Pergamon

Tetrahedron Letters 42 (2001) 5017–5019

TETRAHEDRON LETTERS

A new convenient procedure for the preparation of enantiopure C10-S- and C10-Se-substituted camphor-derived sulfides and selenides

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Received 7 May 2001; revised 28 May 2001; accepted 29 May 2001

Abstract—The enantiospecific preparation of two novel C10-S(II)- and C10-Se(II)-substituted camphor derivatives (arylsulfide and arylselenide) from readily available camphor is described. The established three-step route constitutes a model procedure for the straightforward preparation of interesting enantiopure C10-S- and C10-Se-substituted camphor-derived chiral sources. The key-step of the described route is an enantiospecific Wagner–Meerwein rearrangement of 3,3-dimethyl-2-methylenenorbornan-1-ol **6** under electrophilic treatment with an arylsulfenyl (or arylselenyl) chloride.

Enantiopure C10-S-substituted camphor derivatives are an important class of chiral sources, which have been widely used as chiral reagents (e.g. Davies' oxaziridine), chiral auxiliaries (e.g. Oppolzer's sultame), chiral resolving agents (e.g. 10-camphorsulfonic acid) and chiral catalysts (e.g. Yus' sulfonamides) for asymmetric synthesis, as well as chiral synthetic intermediates for the preparation of high-value molecules (e.g. in the total synthesis of the natural product taxol).[1] Most of the described C10-S-substituted camphor derivatives are of the type C10-S(VI), due to the fact that they can be easily obtained by transfunctionalization of commercially available 10-camphorsulfonic acid (or 10-camphorsulfonyl halide).[1] Nevertheless some interesting C10-S(II)- and C10-S(IV)-substituted camphor derivatives (generally sulfides and sulfoxides), and also corresponding chalcogenic analogous of the type C10-Se(II) and C10-Se(IV), have been obtained and probed as valuable chirality transfer agents (e.g. derivatives **1**–**4** in Fig. 1).[2]

In this sense camphor derived sulfides and selenides of type **5** (Fig. 1) are key intermediates (together with commercial 10-sulfanylisoborneol) to other interesting C10-S(II)- and C10-S(IV)-substituted camphor derivatives (e.g. via stereoselective camphor C2-functionalization, *m*-CPBA S(II)-to-S(IV)-oxidation, etc.).[3] Unfortunately, this kind of ketosulfides and ketoselenides are usually difficult to prepare (specially arylsulfides and arylselenides), and their syntheses have low overall yields.[4]

On the other hand, we have recently reported that the reaction of 3,3-dimethyl-2-methylenenorbornan-1-ol **6**

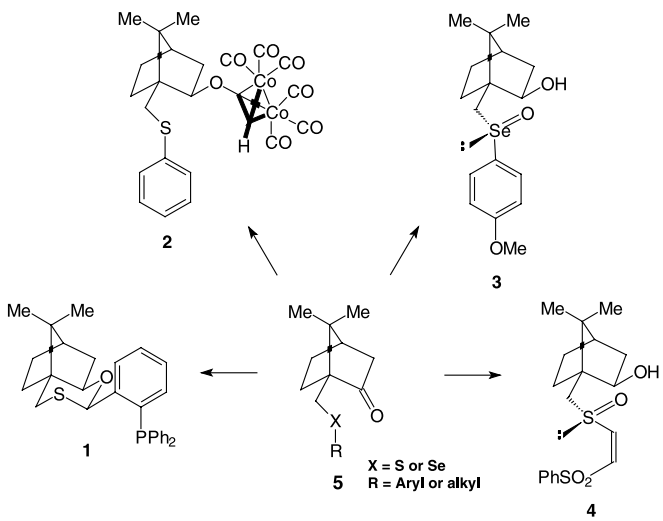

Figure 1. Some interesting C10-S- and C10-Se-substituted camphor derivatives.

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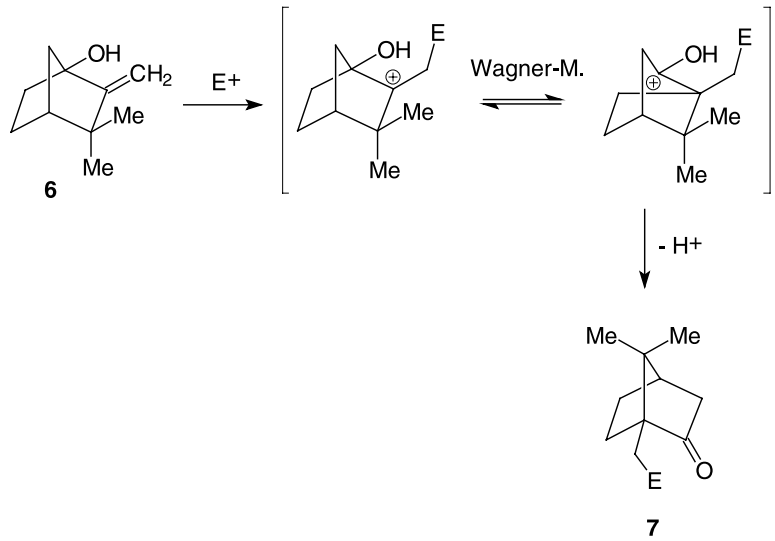
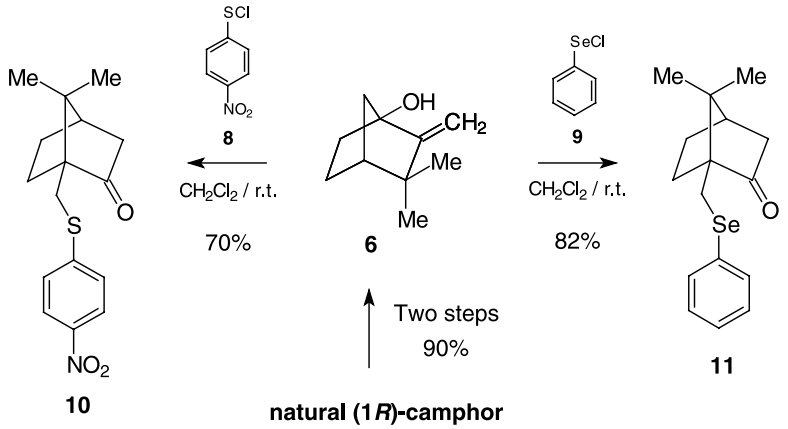
PII: S0040-4039(01)00924-8



Scheme 1. Tandem electrophilic carbon–carbon double-bond addition – Wagner–Meerwein rearrangement in **6**.



Scheme 2. Preparation of enantiopure **10** and **11**: A novel straightforward camphor-based route to C10-S- and C10-Se-substituted camphor-derived sulfides and selenides.

with *N*-bromosuccinimide or *m*-CPBA, as electrophilic reagents ($E^+ = Br^+$ or OH^+), takes place with a regio- and enantiospecific tandem of electrophilic carbon–carbon double-bond addition – Wagner–Meerwein rearrangement, to give straightforwardly the corresponding 10-bromocamphor (**7**, E = Br) and 10-hydroxycamphor (**7**, E = OH) (Scheme 1).[5] Key 2-methylenenorbornane **6** is enantiospecifically obtained from camphor in only two easy steps with 90% overall yield.[5,6]

As a result of this, we have now found that the treatment of (1*R*)-3,3-dimethyl-2-methylenenorbornan-1-ol **6**, obtained from natural (1*R*)-camphor, with the commercial electrophilic sulfanylating and selanylating reagents (4-nitrophenyl)sulfenyl chloride **8** and phenylselenyl chloride **9**, enantiospecifically yields corresponding (1*S*)-10-[(4-nitrophenyl)sulfanyl]camphor **10** or (1*S*)-10-(phenylselanyl)camphor **11** as the only camphor-derived products (Scheme 2).

The reactions take place under mild conditions (methylene dichloride solution at room temperature) and with good yields (70–82%),[7] according to the mechanism described in Scheme 1.

In conclusion, a new enantiospecific route to interesting C10-substituted camphor-derived sulfides and selenides has been established. The synthetic procedure takes place straightforwardly in only three easy individual synthetic steps. The key-step is the reaction of enantiopure 3,3-dimethyl-2-methylenenorbornan-1-ol with sulfenyl (or selenyl) halides, which takes place with a regio- and enantiospecific tandem of electrophilic carbon–carbon double-bond addition – Wagner–Meerwein rearrangement. The easy access to 10-(arylselanyl)camphors of the type of **11** opens the way for the preparation of novel interesting γ-hydroxyselenoxides analogous to **3** (see Fig. 1), which could be used as a good chiral reagents for the asymmetric protonation of enolates.[2d]

Acknowledgements

We would like to thank the Ministerio de Educación y Ciencia (MEC) of Spain (DGICYT, research project PB97-0264) for the financial support of this work. B.L.M. wishes to thank MEC for a post-graduate grant.

References

1. For a review, see: (a) Oppolzer, W.; *Tetrahedron* **1987**, 1969; (b) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 335. Some recent examples are, related to Davis' oxaziridine: (c) Cermak, D. M.; Du, Y.; Wiemer, D. F. *J. Org. Chem.* **1999**, *64*, 388; (d) Wang, C.-C.; Li, J. J.; Huang, H.-C.; Lee, L.-F.; Reitz, D. B. *J. Org. Chem.* **2000**, *65*, 2711; related to Oppolzer's sultame: (e) Miyabe, H.; Ushiro, C.; Ueda, M.; Yamakawa, K.; Naito, T. *J. Org. Chem.* **2000**, *65*, 176; (f) Ponsinet, R.; Chassaing, G.; Vaissermann, J.; Lavielle, S. *Eur. J. Org. Chem.* **2000**, 83; related to 10-camphorsulfonic acid: (g) Yoshioka, R.; Hiratmatsu, H.; Okamura, K.; Tsujioka, I.; Yamada, S. *J. Chem. Soc., Perkin Trans. 2* **2000**, *10*, 2121; (h) Kaptein, B.; Elsenberg, H.; Grimbergen, R. F. P.; Broxterman, Q. B.; Hulshof, L. A.; Pouwer, L. A.; Vries, T. R. *Tetrahedron: Asymmetry* **2000**, *11*, 1343; related to Yus′ 10-camphorsulfonamides; (i) Prieto, O.; Ramon, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2000**, *11*, 1629; related to taxol synthesis: (j) Paquette, L. A.; Zhao, M. *J. Am. Chem. Soc.* **1998**, *120*, 5203.
2. Some selected examples are, concerning to asymmetric Diels–Alder reactions: (a) De Lucchi, O.; Luchini, V.; Marchioro, C.; Valle, G.; Modena, G. *J. Org. Chem.* **1986**, *51*, 1457; (b) Aversa, M. C.; Baratucci, A.; Bonaccorsi, P.; Giannetto, P. *J. Org. Chem.* **1997**, *62*, 4376; (c) Aversa, M. C.; Baratucci, A.; Bonaccorsi, P.; Gianneto, P. *J. Org. Chem.* **1999**, *64*, 2114; concerning to the asymmetric protonation of enolates: (d) Takahashi, T.; Nakao, N.; Koizumi, T. *Tetrahedron: Asymmetry* **1997**, *8*, 3293; concerning to the catalytic asymmetric epoxidation of aldehydes: (e) Furukawa, N.; Sugihara, Y.; Fujihara, H. *J. Org. Chem.* **1989**, *54*, 4222; (f) Aggarwal, V. K.; Ford, J. G.; Fonquerna, S.; Adams, H.; Jones, R. V. H.; Fieldhouse, R. *J. Am. Chem. Soc.* **1998**, *120*, 8328; concerning to asymmetric Pauson–Khand reactions: (g) Verdaguer, X.; Vázquez, J.; Fuster, G.; Barnardes-Génisson, V.; Greene, A. E.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 7037; concerning to the asymmetric reduction of ketones: (h) Fiaud, J.-C.; Mazé, F.; Kagan, H. B. *Tetrahedron: Asymmetry* **1998**, *9*, 3647, (i) Node, M.; Nishide, K.; Shigeta, Y.; Shiraki, H.; Obata, K. *J. Am. Chem. Soc.* **2000**, *122*, 1927; concerning to asymmetric paladium-catalyzed allylic substitutions: (j) Nakano, H.; Okuyama, Y.; Yanagida, M.; Hongo, H. *J. Org. Chem.* **2001**, *66*, 620.
3. For example see: (a) Montenegro, E.; Echarri, R.; Claver, C.; Castillón, S.; Moyano, A.; Pericás, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1996**, *7*, 3553; (b) Sewald, N.; Wendisch, V. *Tetrahedron: Asymmetry* **1996**, *7*, 1269. See also Refs. 2a, 2d and 2g.
4. For example see: Oae, S.; Togo, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3802, and Refs. 2d and 2g.
5. (a) Lora Maroto, B.; de la Moya Cerero, S.; García Martínez, A.; García Fraile, A.; Teso Vilar, E. *Tetrahedron: Asymmetry* **2000**, *11*, 3059; (b) García Martínez, A.; Teso Vilar, E.; García Fraile, A.; de la Moya Cerero, S.; Lora Maroto, B. *Tetrahedron: Asymmetry* **2000**, *11*, 4437.
6. García Martínez, A.; Teso Vilar, E.; García Fraile, A.; Ruano Franco, C.; Soto Salvador, J.; Subramanian, L. R.; Hanack, M. *Synthesis* **1987**, 321.
7. Over a solution of alcohol **6** (0.5 mmol) in 5 mL of dry CH_2Cl_2, under argon atmosphere, 1.5 mmol of **8** (or **9**) were added. The reaction mixture was stirred at room temperature for 24 h (the reaction progress was monitored by GC). After that, the reaction was quenched with saturated $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with brine and dried over anhydrous magnesium sulfate. After filtration and solvent evaporation the residue was purified by column chromatography (silica gel, hexane/CH_2Cl_2 80:20) to yield pure **10** (or **11**). **10:** Pale brown solid, 70% yield, decomposes at 100°C, $[\alpha]_D^{20}$ +7.1 (0.22, CH_2Cl_2). IR (CCl_4) ν 1745, 1583, 1520, 1338 cm^{-1}. EM m/z 305 [$M^{+\bullet}$ (^{32}S), 25], 307 [$M^{+\bullet}$ (^{34}S), 1], 151 (17), 41 (100). HRMS m/z 305.108980 [calcd for $C_{16}H_{19}NO_3S$ (^{32}S) 305.108565]. ^1H NMR ($CDCl_3$, 200 MHz): δ 8.13 and 7.37 (AA′XX′ system, 4H), 3.37 (d, $J=12.6$ Hz, 1H), 2.99 (d, $J=12.6$ Hz, 1H), 2.52–2.37 (dm, $J=18.5$ Hz, 1H), 2.17–1.94 (m, 3H), 1.94 (d, $J=18.5$ Hz, 1H), 1.62–1.35 (m, 2H), 1.21 (s, 3H), 0.98 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ 216.4, 148.6, 145.0, 126.1, 123.9, 60.4, 48.0, 43.5, 43.0, 29.2, 26.9, 26.7, 20.3, 20.2 ppm. **11:** Pale brown solid, 82% yield, mp 36–38°C, $[\alpha]_D^{20}$ −51.8 (0.22, CH_2Cl_2). IR (CCl_4) ν 2959, 1742, 1578, 1477 cm^{-1}. EM m/z 304 [$M^{+\bullet}$ (^{76}Se), 4], 305 [$M^{+\bullet}$ (^{77}Se), 4], 306 [$M^{+\bullet}$ (^{78}Se), 12], 308 [$M^{+\bullet}$ (^{80}Se), 24], 310 [$M^{+\bullet}$ (^{82}Se), 4], 151 (18), 81 (100). HRMS 308.067870 [calcd. for $C_{16}H_{20}OSe$ (^{80}Se) 308.067936]. ^1H NMR ($CDCl_3$, 200 MHz): δ 7.56–7.51 (m, 2H), 7.26–7.22 (m, 3H), 3.26 (d, $J=12.2$ Hz, 1H), 2.78 (d, $J=12.2$ Hz, 1H), 2.40 (dm, $J=18.4$ Hz, 1H), 2.12–2.09 (m, 1H), 2.00–1.87 (m, 2H), 1.89 (d, $J=18.3$ Hz, 1H), 1.69 (dd, $J=9.0$ Hz, $J=9.0$ Hz, 1H), 1.38 (dd, $J=9.0$ Hz, $J=9.0$ Hz, 1H), 1.02 (s, 3H), 0.91 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ 217.3, 132.6, 132.4, 129.0, 126.6, 61.3, 48.1, 43.5, 43.1, 27.8, 26.8, 25.3, 20.1, 20.0 ppm.