liquid. The mixture was performed at 25 °C for 16 h. The volatile reagents were evaporated under reduced pressure. The product was purified by silica gel chromatography or Puriflash to afford the desired compound.

## Acknowledgements

This work has been partially supported by University of Rouen Normandy, INSA Rouen Normandy, the Centre National de la Recherche Scientifique (CNRS), European Regional Development Fund (ERDF), Labex SynOrg (ANR-11-LABX-0029), Carnot Institute I2C, the graduate school for research XL-Chem (ANR-18-EURE-0020 XL CHEM), and by Region Normandy. M.G., M.V. and T.B. thank the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement no. 758710). M.G. thanks the Region Normandy for a doctoral fellowship.

## Keywords

Chiral sources • Difunctionalization of alkenes • Electrophilic reagent • Synthetic methods • Thiocyanation

[1] For selected examples, see: a) Yasman, R. A. Edrada, V. Wray, P. Proksch, *J. Nat. Prod.* 2003, 66, 1512-1514; b) E. Zubía, M. J. Ortega, J. L. Carballo, *J. Nat. Prod.* 2008, 71, 2004-2010; c) S. Dutta, H. Abe, S. Aoyagi, C. Kibayashi, K. S. Gates, *J. Am. Chem. Soc.* 2005, 127, 15004-15005; d) J. F. Liu, C. H. Heathcock, *J. Org. Chem.* 1999, 64, 8263-8266; e) S. S. Roy, P. Ghosh, U. H. Sk, P. Chakraborty, J. Biswas, S. Mandal, A. Bhattacharjee, S. Bhattacharya, *Bioorg. Med. Chem. Lett.* 2010, 20, 6951-6955; f) D. Plano, D. N. Karelia, M. K. Pandey, J. E. Spallholz, S. Amin, A. K. Sharma, *J. Med. Chem.* 2016, 59, 1946-1959; g) W. Ali, M. Álvarez-Pérez, M. A. Maré, N. Salardón-Jiménez, J. Handzlik, E. Domínguez-Álvarez, *Curr. Pharmacol. Rep.* 2018, 4, 468-481.

[2] For selected reviews, see: a) T. Castanheiro, J. Suffert, M. Donnard, M. Gulea, *Chem. Soc. Rev.* 2016, 45, 494-505 and references cited therein; b) X. Qing, Z. Lianyang, F. Gaofeng, J. Chengan, *Chin. J. Org. Chem.* 2019, 39, 287-300 and references cited therein; c) A. W. Erian, S. M. Sherif, *Tetrahedron* 1999, 55, 7957-8140; d) M. Gulea, M. Donnard, *Curr. Green Chem.* 2020, 7, 201-216; e) L. Zhang, C. Niu, X. Yang, H. Qin, J. Yang, J. Wen, H. Wang, *Chin. J. Org. Chem.* 2020, 40, 1117-1128.

[3] For selected examples, see: a) R. G. Guy in *The Chemistry of Cyanates*

and their Thio Derivatives, John Wiley & Sons, New York, 1977; b) B. Bayarmagnai, C. Matheis, K. Jouvin, L. J. Gooßen, *Angew. Chem. Int. Ed.* 2015, 54, 5753-5756; *Angew. Chem.* 2015, 127, 5845-5848; c) Z. Zhang, L. S. Liebeskind, *Org. Lett.* 2006, 8, 4331-4333; d) H.-Y. Xiong, A. Bayle, X. Pannecoucke, T. Besset, *Angew. Chem. Int. Ed.* 2016, 55, 13490-13494; *Angew. Chem.* 2016, 128, 13688-13692; e) M. V. Ivanova, A. Bayle, T. Besset, X. Pannecoucke, T. Poisson, *Angew. Chem. Int. Ed.* 2016, 55, 14141-14145; *Angew. Chem.* 2016, 128, 14347-14351; f) M. V. Ivanova, A. Bayle, T. Besset, X. Pannecoucke, T. Poisson, *Chem. Eur. J.* 2017, 23, 17318-17338; g) M. V. Ivanova, A. Bayle, X. Pannecoucke, T. Besset, T. Poisson, *Eur. J. Org. Chem.* 2017, 2475-2480; h) J. Wang, H.-Y. Xiong, E. Petit, L. Bailly, X. Pannecoucke, T. Poisson, T. Besset, *Chem. Commun.* 2019, 55, 8784-8787; i) F. Petit-Cancelier, B. François, X. Pannecoucke, S. Couve-Bonnaire, T. Besset, *Adv. Synth. Catal.* 2020, 362, 760-764; j) Y. Ou, L. J. Gooßen, *Asian J. Org. Chem.* 2019, 8, 650-653; k) M.-Y. Chen, X. Pannecoucke, P. Jubault, T. Besset, *J. Org. Chem.* 2019, 84, 13194-13202.

[4] For selected examples, see: a) W. Guo, W. Tan, M. Zhao, L. Zheng, K. Tao, D. Chen, X. Fan, *J. Org. Chem.* 2018, 83, 6580-6588; b) D. Zhu, D. Chang, L. Shi, *Chem. Commun.* 2015, 51, 7180-7183; c) T. Castanheiro, M. Gulea, M. Donnard, J. Suffert, *Eur. J. Org. Chem.* 2014, 7814-7817; d) F. Teng, J.-T. Yu, H. Yang, Y. Jiang, J. Cheng, *Chem. Commun.* 2014, 50, 12139-12141; e) K. Yamaguchi, K. Sakagami, Y. Miyamoto, X. Jin, N. Mizuno, *Org. Biomol. Chem.* 2014, 12, 9200-9206.

[5] For selected examples of thiocyanation reactions, see: a) Z. Yang, Y. Wang, L. Hu, J. Yu, A. Li, L. Li, T. Yang, C. Zhou, *Synthesis* 2020, 52, 711-718; b) F. Meng, H. Zhang, H. He, N. Xu, Q. Fang, K. Guo, S. Cao, Y. Shi, Y. Zhu, *Adv. Synth. Catal.* 2020, 362, 248-254; c) X. Mao, J. Ni, B. Xu, C. Ding, *Org. Chem. Front.* 2020, 7, 350-354; d) T. Kittikool, S. Yotphan, *Eur. J. Org. Chem.* 2020, 961-970; e) M. Dyga, D. Hayrapetyan, R. K. Rit, L. J. Gooßen, *Adv. Synth. Catal.* 2019, 361, 3548-3553; f) X. Bao, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* 2019, 58, 2139-2143; g) V. A. Kokorekin, R. R. Yaubasarova, S. V. Neverov, V. A. Petrosyan, *Eur. J. Org. Chem.* 2019, 4233-4238; h) M. Li, W. Song, K. Dong, Y. Zheng, *Tetrahedron Lett.* 2020, 61, 151503-151507; i) X. Zeng, B. Chen, Z. Lu, G. B. Hammond, B. Xu, *Org. Lett.* 2019, 21, 2772-2776; j) Z. Yang, L. Hu, T. Cao, L. An, L. Li, T. Yang, C. Zhou, *New J. Chem.* 2019, 43, 16441-16444; k) A. Dey, A. Hajra, *Adv. Synth. Catal.* 2019, 361, 842-849; l) V. Rathore, S. Kumar, *Green Chem.* 2019, 21, 2670-2676; m) K. Gullapalli, S. Vijaykumar, *Org. Biomol. Chem.* 2019, 17, 2232-2241; n) P. Chauhan, Ritu, Preeti, S. Kumar, N. Jain, *Eur. J. Org. Chem.* 2019, 4334-4340; o) Y. Gao, Y. Liu, J.-P. Wan, *J. Org. Chem.* 2019, 84, 2243-2251; p) I. Ghosh, J. Khamrai, A. Savateev, N. Shlapakov, M. Antonietti, B. König, *Science* 2019, 365, 360-366; q) S. Samanta, R. Chatterjee, S. Santra, A. Hajra, I. A. Khalymbadzha, G. V. Zyryanov, A. Majee, *ACS Omega* 2018, 3, 13081-13088; r) X. Zeng, L. Chen, *Org. Biomol. Chem.* 2018, 16, 7557-7560; s) Y. Chen, S. Wang, Q. Jiang, C. Cheng, X. Xiao, G. Zhu, *J. Org. Chem.* 2018, 83, 716-722; t) C. Feng, Y. Peng, G. Ding, X. Li, C. Cui, Y. Yan, *Chem. Commun.* 2018, 54, 13367-13370; u) P.-F. Yuan, Q.-B. Zhang, X.-L. Jin, W.-L. Lei, L.-Z. Wu, Q. Liu, *Green Chem.* 2018, 20, 5464-5468; v) H. Jiang, W. Yu, X. Tang, J. Li, W. Wu, *J. Org. Chem.* 2017, 82, 9312-9320; w) Z. Wang, L. Wang, Q. Chen, M. He, *Synth. Commun.* 2018, 48, 76-84; x) Q. Chen, Y. Lei, Y. Wang, C. Wang, Y. Wang, Z. Xu, H. Wang, R. Wang, *Org. Chem. Front.* 2017, 4, 369-372; y) H. Zhang, Q. Wei, Q. Wei, J. Qu, B. Wang, *Eur. J. Org. Chem.* 2016, 3373-3379; z) R. Frei, T. Courant, M. D. Wodrich, J. Waser, *Chem. Eur. J.* 2015, 21, 2662-2668; aa) M. Gao, M.-Y. Chen, X. Pannecoucke, P. Jubault, T. Besset, *Chem. Eur. J.* 2020, 26, 15497-15500.

[6] M. Gao, M. Vuagnat, M.-Y. Chen, X. Pannecoucke, P. Jubault, T. Besset, *Chem. Eur. J.* 2021, 27, 6145-6160 and references cited therein.

[7] a) E. Differding, R. W. Lang, *Tetrahedron Lett.* 1988, 29, 6087-6090; b) F. A. Davis, P. Zhou, C. K. Murphy, *Tetrahedron Lett.* 1993, 34, 3971-3974; c) F. A. Davis, P. Zhou, C. K. Murphy, G. Sundarababu, H. Qi, W. Han, R. M. Przeslawski, B. C. Chen, P. J. Carroll, *J. Org. Chem.* 1998, 63, 2273-2280; d) H. Zhang, X. Leng, X. Wan, Q. Shen, *Org. Chem. Front.* 2017, 4, 1051-1057; e) H. Zhang, X. Wan, Q. Shen, *Chin. J. Chem.* 2019, 37, 1041-1050.

[8] a) L. Duhamel, G. Plé, P. Angibaud, J. R. Desmurs, *Synth. Commun.* 1993, 23, 2423-2433; b) Fan, Z.; Lu, H.; Cheng, Z.; Zhang, A. *Chem. Commun.* 2018, 54, 6008-6011.

[9] Note that working at 0 °C was important to avoid the degradation of N-chloro-(1S)-(-)-2,10-camphorsultam 2a into 1a.

[10] In case of the aniline 4a, an extra acetylation step was required to circumvent purification issues.

[11] For selected reviews, see: a) E. Merino, C. Nevado, *Chem. Soc. Rev.* 2014, 43, 6598-6608; b) H. Egami, M. Sodeoka, *Angew. Chem., Int. Ed.* 2014, 53, 8294-8308; c) T. Besset, T. Poisson, X. Pannecoucke, *Chem. Eur. J.* 2014, 20, 16830-16845; d) X.-W. Lan, N.-X. Wang, Y. Xing, *Eur. J. Org. Chem.* 2017, 5821-5851; e) X. Bao, J. Li, W. Jiang, C. Huo, *Synthesis* 2019, 51, 4507-4530; f) X. Fu, W. Zhao, *Chin. J. Org. Chem.* 2019, 39, 625-647; g) H. Yao, W. Hu, W. Zhang, *Molecules* 2020, 26, 105-135; h) B. Wang, Y. Zhou, S. Luo, X. Luo, W. Chen, S. Yang, Z. Wang, *Chin. J. Org. Chem.* 2021, 41, 171-184; i) Z. Hossaini, E. A. Mahmood, M. R. P. Heravi, A. G. Ebadi, E. Vessally, *E. RSC Adv.* 2021, 11, 21651-21665.

[12] For selected examples of difunctionalization of alkenes with the SCN moiety, see: a) A. B. Angus, R. G. R Bacon, *J. Chem. Soc.* 1958, 774-778; b) G. R. Guy, I. Pearson, *J. Chem. Soc. Perkin Trans. 1* 1973, 281-284; c) G. R. Guy, I. Pearson, *Bull. Chem. Soc. Jap.* 1976, 49, 2310-2314; d) J. Goerdeler, P. Rosenthal, *Tetrahedron Lett.* 1964, 48, 3665-3666; e) A.-H. Ye, Y. Zhang, Y.-Y. Xie, H.-Y. Luo, J.-W. Dong, X.-D. Liu, X.-F. Song, T. Ding, Z.-M. Chen, *Org. Lett.* 2019, 21, 5106-5110; f) D. Zhang, H. Wang, C. Bolm, *Chem. Commun.* 2018, 54, 5772-5775; g) C. Li, P. Long, H. Wu, H. Yin, F.-X. Chen, *Org. Biomol. Chem.* 2019, 17, 7131-7134; h) X.-F. Song, A.-H. Ye, Y.-Y. Xie, J.-W. Dong, C. Chen, Y. Zhang, Z.-M. Chen, *Org. Lett.* 2019, 21, 9550-9554.

[13] For more details, see the Supporting Information.

[14] Note that an attempt to get the enantioenriched compound 7j by carrying the reaction at -20 °C using 3a failed.

[15] For selective examples of enantioselective thiocyanation reaction, see: a) J. Qiu, D. Wu, P. G. Karmaker, H. Yin, F.-X. Chen, *Org. Lett.* 2018, 20, 1600-1603; b) J. Qiu, D. Wu, L. Yuan, P. Long, H. Yin, F.-X. Chen, *J. Org. Chem.* 2019, 84, 7917-7926.