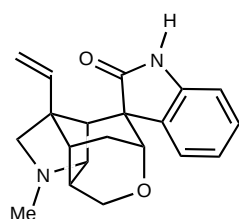


Total Synthesis of (+)-Gelsedine

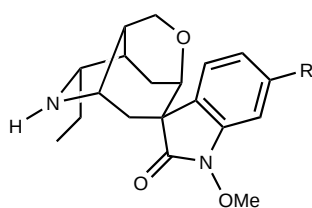
Winfred G. Beyersbergen
van Henegouwen,
Rutger M. Fieseler,
Floris P. J. T. Rutjes, and
Henk Hiemstra*

Species of the plant genus *Gelsemium* (Loganiaceae) constitute a rich source of indole alkaloids with remarkably complex and diverse structures.^[1] Among these are gelsemine (**1**) and gelsedine (**2**). Recently, we^[2] and others^[3] have published total syntheses of racemic gelsemine. Here we present the first total synthesis of gelsedine in enantiopure form. Our studies are motivated by the challenging molecular architecture of the *Gelsemium* alkaloids and by the interesting biological activity that some of these natural products display. In fact, extracts from *Gelsemium* species have a rich medicinal history, particularly in China.^[1]

Gelsedine (**2**) was isolated from Carolina jasmine (*Gelsemium semper-virens*) in 1953 by Schwarz and Marion^[4] and was later also found to occur in *G. elegans*.^[5] Its structure was elucidated by Wenkert et al.^[6] in 1962 on the basis of a spectroscopic comparison with its 11-methoxy analogue gelsemicine (**3**), whose structure had already been determined in 1961 through X-ray crystallography by Przybylska and Marion.^[7]

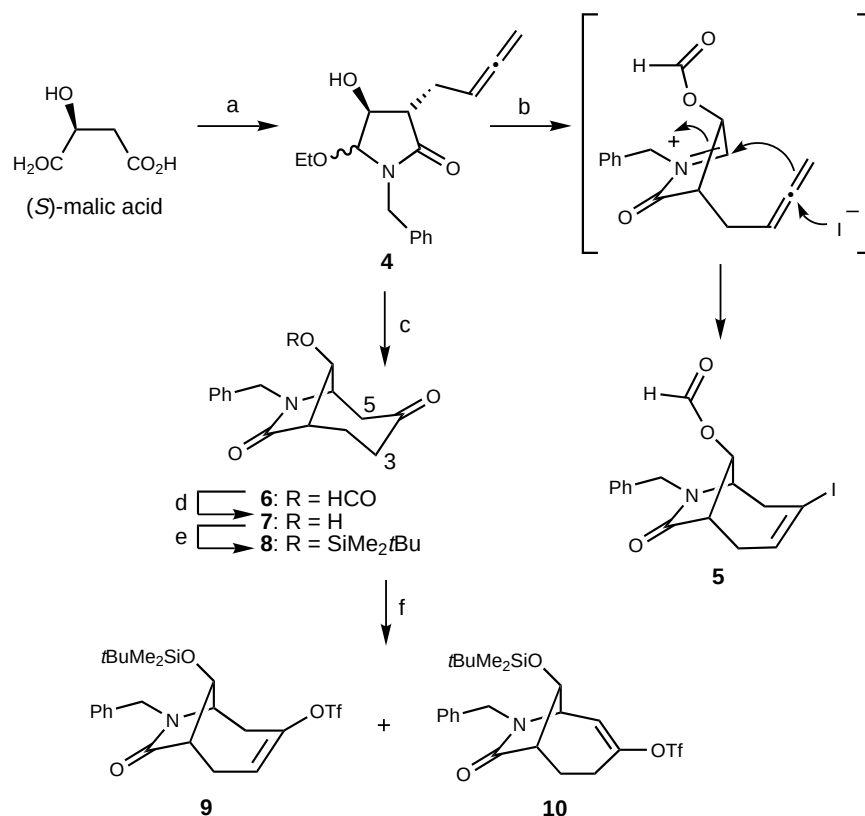


1: gelsemine



2: gelsedine, R = H
3: gelsemicine, R = OMe

Being a minor constituent in Carolina jasmine, gelsedine has not received as much attention as the parent alkaloid gelsemine. From a synthetic point of view, both alkaloids present the formidable challenge of a compact tricyclic skeleton adorned with a spiro-oxindole moiety. Gelsedine



Scheme 1. Cyclization of **4**. a) Reference [11]; b) NaI (20 equiv), HCO₂H (0.2 M), 85 °C, 18 h, 42 % of **5** + 34 % of **6**; c) HCO₂H, 85 °C, 18 h; d) satd NH₃ in MeOH, RT (room temperature), 15 min, 79 % over two steps; e) TBDMSCl (3 equiv), imidazole (4 equiv), DMAP (0.2 equiv), CH₂Cl₂, RT, 18 h, 96 %; f) LiHMDS (1.5 equiv), THF, –78 °C, 0.5 h, then PhNTf₂ (1.5 equiv), –78 °C → RT, 18 h, 45 % of **10**. DMAP = 4-(dimethylamino)pyridine, HMDS = hexamethyldisilazane, TBDMS = *tert*-butyldimethylsilyl, Tf = trifluoromethanesulfonyl.

raises additional problems, such as the introduction of the ethyl substituent in the correct stereochemical sense and the special functionalization of the seven-membered ring. Until now, three groups have reported studies towards a total synthesis of gelsedine.^[8, 9] The elegant approach by Kende and co-workers is particularly noteworthy, but the formation of the undesired stereoisomer in the final spirocyclization step has prevented real success.^[9] Furthermore, in 1994 a semisynthesis of gelsedine starting from koumidine was accomplished by Takayama et al.^[10] We now report the first totally chemical synthesis of gelsedine based on the unique reaction sequence of a novel iodide-promoted cyclization of an allene onto an *N*-acyliminium ion followed by palladium-catalyzed carbonylation and Heck spirocyclization. The synthesis starts with inexpensive (*S*)-malic acid and leads to the enantiomer of natural gelsedine.

Previously, we have reported an efficient five-step synthesis of ethoxylactam **4** from (*S*)-malic acid, and cyclization of the *N*-acyliminium ion of **4** in neat formic acid to bicyclic ketone **6** in 79 % yield (Scheme 1).^[11] Because a successful route to gelsedine starting from ketone **6** requires functionalization at C4, we tried to prepare vinyl triflate **9** from **6** via hydroxy ketone **7** and silyl ether **8**. However, we were unable to generate **9** from **8**; the regioisomer **10** was always the sole product obtained.^[12] We then considered the possibility of a more direct and elegant pathway to arrive at vinyl iodide **5**,

[*] Prof. Dr. H. Hiemstra, W. G. Beyersbergen van Henegouwen, R. M. Fieseler, Dr. F. P. J. T. Rutjes
Laboratory of Organic Chemistry, Institute of Molecular Chemistry
University of Amsterdam
Nieuwe Achtergracht 129
1018 WS Amsterdam (The Netherlands)
Fax: (+31) 20-5255670
E-mail: henkh@org.chem.uva.nl

which is a synthetic equivalent of **9**. The successful one-step transformation of **4** into **5** appeared to be the key to success.

Cyclizations of allenones onto *N*-acyliminium ions are scarce in the literature,^[13] and iodide-promoted variants are unknown, to the best of our knowledge. Overman and Brosius have reported examples of the beneficial effect of iodide as a powerful nucleophile in cationic cyclizations of alkenes.^[14] When allene **4** was dissolved in formic acid in the presence of a large excess of sodium iodide and heated to 85 °C for 18 h, we were delighted to find **5** as the main product in 42 % yield (Scheme 1, Table 1). In spite of extensive experimentation

for the Heck spirocyclization.^[16] This reaction proceeded best in acetonitrile in a sealed tube at 120 °C. We obtained oxindole **15** as the sole product with the desired spiroster-chemistry in 90 % yield.^[17]

The installation of the tetrahydropyran ring was the next phase of the synthesis. Hydroboration of **15** with dicyclohexylborane^[18] gave exclusively the desired stereoisomer **16** in 79 % yield (Table 1). Ring closure was effected by treatment with Hg(O₂CCF₃) followed by addition of saturated aqueous NaCl to produce chloromercurial **17** in excellent yield. Only the six-membered ring ether was formed. After extensive experimentation we found that demercuration was most cleanly achieved by reduction with *n*Bu₃SnH^[19] to furnish **18**, which already features the complete skeleton of gelsedine.

Introduction of the ethyl moiety required prior reductive removal of the benzyl group from the saturated lactam nitrogen atom. However, to achieve this through reduction by a dissolved metal, the oxindole ring would need protection as the anion. Therefore, the oxindole methyl group should be removed first. This latter chore was readily accomplished by using a procedure which is known for removal of an *N*-methyl group from an indole.^[20] Treatment of **18** with dibenzoyl peroxide followed by saturated NH₃ in methanol gave **19** in a remarkable 74 % yield. Removal of the benzyl group now proceeded smoothly to give the very polar compound **20**.

The appropriate lactam carbonyl group was activated towards Grignard addition by double protection with *tert*-butoxycarbonyl (Boc) to give **21**. Treatment of biscarbamate **21** with excess EtMgBr (6 equiv) gave the highly useful hemiaminal **22** in a surprisingly efficient transformation. We assume that attack of the Grignard reagent takes place on the carbonyl moiety of the Boc group that is then removed (R² in **21**) because the oxindole carbonyl moiety is too sterically hindered. Although **22** was stable at room temperature, it was treated in crude form with trifluoroacetic acid (TFA) to generate *N*-acyliminium ion **23**, which was reduced in situ with triethylsilane. On addition of more TFA the Boc group was removed, and the TFA salt of desmethoxygelsedine (**24**) was obtained in good yield (Table 1).^[17]

For the final stage—that is, the introduction of the *N*-methoxy group—we followed a procedure which was especially designed for this purpose.^[10, 21] Protection of the amine in **24** with 2,2,2-trichloroethyl chloroformate gave **25**, and subsequent reduction of the oxindole carbonyl group with borane afforded spiro-indoline **26**. The oxidation of this indoline (urea · H₂O₂, Na₂WO₄ · 2H₂O, 10 % aq MeOH) proceeded rather slowly, but did produce **27** after subsequent treatment with diazomethane. Deprotection of **27** with zinc in acetic acid gave (+)-gelsedine, which was identical to natural (–)-gelsedine^[22] (¹H (400 MHz) and ¹³C NMR spectroscopy (100 MHz), high-resolution mass spectrometry (FAB)), except for the optical rotation (synthetic (+)-gelsedine: [α]_D²⁵ = +120 (*c* = 0.25, CHCl₃); natural (–)-gelsedine: [α]_D²⁵ = –159 (*c* = 1.35, CHCl₃)).^[4]

In conclusion, we have successfully completed the first total synthesis of (+)-gelsedine in 21 steps from (*S*)-malic acid. This synthetic endeavour produces a single enantiomer, proceeds with complete stereoselectivity, and has brought forth a number of novel transformations which may find further

Table 1. Selected physical properties of compounds **5**, **16**, and **24**.

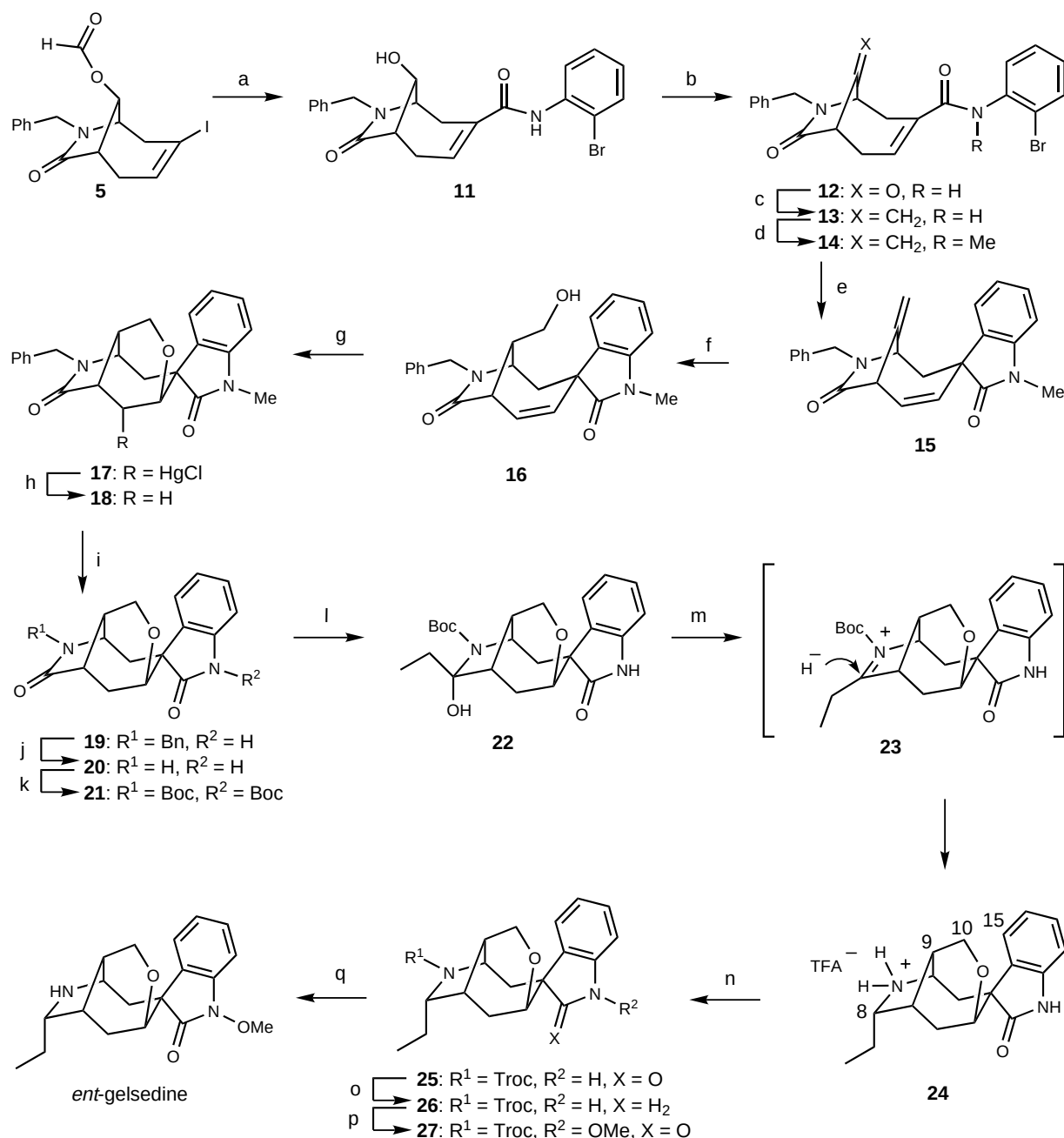
5: *R*_f = 0.31 (EtOAc/petroleum ether (60–80) 1/1); [α]_D²⁵ = +10.3 (*c* = 1.0, CHCl₃); IR (thin film): $\tilde{\nu}$ = 2920, 1735, 1682, 1495, 1446, 1165 cm^{–1}; ¹H NMR (400 MHz, CDCl₃): δ = 7.97 (s, 1H), 7.30 (m, 5H), 6.34 (s, 1H), 5.02 (s, 1H), 4.86 (d, *J* = 15.3 Hz, 1H), 4.12 (d, *J* = 15.3 Hz, 1H), 3.44 (t, *J* = 3.3 Hz, 1H), 2.99 (d, *J* = 18.7 Hz, 1H), 2.83 (d, *J* = 18.9 Hz, 1H), 2.77 (s, 1H), 2.70 (d, *J* = 18.5 Hz, 1H), 2.57 (d, *J* = 18.5 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 173.0, 159.8, 137.3, 135.4, 128.7, 127.6, 127.5, 93.1, 75.4, 61.9, 45.8, 45.2, 44.2, 32.5; HR-MS (EI) calcd for C₁₆H₁₆INO₃: 397.0174, found: 397.0146.

16: *R*_f = 0.37 (CH₂Cl₂/acetone 1/1); m.p. 87–89 °C; [α]_D²⁵ = –13.4 (*c* = 1.0, CHCl₃); IR (thin film): $\tilde{\nu}$ = 3394, 2932, 1699, 1682, 1610, 1495, 1342, 1252 cm^{–1}; ¹H NMR (400 MHz, CDCl₃): δ = 7.26 (m, 7H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.00 (dd, *J* = 9.1, 11.6 Hz, 1H), 5.33 (d, *J* = 15.7 Hz, 1H), 5.20 (d, *J* = 11.7 Hz, 1H), 4.07 (m, 2H), 3.86 (d, *J* = 15.7 Hz, 1H), 3.78 (t, *J* = 4.5 Hz, 1H), 3.26 (dd, *J* = 6.8, 8.7 Hz, 1H), 3.19 (s, 3H), 2.77 (m, 1H), 2.30 (dd, *J* = 4.3, 16.3 Hz, 1H), 2.21 (dd, *J* = 1.6, 16.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 176.6, 174.9, 142.2, 137.2, 135.1, 132.4, 128.5, 128.4, 128.2, 127.7, 127.2, 123.2, 123.0, 107.9, 59.3, 56.9, 55.3, 45.3, 45.1, 45.0, 32.7, 26.5; HR-MS (EI) calcd for C₂₄H₂₄N₂O₅: 370.1787, found: 370.1787.

24: *R*_f = 0.42 (CH₂Cl₂/MeOH 4:1); m.p. 110–112 °C; [α]_D²⁵ = +83.0 (*c* = 1.0, MeOH); IR (thin film): $\tilde{\nu}$ = 2971, 1679, 1620, 1472, 1435, 1201, 1124 cm^{–1}; ¹H NMR (400 MHz, CDCl₃): δ = 11.5 (s, 1H), 11.3 (s, 1H), 9.32 (s, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 4.51 (s, 1H), 4.27 (m, 2H), 3.80 (s, 1H), 3.72 (d, *J* = 6.5 Hz, 1H), 2.88 (s, 1H), 2.56 (s, 1H), 2.35 (dd, *J* = 16.4, 3.4 Hz, 1H), 2.26 (d, *J* = 15.5 Hz, 1H), 2.18 (m, 2H), 2.00 (m, 2H), 1.08 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD): δ = 184.2, 163.4 (q, *J*(C,F) = 35.4 Hz), 141.5, 136.5, 129.9, 126.0, 124.4, 118.3 (q, *J*(C,F) = 290.6 Hz), 111.5, 76.6, 66.4, 63.7, 61.3, 60.9, 40.9, 35.2, 32.0, 22.1, 20.6, 11.4; ¹⁹F NMR (282 MHz, CD₃OD): δ = –77.4; HR-MS (EI) calcd for C₁₈H₂₂N₂O₂: 298.1682, found: 298.1679.

(varying temperature, concentration, iodide source), we were unable to prevent competitive attack of formic acid as a nucleophile, and **6** (after unavoidable in situ hydrolysis of the intermediate vinyl formate) was always obtained as a by-product (34 %). Iodide **5** was readily separated from **6** by flash chromatography, so that sufficient quantities of **5** could be obtained to proceed with the total synthesis of gelsedine.

The construction of the spiro-oxindole moiety onto **5** commenced with a Pd-catalyzed aminocarbonylation^[15] to give anilide **11** after subsequent deformylation (Scheme 2). To render the molecular architecture more favorable for the desired stereochemical course of the Heck spirocyclization, we deemed an sp²-hybridized bridging carbon atom to be desirable. The approach of the arylpalladium complex from the *exo* direction would then be least sterically encumbered. Therefore, alcohol **11** was first oxidized with PCC to ketone **12** and subjected to a Wittig reaction to provide **13** in good overall yield. The nitrogen atom in anilide **13** was then protected with a methyl group to give **14**, which set the stage



Scheme 2. Synthesis of *ent*-gelsedine. a) 1. *o*-Bromoaniline (3 equiv), Pd(OAc)₂ (0.15 equiv), PPh₃ (0.30 equiv), Et₃N (5 equiv), CO (balloon), DMF, 40 °C, 20 h; 2. satd NH₃ in MeOH, RT, 15 min, 64 %; b) PCC (5 equiv), CH₂Cl₂, 40 °C, 24 h, 66 %; c) Ph₃PMeBr (2.5 equiv), *n*BuLi (1.6 M in hexanes, 2.45 equiv), THF, 0 °C, then **12**, reflux, 18 h, 83 %; d) MeI (2.5 equiv), NaH (3 equiv), THF, RT, 4.5 h, 78 %; e) [Pd(PPh₃)₄] (0.2 equiv), Et₃N (10 equiv), MeCN, sealed tube, 120 °C, 40 h, 90 %; f) (Chx)₂BH (2 equiv), THF, 0 °C, 2 h, then 3 M NaOH/H₂O₂, 1 h, RT, 79 %; g) Hg(O₂CCF₃)₂ (2 equiv), THF, 5 h, then satd aq NaCl, RT, 3 h, 88 %; h) *n*Bu₃SnH (2.5 equiv), AIBN (0.1 equiv), toluene (0.5 M of **17**), RT → 55 °C, 2 h, 80 %; i) 1. (PhCO₂)₂ (2 equiv), CH₂Cl₂, sealed tube, 80 °C, 18 h; 2. satd NH₃ in MeOH, RT, 20 h, 74 %; j) Li (10 equiv), NH₃, -78 °C, 30 min, then isoprene (25 equiv), -78 °C → RT, 79 %; k) Boc₂O (8 equiv), DMAP (6 equiv), THF, RT, 4 h, 78 %; l) EtMgBr (1 M in THF, 6 equiv), THF, -78 → 0 °C, 30 min, then satd aq NH₄Cl; m) TFA (12 equiv), Et₃SiH (8 equiv), CH₂Cl₂, 0 °C → RT, 4 h, then extra TFA, RT, 18 h, 61 % over two steps; n) TrocCl (2.2 equiv), pyridine, CH₂Cl₂, RT, 18 h, 67 %; o) BH₃·SMe₂ (20 equiv), THF, 0 → 70 °C, 18 h, then Me₃NO (5 equiv), MeOH, reflux, 2 h, 72 %; p) 1. urea·H₂O₂ (20 equiv), Na₂WO₄·2H₂O (0.6 equiv), 10 % aq MeOH, RT, 4 h; 2. CH₂N₂ (excess), Et₂O, 1 h, 31 % over two steps; q) Zn (40 equiv), AcOH, RT, 20 h, 84 %. AIBN = 2,2'-azobisisobutyronitrile, Boc = *tert*-butoxycarbonyl, Chx = cyclohexyl, DMAP = 4-(dimethylamino)pyridine, PCC = pyridinium chlorochromate, TFA = trifluoroacetic acid, TrocCl = 2,2,2-trichloroethyl chloroformate.

application. The unique combination of the iodide-promoted cationic allene cyclization to produce a vinyl iodide and palladium-catalyzed elaboration of the latter in carbonylation and subsequent Heck chemistry has been the key to success. In addition, methyl has shown to be a good protecting group for the oxindole nitrogen atom. Finally, the fully chemo- and

stereoselective introduction of the ethyl group provides another illustration of the powerful utility of *N*-acyliminium ions as intermediates in modern synthesis.

Received: January 28, 1999

Revised version: April 6, 1999 [Z12971IE]

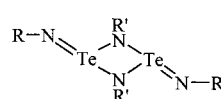
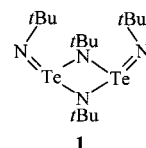
German version: *Angew. Chem.* **1999**, *111*, 2351–2355

Keywords: alkaloids • allenes • natural products • spiro compounds • total synthesis

Coinage Metal Complexes of a Tellurium Diimide: *cis* → *trans* Isomerization and Metal–Metal Interactions**

Tristram Chivers,* Masood Parvez, and Gabriele Schatte

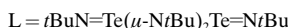
The unique properties of inorganic polymers, especially those with metal atoms in the backbone, provide an incentive for the investigation of novel systems.^[1] The versatile ligand behavior of sulfur(IV) diimides encompasses $\sigma(N)$, $\sigma(N,N')$, and, less commonly, $\sigma(S)$ and $\pi(N,S)$ bonding modes.^[2] The only known complex of a selenium(IV) diimide, $\text{SnCl}_4(\text{tBuN}=\text{Se}=\text{NtBu})$, displays $\sigma(N,N')$ chelation.^[3] Unlike their lighter congeners $\text{RN}=\text{E}=\text{NR}$ ($\text{E} = \text{S}, \text{Se}$), which adopt monomeric structures with *syn,syn* or *syn,anti* conformations in the solid state^[4,5] and gas phase,^[6] tellurium diimides are dimeric and form *cis* or *trans* isomers in the solid state.^[7–9] The *cis* isomer **1** is obtained with an *endo,endo* arrangement of terminal *t*Bu groups,^[8] whereas in the *trans* isomers **2b** and **2c** the terminal groups occupy *exo* positions with respect to the



2a, $\text{R} = \text{R}' = \text{tBu}$
2b, $\text{R} = \text{PPh}_2\text{NSiMe}_3$, $\text{R}' = \text{tBu}$
2c, $\text{R} = \text{PPh}_2\text{NSiMe}_3$, $\text{R}' = \text{tOct}$

Te_2N_2 ring.^[9] In solution **2b** and **2c** slowly convert into the corresponding *cis* isomers.^[9]

As part of our investigations of the coordination chemistry of tellurium diimide dimers the generation of a polymer in which ligands of type **2** are bridged by metal ions seemed especially intriguing. We describe here the synthesis and X-ray structures of **3** and **4**, the first metal complexes of a tellurium diimide dimer. The ligand **1** exhibits remarkably different ligand behavior towards Cu^+ and Ag^+ . In particular, Cu^+ promotes *cis* → *trans* isomerization (**1** → **2a**) in the formation of **3**. In contrast, the dinuclear complex **4** with a metal–metal (d^{10} – d^{10}) interaction is produced in the presence of Ag^+ .



Complex **3** was obtained by a two-step process in which **5** was prepared from stoichiometric amounts of copper(I) trifluoromethanesulfonate and **1**.^[10] Subsequently, **5** was

[*] Prof. Dr. T. Chivers, Dr. M. Parvez, Dr. G. Schatte
 Department of Chemistry
 University of Calgary
 Calgary, AB T2N 1N4 (Canada)
 Fax: (+1) 403-289-9488
 E-mail: chivers@ucalgary.ca

[**] We gratefully acknowledge the Natural Sciences and Engineering Research Council (Canada) for financial support.

- [1] Reviews on *Gelsemium* alkaloids: a) J. E. Saxton in *The Alkaloids*, Vol. 8 (Ed.: R. H. F. Manske), Academic Press, New York, **1965**, pp. 93–117; b) Z.-J. Liu, R.-R. Lu in *The Alkaloids*, Vol. 33 (Ed.: A. Brossi), Academic Press, New York, **1988**, pp. 83–140; c) H. Takayama, S. Sakai in *Studies in Natural Products Chemistry*, Vol. 15 (Ed.: A. Rahman), Elsevier, Amsterdam, **1995**, pp. 465–518.
- [2] N. J. Newcombe, Y. Fang, R. J. Vijn, H. Hiemstra, W. N. Speckamp, *J. Chem. Soc. Chem. Commun.* **1994**, 767–768.
- [3] a) J. K. Dutton, R. W. Steel, A. S. Tasker, V. Popsavin, A. P. Johnson, *J. Chem. Soc. Chem. Commun.* **1994**, 765–766; b) D. Kuzmich, S. C. Wu, D.-C. Ha, C.-S. Lee, S. Ramesh, S. Atarashi, J.-K. Choi, D. J. Hart, *J. Am. Chem. Soc.* **1994**, *116*, 6943–6944; c) T. Fukuyama, L. Gang, *J. Am. Chem. Soc.* **1996**, *118*, 7426–7427; d) S. Atarashi, J.-K. Choi, D.-C. Ha, D. J. Hart, D. Kuzmich, C.-S. Lee, S. Ramesh, S. C. Wu, *J. Am. Chem. Soc.* **1997**, *119*, 6226–6241.
- [4] H. Schwarz, L. Marion, *Can. J. Chem.* **1953**, *31*, 958–975.
- [5] H. L. Jin, R. S. Xu, *Acta Chim. Sinica* **1982**, *40*, 1129–1135.
- [6] E. Wenkert, J. C. Orr, S. Garratt, J. H. Hansen, B. Wickberg, C. L. Leicht, *J. Org. Chem.* **1962**, *27*, 4123–4126.
- [7] M. Przybylska, L. Marion, *Can. J. Chem.* **1961**, *39*, 2124–2127.
- [8] a) S. W. Baldwin, R. J. Doll, *Tetrahedron Lett.* **1979**, *20*, 3275–3278; b) N. K. Hamer, *J. Chem. Soc. Chem. Commun.* **1990**, 102–103.
- [9] a) A. S. Kende, M. J. Luzzio, J. S. Mendoza, *J. Org. Chem.* **1990**, *55*, 918–924; b) M. J. Luzzio, Dissertation, University of Rochester, USA, **1987**. We thank Professor A. S. Kende of the University of Rochester for sending us a copy of this thesis.
- [10] H. Takayama, Y. Tominaga, M. Kitajima, N. Aimi, S. Sakai, *J. Org. Chem.* **1994**, *59*, 4381–4385.
- [11] W. G. Beyersbergen van Henegouwen, H. Hiemstra, *J. Org. Chem.* **1997**, *62*, 8862–8867.
- [12] More detailed information about these reactions will be provided in a full paper.
- [13] a) P. M. M. Nossin, W. N. Speckamp, *Tetrahedron Lett.* **1981**, *22*, 3289–3292; b) P. M. M. Nossin, J. A. M. Hamersma, W. N. Speckamp, *Tetrahedron Lett.* **1982**, *23*, 3807–3810; c) P. M. M. Nossin, Dissertation, University of Amsterdam, The Netherlands, **1983**; for intermolecular reactions of N-acyliminium ions with allenes, see d) R. L. Danheiser, C. A. Kwasigroch, Y.-M. Tsai, *J. Am. Chem. Soc.* **1985**, *107*, 7233–7235; e) J. S. Prasad, L. S. Liebeskind, *Tetrahedron Lett.* **1988**, *29*, 4257–4260; f) W. F. J. Karstens, F. P. J. T. Rutjes, H. Hiemstra, *Tetrahedron Lett.* **1997**, *38*, 6275–6278.
- [14] A. D. Brosius, L. E. Overman, *J. Org. Chem.* **1997**, *62*, 440–441.
- [15] S. Cacchi, E. Morera, G. Ortari, *Tetrahedron Lett.* **1985**, *26*, 1109–1112.
- [16] a) M. M. Abelman, T. Oh, L. E. Overman, *J. Org. Chem.* **1987**, *52*, 4130–4133; b) A. Madin, L. E. Overman, *Tetrahedron Lett.* **1992**, *33*, 4859–4862; c) A. Ashimori, B. Bachand, L. E. Overman, D. J. Poon, *J. Am. Chem. Soc.* **1998**, *120*, 6477–6487.
- [17] The stereochemistry of the oxindole and ethyl group was proven unambiguously in **24**. Distinct NOEs between C10 and C15 protons and C8 and C9 protons were observed.
- [18] H. C. Brown, A. K. Mandal, S. U. Kulkarni, *J. Org. Chem.* **1977**, *42*, 1392–1398.
- [19] D. A. Evans, S. L. Bender, J. Morris, *J. Am. Chem. Soc.* **1988**, *110*, 2506–2526.
- [20] S. Nakatsuka, O. Asano, T. Goto, *Heterocycles* **1986**, *24*, 2791–2792. We thank Professor C. Szántay of the Technical University of Budapest (Hungary) for drawing our attention to this article.
- [21] a) S.-I. Murahashi, T. Oda, T. Sugahara, Y. Masui, *J. Org. Chem.* **1990**, *55*, 1744–1749; b) M. Kitajima, H. Takayama, S. Sakai, *J. Chem. Soc. Perkin Trans. 1* **1994**, 1573–1578.
- [22] We are very grateful to Professor H. Takayama of Chiba University (Japan) for NMR spectra and a sample of (–)-gelsedine.