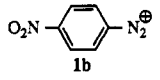
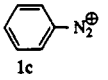
oxidatively be desilylated by treatment with aryldiazonium ions.

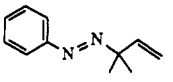
Preliminary experiments showed that among the allylsilanes used in this work all but **2i** and **2j** also react with the less electrophilic *p*-nitrobenzenediazonium ion **1b**. The highly alkylated allylsilanes **2b** and **2g** even react with the unsubstituted benzenediazonium ion **1c** to give **3b′** and **3g′** in 51 and 74% yield, respectively. In accord with our previous report that allylstannanes are more nucleophilic than structurally analogous allylsilanes by several orders of magnitude,[6d] tri-*n*-butylprenylstannane also reacted with the parent benzenediazonium ion **1c** to afford 49% of **3a′**. Though the correlation between reactivities toward carbenium and diazonium ions does not seem to be perfect, Table II shows that the nucleophilicity scale developed with respect to diarylcarbenium ions[6] also allows one to roughly predict the feasibility of electrophilic attack of diazonium ions at allylsilanes.



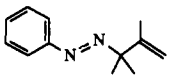
1b



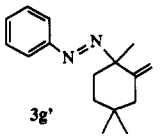
1c



3a′



3b′



3g′

Registry No. **1a**, 345-12-0; **1b**, 456-27-9; **1c**, 369-57-3; **2a**, 18293-99-7; **2b**, 64545-12-6; **2c**, 83438-58-8; **2d**, 63922-76-9; **2e**, 138061-12-8; **2f**, 138061-13-9; **2g**, 138061-14-0; **2h**, 18292-38-1; **2i**, 762-72-1; **2j**, 14579-08-9; **3a**, 138061-15-1; **3a′**, 31928-42-4; **3b**, 138061-16-2; **3b′**, 138061-17-3; **3c**, 138061-18-4; **3d**, 138061-19-5; **3e**, 138061-20-8; **3f**, 138061-21-9; **3g**, 138061-22-0; **3g′**, 138061-23-1.

(*R*)-1-Acetyl-5-isopropoxy-3-pyrrolin-2-one: A Versatile Chiral Dienophile from (*S*)-Malic Acid

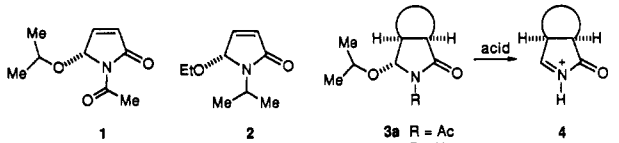
Wim-Jan Koot, Henk Hiemstra,* and W. Nico Speckamp*

Department of Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands

Received October 28, 1991

Summary: The title compound, readily prepared from (*S*)-malic acid, reacts as a Diels–Alder dienophile with several 1,3-dienes with excellent regio- and stereoselectivity without loss of enantiomeric purity. The synthesis of an enantiomerically pure intermediate in a projected synthesis of gelsemine is detailed.

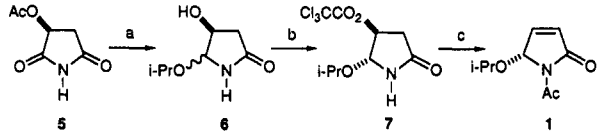
Of the various ways to control the absolute stereochemistry of an intermolecular Diels–Alder reaction, the approach involving the use of an enantiomerically pure dienophile has proven to be most practicable.[1] In this paper we wish to present the synthesis and utility of the chiral dienophile (*R*)-1-acetyl-5-isopropoxy-3-pyrrolin-2-one (**1**), which in essence can be viewed as an enantiomerically pure synthetic equivalent of maleimide.[2]



1 **2** **3a** R = Ac, **3b** R = H **4**

The choice for the structural features present in **1** was eventually made, when we had found that other Δ^3-pyrrolin-2-ones such as **2**[3] were unsuitable for our purposes. The isopropoxy function at C-5 in **1** is meant to direct 1,3-dienes to react at the opposite face of the molecule to give **3a**.[4] The significance of an alkoxy function at C-5 becomes apparent after removal of the *N*-acetyl function, as **3b** is expected to allow the introduction of a variety of substituents via *N*-acyliminium intermediate **4**.[5] The presence of the *N*-acetyl function in **1** is required to prevent racemization and enhance the reactivity and regiochemical bias of the dienophile.[6]

Scheme I[a]



5 **6** **7** **1**

[a] Reagents and conditions: (a) (i) $LiBH_4$ (1.0 equiv), THF, −20 → 0 °C, (ii) H_2SO_4 in i-PrOH (pH = 3), 0 °C → reflux, 55%; (b) $(Cl_3CCO)_2O$ (1.1 equiv), DMAP (1.1 equiv), Et_2O, −60 °C → rt, 86%; (c) Ac_2O/pyridine, DMAP (cat.), 0 °C → rt, 85%.

The synthesis of (*R*)-**1** is detailed in Scheme I. (*S*)-3-Acetoxysuccinimide (**5**), readily prepared on large scale from (*S*)-malic acid,[7] was regioselectively reduced with lithium borohydride in THF at −20 °C. The crude reaction mixture was acidified with sulfuric acid. The solvent THF was then substituted for 2-propanol and the resulting mixture heated at reflux for 18 h to effect both isopropanolysis and transesterification, to give **6** as a 1:4

(1) For reviews, see: (a) Paquette, L. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, Chapter 7. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876.

(2) For recent alternative approaches, see: (a) Arai, Y.; Matsui, M.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1991**, *56*, 1983. (b) Baldwin, S. W.; Greenspan, P.; Alaimo, C.; McPhail, A. T. *Tetrahedron Lett.* **1991**, *32*, 5877. For a chiral synthetic equivalent for maleic anhydride, see: (c) Feringa, B. L.; de Jong, J. C. *J. Org. Chem.* **1988**, *53*, 1125. (d) de Jong, J. C.; Jansen, J. F. G. A.; Feringa, B. L. *Tetrahedron Lett.* **1990**, *31*, 3047.

(3) The study of **2** originated from our work on the synthesis of the indole alkaloid peduncularine and will be described in a full paper; see: Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *J. Am. Chem. Soc.* **1989**, *111*, 2588.

(4) For Diels–Alder additions to Δ^3-pyrrolin-2-ones with carbon substituents at C-5, see: (a) Vedejs, E.; Campbell, J. B., Jr.; Gadwood, R. C.; Rodgers, J. D.; Spear, K. L.; Watanabe, Y. *J. Org. Chem.* **1982**, *47*, 1534. (b) Stork, G.; Nakahara, Y.; Nakahara, Y.; Greenlee, W. J. *J. Am. Chem. Soc.* **1978**, *100*, 7775. (c) Ohfune, Y.; Tamita, M. *J. Am. Chem. Soc.* **1982**, *104*, 3511. (d) Harkin, S. A.; Singh, O.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1489. (e) Ackermann, J.; Matthes, M.; Tamm, C. *Helv. Chim. Acta* **1990**, *73*, 122. (f) Meyers, A. I.; Busacca, C. A. *Tetrahedron Lett.* **1989**, *30*, 6973.

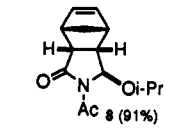
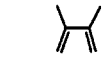
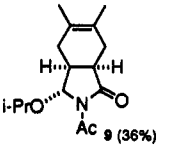
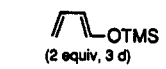
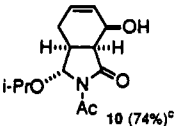
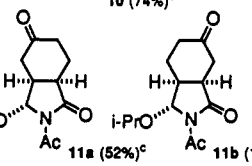
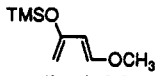
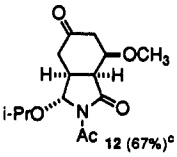
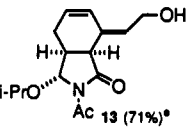
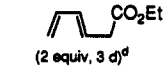
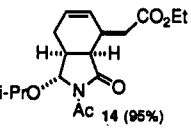
(5) For a review, see: Hiemstra, H.; Speckamp, W. N. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon: Oxford, 1991; Vol. 2, Chapter 4.5.

(6) (a) Vedejs, E.; Gadwood, R. C. *J. Org. Chem.* **1978**, *43*, 376. (b) Baker, J. T.; Sifniades, S. *J. Org. Chem.* **1979**, *44*, 2798. (c) Schmidlin, T.; Tamm, C. *Helv. Chim. Acta* **1980**, *63*, 121.

(7) (a) Chamberlin, A. R.; Chung, Y. L. *J. Am. Chem. Soc.* **1983**, 105, 3653. (b) Hart, D. J.; Yang, T.-K. *J. Org. Chem.* **1985**, *50*, 235.

0022-3263/92/1957-1059$03.00/0

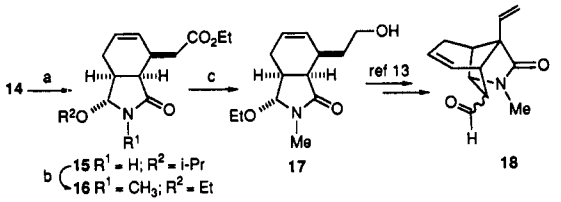
Table I. Diels–Alder Reactions with Pyrrolinone 1

entry	diene (equiv, reactn time)[a]	product(s) (yield)[b]	specific rotation
1	 (3 equiv, 4.5 h)	 **8** (91%)	$[\alpha]^{20}_D$ -125° (c 1.08, $CHCl_3$)
2	 (5 equiv, 3 d)	 **9** (36%)	$[\alpha]^{20}_D$ +115° (c 1.26, $CHCl_3$)
3	 (2 equiv, 3 d)	 **10** (74%)[c]	$[\alpha]^{20}_D$ +74° (c 0.66, $CHCl_3$)
4	 (2 equiv, 3 d)	 **11a** (52%)[c] **11b** (10%)[c]	**11a**: $[\alpha]^{20}_D$ +22° (c 1.06, $CHCl_3$)
5	 (2 equiv, 3 d)	 **12** (67%)[c]	$[\alpha]^{20}_D$ +65° (c 3.15, $CHCl_3$)
6	 (2 equiv, 18 h)[d]	 **13** (71%)[e]	$[\alpha]^{20}_D$ +49° (c 1.05, $CHCl_3$)
7	 (2 equiv, 3 d)[d]	 **14** (95%)	$[\alpha]^{20}_D$ +49° (c 1.01, $CHCl_3$)

[a] Conditions: toluene, sealed tube, 100–110 °C. [b] Yields are not optimized, except for 14. [c] The Diels–Alder product was desilylated ($(n\text{-}Bu)_4NF$ (cat.), KF (2 equiv), THF, rt) before purification. [d] For the synthesis of this diene, see ref 15. [e] >90% pure; some small signals of an unidentified byproduct were detected by NMR.

cis/trans mixture. The hydroxy function was acylated by using trichloroacetic anhydride and DMAP. Surprisingly, the trans lactam **7** was obtained as the sole product ($[\alpha]^{20}_D$ + 16° (c 0.60, $CHCl_3$), mp 100–102 °C) in 86% yield. Apparently, epimerization at C-5 has occurred during acylation. Although the mechanism of this epimerization is not clear (it could be either acid or base catalyzed), a beneficial effect on the overall yield is evident. The last two steps were achieved in a tandem fashion. By stirring lactam **7** with acetic anhydride in pyridine, *N*-acylation occurred first, followed by elimination of the trichloroacetoxy group to give the desired dienophile **1** ($[\alpha]^{20}_D$ –149° (c 0.50, $CHCl_3$), mp 49–49.5 °C)[8] in 40% overall yield from **5**. Without purification of intermediates a comparable yield of **1** from **5** was attained on a 50-g scale. Pyrrolinone **1** was also synthesized from **6** via diacylation with acetic anhydride in pyridine. However, refluxing triethylamine was now required for the final elimination step. Prepared

Scheme II[a]



[a] Reagents and conditions: (a) Me_2NH, DMF, rt, 18 h, 100%; (b) (i) NaH (1.1 equiv), DMF, rt, 5 min, (ii) MeI (1.1 equiv), DMF, rt, 3 h, (iii) $EtOH/H_2SO_4$ (pH = 2), rt, 2 h, 60%; (c) $LiBH_4$ (1.1 equiv), $LiEt_3BH$ (cat.), THF/Et_2O, rt, 2 h, 80%.

in this way, **1** showed a specific rotation $[\alpha]^{20}_D$ –100° (c 1.79, $CHCl_3$), corresponding with an optical purity of 67%, thus clearly demonstrating the need of a better leaving group at C-4.

The enantiomeric purity of (*R*)-**1** was determined by using the chiral shift reagent $Eu(hfc)_3$[9] in ^1H NMR, which did not reveal the presence of any of the enantiomeric (*S*)-**1**.[10] The stereochemical stability of (*R*)-**1** was also carefully checked. Although stable in chloroform at rt for at least 3 days and in refluxing toluene for at least 20 h, considerable racemization occurred on prolonged heating in neat triethylamine (vide supra), clearly demonstrating the somewhat acidic character of the proton at C-5. Further structural information about (*R*)-**1** was obtained from an X-ray crystal structure determination,[11] which showed a virtually planar pyrrolinone ring, with which the plane of the acetyl substituent makes an angle of less than 5°.

The results of the Diels–Alder reactions of (*R*)-**1** with seven different 1,3-dienes are shown in Table I. All reactions were carried out with ca. 2–3 equiv of diene in a sealed tube with toluene as solvent at ca. 100 °C. Reaction times varied from a few hours for cyclopentadiene to 72 h for less reactive dienes. When (silyloxy)butadienes were used (entries 3–5), the crude products were first desilylated with fluoride in THF before purification. The products shown in entries 1–5 and 7 were the only products that could be detected by ^1H and ^{13}C NMR. The stereochemistry of the products could be assigned by using ^1H NMR, in particular NOE difference techniques. In the case of adduct **13** (entry 6) the ^1H NMR spectrum showed some minor signals caused by a byproduct, which could not be identified. All Diels–Alder products were obtained as oils. Adduct **8** (entry 1) was readily deacylated with dimethylamine to give the N-unsubstituted lactam as colorless crystals in 92% yield ($[\alpha]^{20}_D$ –19° (c 0.31, $CHCl_3$), mp 166–168 °C dec).[12]

The above results show that the π-facial selectivity of the Diels–Alder process was very high in all cases. Where endo/exo selectivity is involved (entries 1, 3, 5–7), the reactions proceeded with high endoselectivity. The regioselectivity was only moderate when 2-[(trimethyl-

(8) Spectral data of **1**: IR ($CHCl_3$) 2970, 2925, 1740, 1700, 1370 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.19, 1.23 (2 d, 3 H, *J* = 6.2 Hz, $CH(CH_3)_2$), 2.53 (s, 3 H, Ac), 4.28 (sept, 1 H, *J* = 6.2 Hz, $CH(CH_3)_2$), 5.96 (d, 1 H, *J* = 1.7 Hz, H-5), 6.10 (d, 1 H, *J* = 6.1 Hz, H-3), 7.01 (dd, 1 H, *J* = 1.9, 6.0 Hz, H-4); ^{13}C NMR (50 MHz, $CDCl_3$) 169.6, 168.5, 147.6, 126.6, 86.2, 72.8, 24.7, 22.9, 22.8.

(9) Tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III) derivative, purchased from Aldrich.

(10) Racemic **1**, prepared in the same way from racemic malic acid, clearly showed double peaks for the ring protons in its NMR spectrum in the presence of $Eu(hfc)_3$.

(11) Details of the X-ray crystal structure determination will be reported elsewhere.

(12) Spectral data: IR ($CHCl_3$) 3430, 2990, 2970, 2930, 2870, 1685 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.16, 1.17 (2 d, 3 H, *J* = 6.1 Hz, $CH(CH_3)_2$), 1.38 (br d, 1 H, *J* = 8.4 Hz, *H*CH), 1.59 (br d, 1 H, *J* = 8.4 Hz, HC*H*), 2.77 (dd, 1 H, *J* = 4.2, 8.4 Hz, C*H*-CH-N), 3.13 (m, 2 H), 3.22 (m, 1 H), 3.67 (sept, 1 H, *J* = 6.1 Hz, $CH(CH_3)_2$), 4.38 (d, 1 H, *J* = 0.8 Hz, O-C*H*-N), 6.10 (dd, 1 H, *J* = 2.9, 5.6 Hz, *H*C=CH), 6.18 (dd, 1 H, *J* = 2.9, 5.6 Hz, HC=C*H*), 6.48 (br s, 1 H, N-*H*); ^{13}C NMR (50 MHz, $CDCl_3$) 178.7, 136.2, 133.3, 85.7, 69.4, 51.3, 48.4 (2×), 44.8, 44.7, 23.2, 22.4.

silyl)oxy]-1,3-butadiene was used (entry 4) but high in all other cases (entries 3, 5-7).

As an illustration of the applicability of 1 in synthesis, Diels-Alder adduct 14 (entry 7) was transformed into alcohol 17 (Scheme II), a crucial intermediate in a projected synthesis of gelsemine.[13] The acetyl function was easily removed from 14 through treatment with dimethylamine. Lactam 15 ($[\alpha]^{20}_D$ +55° (c 0.90, $CHCl_3$)) was then methylated with sodium hydride and methyl iodide, followed by an isopropoxy/ethoxy exchange to give lactam 16 ($[\alpha]^{20}_D$ +11° (c 1.15, $CHCl_3$)). This exchange was necessary, because the eventual BF_3·Et_2O-induced *N*-acyliminium cyclization to the tricyclic product 18[13] did not proceed well with isopropoxy as leaving group. Finally, the ester group in 16 was reduced with lithium borohydride in the presence of $LiBEt_3H$ to give alcohol 17 in 80% yield.[14] All spectroscopic data of 17 except rotation ($[\alpha]^{20}_D$ +5° (c 2.85, MeOH)) were in complete agreement with those of the racemic alcohol prepared before.[13] The product appeared to be enantiomerically pure within detection limits, according to analysis of its ^1H NMR spectrum with $Eu(hfc)_3$.[9]

In conclusion, we have shown that enantiomerically pure (*R*)-1-acetyl-5-isopropoxy-3-pyrrolin-2-one (1) can be readily prepared from (*S*)-malic acid and reacts with excellent stereo- and regioselectivity in Diels-Alder reactions without loss of enantiomeric purity. Further applications of this methodology as well as stereoselective conjugate additions to 1 will be reported in due course.

Acknowledgment. We are grateful to J. Fraanje and K. Goubitz of the Department of Crystallography of this University for the X-ray crystal structure determination. We thank C. Kruk and his staff for their help in obtaining and interpreting the NMR spectra, R. H. Balk and W. J. M. Steeman for the preparation of starting materials on large scale, and M. Avis and R. M. Schonk for pioneering experiments with 2. This investigation was supported by the Netherlands' Foundation for Chemical Research (SON) with financial aid from the Netherlands' Organization for the Advancement of Pure Research (NWO).

Registry No. 1, 138259-70-8; 5, 85319-59-1; *trans*-6, 138259-71-9; *cis*-6, 138259-72-0; 7, 138259-73-1; 8, 138259-74-2; 8 deacylated derivative, 138259-75-3; 9, 138259-76-4; 10, 138259-77-5; 11a, 138259-78-6; 11b, 138259-79-7; 12, 138259-80-0; 13, 138259-81-1; 14, 138259-82-2; 15, 138259-83-3; 16, 138259-84-4; 17, 138332-58-8; cyclopentadiene, 542-92-7; 2,3-dimethyl-1,3-butadiene, 513-81-5; 1-[(trimethylsilyl)oxy]-1,3-butadiene, 6651-43-0; 2-[(trimethylsilyl)oxy]-1,3-butadiene, 38053-91-7; 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene, 59414-23-2; 3,5-hexadien-1-ol, 5747-07-9; ethyl 3,5-hexadienoate, 81838-64-4.

Supplementary Material Available: Experimental procedures, physical properties, and spectral data (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(13) (a) Vijn, R. J.; Hiemstra, H.; Kok, J. J.; Knotter, M.; Speckamp, W. N. *Tetrahedron* **1987**, *43*, 5019. (b) Hiemstra, H.; Vijn, R. J.; Speckamp, W. N. *J. Org. Chem.* **1988**, *53*, 3882. (c) Fang, Y. Forthcoming Thesis, University of Amsterdam.
(14) Brown, H. C.; Narasimhan, S. *J. Org. Chem.* **1982**, *47*, 1604.
(15) (a) Martin, S. F.; Tu, C.; Chou, T. *J. Am. Chem. Soc.* **1980**, *102*, 5274. (b) Stevens, R. V.; Cherpeck, R. E.; Harrison, B. L.; Lai, J.; Lapalme, R. *J. Am. Chem. Soc.* **1976**, *98*, 6317.

Facile Electroreduction of Methyl Esters and *N*,*N*-Dimethylamides of Aliphatic Carboxylic Acids to Primary Alcohols[1]

Tatsuya Shono,* Haruhisa Masuda, Hiroaki Murase, Masatoshi Shimomura, and Shigenori Kashimura

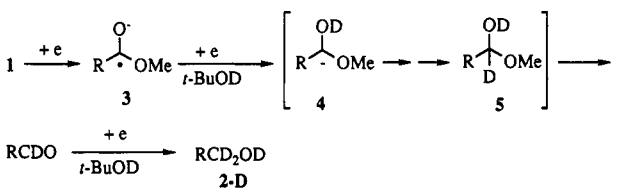
Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Sakyo, Kyoto 606-01, Japan

Received September 23, 1991

Summary: In the presence of *t*-BuOH, methyl esters and *N*,*N*-dimethylamides of aliphatic carboxylic acids are electroreduced at a Mg cathode to the corresponding primary alcohols. In the presence of *t*-BuOD instead of *t*-BuOH, the electroreduction of the esters gives the corresponding 1,1-dideuterated alcohol. In all cases, the yields are excellent.

The transformation of esters of aromatic carboxylic acids to benzyl-type alcohols can be achieved by electrochemical reduction.[2,3] However, the electroreduction of esters of aliphatic carboxylic acids to primary alcohols has never been achieved because such esters display highly negative reduction potentials (~-3.0 V vs SCE).[4-6]

Scheme I



We have found that when Mg is used as the electrode material, the electroreduction of esters of aliphatic carboxylic acids 1 is possible. Thus, the electroreduction of 1 at a Mg cathode in the presence of a proton donor like *t*-BuOH gives primary alcohols 2 (RCH_2OH) in excellent

(1) Electroorganic chemistry. 134. For part 133, see: Shono, T.; Nozoe, T.; Yamaguchi, Y.; Ishifune, M.; Sakaguchi, M.; Masuda, H.; Kashimura, S. *Tetrahedron Lett.* **1991**, *32*, 1051.
(2) Coleman, G. H.; Johnson, H. L. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 61.
(3) Popp, F. D.; Schultz, H. P. *Chem. Rev.* **1962**, *62*, 19 and references cited therein.
(4) Weinberg, N. L.; Ed. *Technique of Electroorganic Synthesis*; John Wiley: New York, 1974-1982; Vols. 1-3.
(5) Baizer, M. M.; Lund, H., Eds. *Organic Electrochemistry*, 2nd ed.; Marcel Dekker: New York, 1983.
(6) Belotti, D.; Cossy, J.; Pete, J. P.; Portella, C. *J. Org. Chem.* **1986**, *51*, 4196.

0022-3263/92/1957-1061$03.00/0