Alkene–alkyne metathesis and 1,4-*cis*-hydrogenation as a route to tetrasubstituted (*Z*)-olefins

Andrei A. Vasil'ev,*[a] Lars Engman[b] and Edward P. Serebryakov[a]

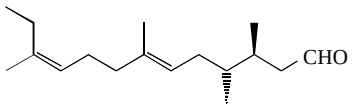
[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation. Fax: + 7 095 135 5328; e-mail: vasiliev@ioc.ac.ru*

[b] *Department of Organic Chemistry, Institute of Chemistry, Uppsala University, S-751 21 Uppsala, Sweden*

10.1070/MC2000v010n03ABEH001303

Stereospecific synthesis of *erythro*-5-benzyloxy-2,3-dimethylpentan-1-ol, a building block for the preparation of faranal and lasiol, was performed starting from 5-benzyloxypent-2-yn-1-ol using the title methodology followed by 1,2-*syn*-hydrogenation.

Faranal **1** [(3*S*,4*R*,6*E*,10*Z*)-3,4,7,11-tetramethyltrideca-6,10-dienal, a trail pheromone of the Pharaoh's ant *Monomorium pharaonis*],[1] and lasiol **2** [(2*R**,3*R**)-2,3,6-trimethylhept-5-en-1-ol, the major component of the mandibular gland secretion of the ant *Lasius meridionalis*][2] both contain a vicinal *erythro* dimethyl structural motif. For their preparation, the use of suitably substituted building blocks,[2–7] stereospecific substituent-directed *anti*-alkylation of 3-methylalkanolide carbanions[8,9] and *erythro* addition of alkenylmanganese chloride to methyl crotonate[10] were described. *Syn*-1,2-addition of hydrogen to a double bond of a (*Z*)-1,2-dimethyl tetrasubstituted olefin with heterogeneous catalysis was never attempted for this purpose. Although there are cases where mixtures of *syn*- and *anti*-addition products are formed,[11] the stereochemistry of hydrogenation of tetrasubstituted olefins is not well investigated. We reasoned that Raney nickel can hydrogenate *via syn*-1,2-addition (and in an essentially irreversible manner) rather than by hydride transfer. Remarkably, a diimide is practically inert towards tetrasubstituted olefins.[12]

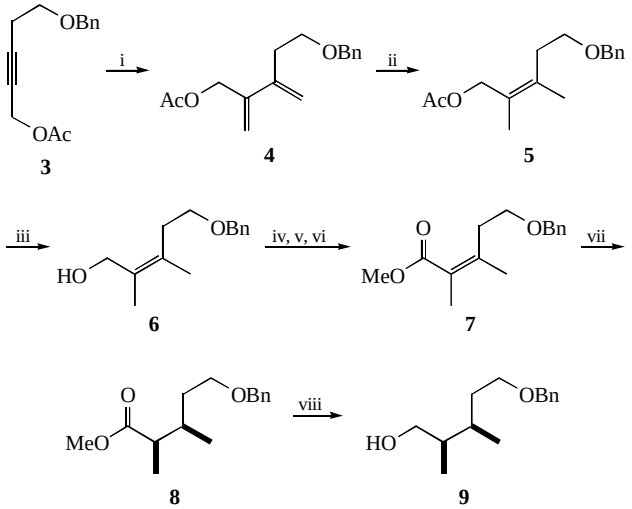


1 **2**

M. Mori and co-workers have recently developed intermolecular alkene–alkyne metathesis[13,14] into a useful method for the preparation of functionalized 2,3-disubtituted butadienes. With our previous experience in the 1,4-*cis*-hydrogenation of conjugated dienes over (arene)tricarbonylchromium catalysts[15,16] (for a review, see ref. 17) we decided to prepare (*Z*)-tetrasubstituted olefins by this route and to investigate their further transformations into *erythro*-configured *vic*-dimethyl derivatives (Scheme 1).

The readily available acetate of 5-benzyloxypent-2-yn-1-ol **3**,[18] upon metathesis with ethylene in CH_2Cl_2 under the Mori conditions,[13,14] afforded target conjugated diene **4** with a maximum conversion of 43%.† Attempts to improve the process were unsuccessful. Thus, running the reaction in an autoclave under a higher ethylene pressure resulted in a low (less than 5%) conversion of the starting material. This may be attributed to the pressure-accelerated degenerate ethylene–ethylene metathesis (due to an increased concentration of ethylene). As a result, this process effectively competes with the reaction between ethylene and acetylenic substrate **3**. Fortunately, compounds **3** and **4** could be readily separated by column chromatography, allowing for recycling of compound **3** to accumulate sufficient amounts of diene **4** for further investigations.

The 1,4-*cis*-hydrogenation of diene **4** over (η^6-naphthalene)-$Cr(CO)_6$ in THF at 45 °C and 1 atm H_2 led cleanly to olefin **5**.‡ The (*Z*)-configuration of the double bond in compound **5** was confirmed by NOE difference experiments. Thus, irradiation of the allylic CH_2CH_2OBn protons at 2.47 ppm gave effects at 1.74 (3.5%), 3.49 (6.5%) and 4.60 (6.5%) ppm. Also, irradiation of the acetoxymethyl protons at 4.60 ppm gave effects at 1.71 (3%) and 2.47 (4%) ppm. Subsequent attempts to hydrogenate the double bond either in acetate **5** or in the corresponding alcohol **6** over Raney nickel mainly caused cleavage of the allylic C–O bond. To avoid this, allylic alcohol **6** was subjected to consecutive Swern and sodium chlorite oxidations followed by diazomethane esterification.§ Hydrogenation of (*Z*)-tetrasubstituted acrylate **7** over Raney nickel in propan-2-ol at room temperature and 15 atm H_2 proceeded smoothly without affecting the ester function to afford a 90% yield of the *erythro*-



Scheme 1 *Reagents and conditions*: i, C_2H_4, $PhCH{=}RuCl_2(PCy_3)_2$, CH_2Cl_2, room temperature, 35% (based on **3** used) and 70% (based on **3** recovered); ii, H_2 (1 atm), $(C_{10}H_8)Cr(CO)_3$, THF, 45 °C, 91%; iii, MeOH, K_2CO_3, room temperature; iv, DMSO, $(COCl)_2$, CH_2Cl_2, then Et_3N, –50 °C; v, $NaClO_2$, 1-methylcyclohexene, Bu^tOH, NaH_2PO_4, room temperature; vi, CH_2N_2, Et_2O, 65% (**5** to **7**); vii, H_2 (15 atm), Ni, Pr^iOH, room temperature; viii, $LiAlH_4$, Et_2O, 74% (**7** to **9**).

† *1-Acetoxy-5-benzyloxy-2,3-dimethylenepentane* **4**. A mixture of 1-acetoxy-5-benzyloxypent-2-yne **3** (0.389 g, 1.67 mmol) and benzylidenebis(tricyclohexylphosphine)dichlororuthenium (Fluka) (0.04 g) in CH_2Cl_2 (17 ml) was stirred in an ethylene atmosphere for 3 days and treated according to a published procedure.[12,13] The crude material was a 43:57 (mol/mol) mixture (^{1}H NMR data) of title compound **4** and unreacted compound **3**. Column chromatography (3–5% EtOAc in pentane, SiO_2) gave 0.154 g (35%) of compound **4** and 0.196 g (50%) of recovered starting material **3**. ^{1}H NMR ($CDCl_3$) δ: 2.08 (s, 3H), 2.62 (t, 2H, *J* 7.0 Hz), 3.61 (t, 2H, *J* 7.0 Hz), 4.52 (s, 2H), 4.77 (s, 2H), 5.09 (s, 1H), 5.15 (s, 1H), 5.27 (s, 1H), 5.33 (s, 1H), 7.22–7.38 (m, 5H). ^{13}C NMR, δ: 21.0 (Me), 34.2 (CH_2), 65.1 (CH_2), 69.1 (CH_2), 72.9 (CH_2), 114.1 (CH_2), 114.9 (CH_2), 127.5 (CH), 127.6 (CH), 128.4 (CH), 138.3 (C), 141.3 (C), 141.6 (C), 170.7 (C).

‡ *(Z)-1-Acetoxy-5-benzyloxy-2,3-dimethylpent-2-ene* **5** was obtained by hydrogenation (1 atm H_2, 45–50 °C, 2 h) of diene **4** (0.154 g, 0.59 mmol) in THF (10 ml) in the presence of (naphthalene)tricarbonylchromium[20] (0.03 g). Column chromatography afforded 0.141 g (91%) of compound **5**. ^{1}H NMR ($CDCl_3$) δ: 1.71 (s, 3H), 1.74 (s, 3H), 2.03 (s, 3H), 2.47 (t, 2H, *J* 7.2 Hz), 3.49 (t, 2H, *J* 7.2 Hz), 4.50 (s, 2H), 4.60 (s, 2H), 7.32 (m, 5H). ^{13}C NMR, δ: 16.9 (Me), 19.4 (Me), 21.0 (Me), 34.7 (CH_2), 65.4 (CH_2), 69.0 (CH_2), 72.8 (CH_2), 125.4 (C), 127.5 (CH, two peaks), 128.3 (CH), 132.5 (C), 138.4 (C), 171.3 (C).

isomer **8**.¶ The configuration of compound **8** was proven by the transformation ($LiAlH_4$ reduction into alcohol **9** and debenzylation over H_2–Pd/C) into known *erythro*-2,3-dimethylpentane-1,5-diol.[19,††]

After transformation of the alcohol into an iodide and coupling with an appropriate alkenyllithium reagent,[3,6] *erythro*-5-benzyloxy-2,3-dimethylpentan-1-ol **9** may serve as a building block in the synthesis of racemic faranal **1**. On the other hand, manipulations with the protective groups in compound **9** provide an opportunity to synthesise lasiol **2** (see ref. 2 for the methodology). Although the route from compound **3** to **9** gives only a 30% yield over eight steps,‡‡ it is still a competitive method for the synthesis of *erythro*-configured compounds.

In conclusion, transition metal catalysed metathesis and *cis*-hydrogenation reactions provide a new useful approach to functionalized (*Z*)-tetrasubstituted olefins.

This work was supported by the Russian Foundation for Basic Research (grant no. 99-03-32992), the Royal Swedish Academy of Sciences (a research grant for cooperation between Sweden and the former Soviet Union) and the Swedish Natural Science Research Council.

§ *Methyl (Z)-5-benzyloxy-2,3-dimethylpent-2-enoate* **7**. Acetate **5** (0.491 g, 1.87 mmol) was stirred overnight in MeOH in the presence of K_2CO_3. The crude alcohol **6** thus obtained was subjected to the standard Swern oxidation.[21] The resulting crude aldehyde was then oxidised with $NaClO_2$ to the corresponding carboxylic acid,[22] which was esterified by treatment with diazomethane. Column chromatography afforded 0.303 g (65%) of ester **7**. ^{1}H NMR ($CDCl_3$) δ: 1.84 (s, 3H), 1.85 (s, 3H), 2.73 (t, 2H, *J* 7.1 Hz), 3.61 (t, 2H, *J* 7.1 Hz), 3.70 (s, 3H), 4.52 (s, 2H), 7.26 (m, 1H), 7.33 (m, 4H). ^{13}C NMR, δ: 15.9 (Me), 21.2 (Me), 36.6 (CH_2), 51.3 (Me), 69.3 (CH_2), 72.7 (CH_2), 124.2 (C), 127.4 (CH), 127.5 (CH), 128.3 (CH), 138.6 (C), 144.1 (C), 169.6 (C).

¶ erythro-*5-Benzyloxy-2,3-dimethylpentan-1-ol* **9**. Unsaturated ester **7** (0.240 g, 0.97 mmol) was hydrogenated (15 atm H_2, 20 °C, 7 h) in propan-2-ol (15 ml) in the presence of Raney nickel (0.3 g). The filtration and evaporation of the solvent left crude methyl *erythro*-5-benzyloxy-2,3-dimethylpentanoate **8** containing *ca.* 10% impurities. ^{1}H NMR ($CDCl_3$) δ: 0.91 (d, 3H, *J* 6.9 Hz), 1.13 (d, 3H, *J* 7.0 Hz), 1.42 (m, 1H), 1.80 (m, 1H), 1.93 (m, 1H), 2.40 (m, 1H), 3.51 (m, 2H), 3.65 (s, 3H), 4.48 and 4.50 (AB system, 2H, *J* 12.0 Hz), 7.28 (m, 1H), 7.34 (m, 4H). ^{13}C NMR, δ: 14.0 (Me), 17.0 (Me), 33.2 (CH), 33.4 (CH_2), 44.5 (CH), 51.3 (Me), 68.4 (CH_2), 72.9 (CH_2), 127.5 (CH), 127.6 (CH), 128.4 (CH), 138.6 (C), 176.4 (C). Reduction with $LiAlH_4$ followed by column chromatography afforded 0.160 g (74%) of *erythro* alcohol **9** as a colourless oil. ^{1}H NMR ($CDCl_3$) δ: 0.85 (d, 3H, *J* 6.9 Hz), 0.91 (d, 3H, *J* 6.9 Hz), 1.32 (m, 1H), 1.64 (m, 1H), 1.77 (m, 2H), 3.45 (m, 2H), 3.55 (m, 2H), 4.50 and 4.52 (AB system, 2H, *J* 11.6 Hz), 1.26–1.37 (m, 5H). ^{13}C NMR, δ: 12.7 (Me), 17.4 (Me), 30.9 (CH), 31.9 (CH_2), 40.3 (CH), 65.8 (CH_2), 69.2 (CH_2), 73.0 (CH_2), 127.6 (CH), 127.7 (CH), 128.4 (CH), 138.3 (C).

†† ^{13}C NMR (D_2O) δ: 13.5 (Me), 16.8 (Me), 31.1 (CH), 34.9 (CH_2), 40.4 (CH), 61.0 (CH_2), 65.6 (CH_2). An authentic sample of the same diol was obtained by the $LiAlH_4$ reduction of *cis*-3,4-dimethylpentan-5-olide.[5]

‡‡ To reduce the number of steps, we tried to use both methyl 5-benzyloxypent-2-ynoate and 5-benzyloxypent-2-ynal dimethyl acetal in the metathesis. However, they remained unchanged (*cf.* ref. 14).

References

1 (*a*) M. Kobayashi, T. Koyama, K. Ogura, S. Seto, F. J. Ritter and I. E. M. Brüggemann-Rotgans, *J. Am. Chem. Soc.*, 1980, **102**, 6602; (*b*) F. J. Ritter, I. E. M. Brüggemann-Rotgans, P. E. J. Verwiel, C. J. Persons and E. Talman, *Tetrahedron Lett*., 1977, **30**, 2617; (*c*) T. Koyama, M. Matsubara and K. Ogura, *Naturwissenschaften*, 1983, **70**, 469.

2 H. A. Lloyd, T. H. Jones, A. Hefetz and J. Tengoe, *Tetrahedron Lett*., 1990, **31**, 5559.

3 R. Baker, D. C. Billington and N. Ekanayake, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1387.

4 D. W. Knight and B. Ojhara, *J. Chem. Soc., Perkin Trans. 1*, 1983, 955.

5 K. Mori and H. Ueda, *Tetrahedron*, 1982, **38**, 1227.

6 K. Mori and N. Murata, *Liebigs Ann. Chem*., 1995, 2089.

7 T. Kasai, H. Watanabe and K. Mori, *Bioorg. Med. Chem*., 1993, **1**, 67.

8 L. Poppe, L. Novak, P. Kolonits, A. Bata and C. Szantay, *Tetrahedron*, 1988, **44**, 1477.

9 S. Kuwahara, Y. Shibata and A. Hiramatsu, *Liebigs Ann. Chem*., 1992, 993.

10 A. N. Kasatkin, T. Yu. Romanova, I. P. Podlipchuk and G. A. Tolstikov, *Khim. Prir. Soedin*., 1993, 459 [*Chem. Nat. Compd.* (*Engl. Transl.*), 1993, **23**, 397].

11 (*a*) E. Ott, *Chem. Ber*., 1928, **61**, 2124; (*b*) S. Siegel and B. Dmuchovsky, *J. Am. Chem. Soc*., 1964, **86**, 2192.

12 D. J. Pasto and R. T. Tayor, *Org. React*., 1991, **40**, 91.

13 A. Kinoshita, N. Sakakibara and M. Mori, *J. Am. Chem. Soc*., 1997, **119**, 12388.

14 A. Kinoshita, N. Sakakibara and M. Mori, *Tetrahedron*, 1999, **55**, 8155.

15 (*a*) A. A. Vasil'ev, A. L. Vlasyuk, G. V. Kryshtal and E. P. Serebryakov, *Izv. Akad. Nauk, Ser. Khim*., 1995, 2026 (*Russ. Chem. Bull*, 1995, **44**, 1946); (*b*) A. A. Vasil'ev and E. P. Serebryakov, *Izv. Akad. Nauk, Ser. Khim*., 1996, 2350 (*Russ. Chem. Bull*, 1996, **45**, 2232).

16 (*a*) A. A. Vasil'ev, G. V. Kryshtal and E. P. Serebryakov, *Mendeleev Commun*., 1995, 41; (*b*) A. A. Vasil'ev, A. A. Vlasyuk, G. L. Gamalevich and E. P. Serebryakov, *Bioorg. Med. Chem*., 1996, **4**, 389; (*c*) A. A. Vasil'ev, L. Engman and E. P. Serebryakov, *Acta Chem. Scand*., 1999, **53**, 611.

17 M. Sodeoka and M. Shibasaki, *Synthesis*, 1993, 643.

18 W. S. Johnson, N. P. Jensen, J. Hooz and E. J. Leopold, *J. Am. Chem. Soc*., 1968, **90**, 5872.

19 R. L. Willer and E. L. Eliel, *J. Am. Chem. Soc*., 1977, **99**, 1925.

20 M. Uemura, T. Minami, K. Hirotsu and Y. Hayashi, *J. Org. Chem*., 1989, **54**, 469.

21 A. J. Mancuso, S.-L. Huang and D. Swern, *J. Org. Chem*., 1978, **43**, 2480.

22 B. S. Bal, W. E. Childers and H. W. Pinnick, *Tetrahedron*, 1981, **37**, 2091.

Received: 17th March 2000; Com. 00/1629