Synthesis of optically pure 3-(1n.pi.*)-(1S,6R)-bicyclo[4.4.0]decane-3,8-dione, a molecule which is chiral in the excited state only

Citation for published version (APA):

DOI:
10.1021/ja00091a015

Document status and date:
Published: 01/01/1994

Document Version:
Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:
• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:
www.tue.nl/taverne

Take down policy
If you believe that this document breaches copyright please contact us at:
openaccess@tue.nl
providing details and we will investigate your claim.
Synthesis of Optically Pure 
3-(1n*-)-(1S,6R)-Bicyclo[4.4.0]decan-3,8-dione, a Molecule Which is Chiral in the Excited State Only

Franciscus W. A. M. Miesen,† Angelino P. P. Wollersheim,† Stefan C. J. Meskers,‡ Harry P. J. M. Dekkers,† and E. W. Meijer†,†

Contribution from the Laboratory of Organic Chemistry, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands, and Gorlaeus Laboratories, Leiden University, P.O. Box 9502, 2300 RA Leiden, The Netherlands

Received October 25, 1993

Abstract: Low-temperature photooxygenation of (1S,6R)-3-(E,Z)-methoxymethylene)bicyclo[4.4.0]decan-8-one (7), prepared in 10 steps from 2,6-dimethoxynaphthalene (5), yields a mixture of four isomeric 1,2-dioxetanes (8a-d) with ee > 98%. Upon thermal decomposition, these 1,2-dioxetanes are all precursors for 3-(1n*)-(1S,6R)-bicyclo[4.4.0]-decan-3,8-dione (1*), an optically active diketone in its locally excited 1n* state. The optical activity of this molecule is evidenced by the nonvanishing circular polarized in the chemiluminescence of 8a-d. The degree of polarization (gS) at 420 nm equals (1.5 ± 0.3) × 10⁻³, a value which is similar to that of the regular fluorescence of optically active (1S,6R,8S)-8-hydroxybicyclo[4.4.0]decan-3-one (6). This similarity implies the absence of substantial racemization in the excited state, whence one concludes that the rate constant for intramolecular 1n* energy transfer in 1* is ≤10⁹ s⁻¹. The chiroptical results show that localization of excitation energy at the carbonyl at the 3-position of 1* can be achieved by the synthetic route applied, yielding enantiomerically pure 3-(1n*)-(1S,6R)-bicyclo[4.4.0]decan-3,8-dione (1*), an optically active molecule whose chirality is due solely to the presence of localized electronic excitation energy.

Introduction

Molecules in which chirality is due solely to small differences between the discriminating groups have always fascinated stereochemists.† Striking examples are chiral tetraalkylmethanes and fullerenes and molecules which are chiral due to isotopic substitution.‡ One of the smallest deviations from achirality is found in systems in which the chirality is due solely to the presence of localized electronic excitation.∗ This can arise in centrosymmetric or meso compounds with two remote enantiotopic chromophores, as shown in Figure 1 for 1, 1*, and related structures 2-4. In the ground state these diketones (R,S) are achiral, while in the excited state two enantiomeric forms (R*,S) and (R,S*) are present, providing the excitation energy is localized.

The excited state can be formed by the irradiation of R,S with circularly polarized light. The difference in concentration of R*,S and S*,R* is then governed by the disymmetry factor in absorption (gS = OD/OD): in fact, the resultant enantiomer excess (ee) equals gS/2. The optical activity of the excited-state species is evidenced by a nonvanishing degree of circular polarization of luminescence (CPL). Such excited-state chirality has experimentally been demonstrated in the 1,7-diketone 2*.5 In the case of the 1,5-diketone 3*, a zero CPL has been found which is ascribed to a fast racemization in the singlet excited state (lifetime τR) due to 1n* energy transfer. In the absence of energy transfer, the circular polarization, as measured in these experiments, equals gSgS/2. Energy transfer reduces the ee, and thus the CPL signal, by a factor of (2kRτS)⁻¹.

Since in photoselection experiments the ee is governed by gS which, for the n→n* band of ketones, will give an ee of at the most ~10%, a major improvement of selectivity has been foreseen by using chemiexcitation to produce R*,S, potentially with an ee of 100%.*6 According to this approach, singlet-excited-state

Figure 1. Meso diketones that contain two carbonyl moieties of opposite chirality. All structures are achiral in the ground state but chiral in the excited state, provided excitation energy is localized at one carbonyl group.

† Eindhoven University of Technology.
‡ Leiden University.
†† Contribution from the Laboratory of Organic Chemistry, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands, and Gorlaeus Laboratories, Leiden University, P.O. Box 9502, 2300 RA Leiden, The Netherlands

0002-7863/94/1516-5129$04.50/0 © 1994 American Chemical Society
2,4-adamantandione (4*) has been prepared by the thermolysis of the corresponding optically active 1,2-dioxetanes.6 These four-membered rings are known to dissociate into two carbonyl fragments accompanied with chemiluminescence. Upon thermal decomposition, one of the carbonyls is produced in its (singlet or triplet) excited state by a nonadiabatic process (chemiexcitation). The radiative transition from the singlet excited state to the ground state following chemiexcitation accounts then for the chemiluminescence. Despite the fact that the excitation is directed chemically to one of the carbonyls only, a vanishingly small circular polarization in chemiluminescence of the 1,2-dioxetanes has been detected. A complete loss of optical activity occurred within the lifetime of 2 ns of 4*; due to the close proximity of both carbonyls in 4, energy transfer is extremely fast.

In this paper we describe the synthesis and the circular polarization of the chemiluminescence of optically pure 3, (1R*)- (1S,6R*)-bicyclo[4.4.0]dec-3,8-dione (1*),7 a diketone in which both carbonyls are more remote. The synthetic route is based on our previous work for the chemiexcitation of 4,6,8 Via thermal decomposition of the optically active 1,2-dioxetanes 8a-d, enantiomerically pure 1* is obtained together with ground-state methyl formate (Scheme 1).

Results and Discussion

Synthesis. The optically active precursor of 1* is synthesized starting from 2,6-dimethoxybenzophenone (5), as outlined in Scheme 2. In six steps and an overall yield of 15%, 5 has been transformed into optically pure (ee > 98%) (1S,6R,8S)-8-hydroxybicyclo[4.4.0]dec-3-ene (6) using in the last step the HLADH-reduction of 1 as pioneered by Jones et al.9 The conversion of 6 into (1S,6R)-3-(E,Z)-methoxy methylene)bicyclo[4.4.0]decane-8-one (7) is achieved in a four-step procedure. Protection of the alcohol with an acetyl group followed by the Wittig reaction with 1.1 equiv of (methoxymethylene)phosphorane in THF gives the E- and Z-isomers of (1S,6R,8S)-3-(methoxy methylene)bicyclo[4.4.0]dec-8-yl acetate in a 1:1 ratio in 25% yield. Hydrolysis of the acetyl group with LiOH and a pyridinium salt oxidizes the alcohol yielded optically pure enol ether (1S,6R)-7. Photooxygenation of 7 with singlet oxygen in dichloromethane at -80 °C, using methylene blue as sensitizer, gives a mixture of four isomeric 1,2-dioxetanes 8a-d (60%) and allylic hydroperoxides 9a-d (40%) as byproducts.3 The ratio of 8 to 9 is strongly influenced by temperature and solvent, as reported for model compounds.10 The 1,2-dioxetanes are purified (removal of byproducts 9a-d) by using low-temperature (-30 °C) column chromatography. The four isomeric (1S,6R)-1,2-dioxetanes 8a-d are formed in approximately equal amounts by the *O₂ attack of

Figure 2. 1H NMR analysis of the decomposition at 60 °C in toluene-d₈ of the four isomeric 1,2-dioxetanes 8a-d by monitoring the intensities of the characteristic protons of the four-membered ring. The upper lines represent the methoxy protons, whereas the lower lines represent the olefinic protons. It should be noted that two proton chemical shifts do coincide (line in the middle).

Figure 3. Emission spectrum of the optically active 1,2-dioxetanes during thermolysis in diglyme at 80 °C. The circular anisotropy g₂ is detected at optimal wavelength λ = 430 nm. In the inset, the decay of chemiluminescence at 80 °C is shown.

Both enol ethers at both sides of the molecule, as is concluded from NMR spectra.

Thermolysis and Chiroptical Properties. In order to investigate the rates of decomposition of the four individual isomeric 1,2-dioxetanes, we have monitored the thermolysis of 8a-d with 1H NMR spectroscopy. First-order rate constants of k₁ = 9.6 × 10⁻³ and k₂ = 6.5 × 10⁻⁴ s⁻¹ for two pairs of 1,2-dioxetanes are estimated from kinetic studies at 60 °C in toluene-d₈ (Figure 2). The difference in stability for the two pairs is thought to arise from the difference in steric interactions in the equatorial and axial positions of the oxygen atoms of the four-membered rings, while no difference is expected for the E- and Z-stereoisomers. The unequal rate constants give rise to a nonexponential decay of the chemiluminescence intensity (Figure 3) as well as the circular dichroism signal at 295 nm (Figure 4). The CD data have been taken on a dilute sample of (1S,6R)-8a-d in bis(2-methoxyethyl) ether (diglyme). After thermolysis at 80 °C, only a trace amount of optically active impurity (probably a trace of one product) gives rise to a small negative residual CD of 8a-d at λmax = 295 nm.

The thermolysis of 8a-d in diglyme at 80 °C is accompanied with chemiluminescent emission, the spectrum of which (Figure 3) closely resembles the fluorescence spectra of 1 and 6. As expected, 1Hπ* species formed in the decomposition reaction are effectively quenched under the experimental conditions used.
Collecting the emission at 430 nm, we observe\(^{11}\) for 8a-d a
dissymmetry factor of chemiluminescence \(g_c = -(1.5 \pm 0.3) \times 10^{-3}\). The effect cannot be due to a CD artifact, because in the
original sample (i.e., before thermolysis) we observe a zero CD
signal at 430 nm.

Thermolysis of the optically active dioxetanes 8a-d furnishes
initially the excited diketone in its locally excited \(1n\pi^*\) state. The optical activity of this molecule is evidenced by the nonvanishing
circular polarization in the chemiluminescence. In the absence of
racemization, the circular anisotropy in emission of the hydroxy
diketone 5, \(g_c\), should be similar to \(g_{\text{chemi}}\) of the chemiluminescent
diketone \(1^*\). The fact that the dissymmetry factor in the
chemiluminescence has the same order of magnitude as the
energy transfer for ketones \(1-a-d\), respectively, the energy transfer is fast
while for the 1,5-diketone 3 and the
1,3-diketone 4, having estimated \(R_{\text{ab}}\) values of 4.47 and 2.50 Å,
respectively, the energy transfer is fast \((k_{ET} \approx 10^{10} \text{ s}^{-1})\).

The chiroptical results indicate that the value of \(g_{\text{chemi}}\) for \(1^*\) is
determined only by optical activity due to the presence of a locally
excited state in a high enantiomeric excess, equally to the \(>98\%
\) ee and de of the hydroxy ketone 6.

**Concluding Remarks**

In conclusion, the results presented in this paper show the
successful synthesis and detection of CPL of enantiomerically
pure \(1n\pi^*\)-excited \(1^*\), whose chirality is due solely to the presence
of localized excitation energy. The localization of excitation energy on the carbonyl at the 3-position of 1 has been accomplished
by enantioselective chemiexcitation of enol ethers 7 to 1,2-
dioxetanes 8a-d, which by decomposition are all isomeric
precursors of 3-(\(1n\pi^*\))-1*. The optical activity was established
from the CPL in the chemiluminescence of the 1,2-dioxetanes.
No racemization, due to relatively slow intramolecular energy
transfer \((k_{ET} \approx 10^{9} \text{ s}^{-1})\) with respect to the singlet-excited-state
lifetime (2 ns), was observed. Furthermore, this concept of
excited-state chirality of ground-state meso molecules can be
used to observe second harmonic generation (SHG) in
centrosymmetric molecules and assemblies by using a circularly

**Figure 4.** (a) Circular dichroism spectrum of the 1,2-dioxetane showing
a negative Cotton effect. (b) The residual CD spectrum after thermolysis
at 80 °C in diglyme. In the inset, the decay at 80 °C of the CD signal
at 430 nm is shown.

**Figure 5.** X-ray structure of \(\text{trans-bicyclo[4.4.0]decane-3,8-dione (1),}\nshowing the distance \(R_{\text{ab}}\) between the carbon atoms of the two carbonyl
groups.
polarized fundamental beam. Following these lines, we have observed already SHG in centrosymmetric crystals of a racemic mixture;\(^9\) design of other systems with localized distortion of centrosymmetry by excitation is in progress.

**Experimental Section**

**General Techniques.** Melting points were determined on a Unicam THMS heating apparatus. Infrared (FT-IR) spectra were recorded on a Perkin-Elmer 1605 FT-IR spectrophotometer. CD spectra were recorded on a Jasco spectropolarimeter J-715. Analyses were performed on a Perkin-Elmer 240 apparatus. Optical rotations were measured on a Spectrochrome CD 440 spectrometer using tetrachloroethylene (TCE, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytik 8200 instrument with FID detection (25 m × 0.25 mm i.d., column type WCOT fused silica, stationary phase CP SIL-5 CB, film thickness 0.25 μm). Chemiluminescence spectra were recorded on a Spex Fluorolog II emission spectrometer.

**Circular Polarization of Luminescence.** Measurements of the circular polarization of the luminescence (CPL) and chemiluminescence were performed at Leiden University on a custom-built spectrometer operating in the photon counting mode. A detailed description of the instrument has been published.\(^1\) The measurements were performed on ~0.05 M solutions in spectrometric grade CHCl₃ for 6 and bis(2-methoxethyl) ether for 1.\(^6\) The bandwidth of the emission channel was chosen to be 30 nm.

**Materials.** Column chromatography was performed using Merck silica gel 60, 230–400 mesh as the stationary phase. Analytical thin-layer chromatography was conducted on precoated TLC plates, silica gel 60, F-254 layer thickness 0.25 mm, using UV (254 nm) and iodine detection.

Preparations of diolates were carried out in a 700-mL reaction vessel. All solvents and commercial reagents were reagent grade. Diethyl ether was dried over CaCl₂ and stored over sodium wire. Dichloromethane was distilled from CaH₂ and pyridine from KOH pellets. Oxygen was dried over molecular sieves containing concentrated sulfuric acid and a KOH pellets. Tetrahydrofuran (THF) was distilled under dry argon from sodium in the presence of benzophenone.

**1(S,6R)-Bicyclo[4.4.0]decane-3,8-dione (1).** \(^1\) trans-Bicyclo[4.4.0]-decane-3,8-dione (1) was prepared according to literature procedures.\(^a\) Anal. Calcd for C₁₀H₁₄O₂: C, 72.26; H, 8.49. Found: C, 72.44; H, 8.46.

**1(S,6R,8S)-8-Acetylbicyclo[4.4.0]decane-3-one (7).** A 0.1 M phosphate buffer (400 mL, pH 7.2) and 15 mL of anhydrous THF in a nitrogen atmosphere was added 3.8 M of 2.5 M n-butylthiourea (9.52 mmol), whereupon the red color of the ethyldiene phosphorane was produced. After the mixture was stirred for about 1 h, a solution of (1S,6R,8S)-8-acetylbicyclo[4.4.0]-decane-3-one (7) (2.0 g, 9.52 mmol) in anhydrous THF was added rapidly to the dark red solution. After the solution was stirred for another 2 h at room temperature, 10 mL of a saturated ammonium chloride solution was added. The solution was acidified (pH 4) and extracted with ether (250 mL) and washed with water (3 × 20 mL). Extraction with ether, drying (MgSO₄), and rotary evaporation of the organic layer afforded a dark red residue. Column chromatography on silica gel (hexane/ethyl acetate, 92:8 elution) gave 1.25 g of (1S,6R,8S)-3-((E)-methoxymethylene)bicyclo[4.4.0]-dec-8-yl acetate as a colorless oil (yield 55%). \(^1\) H NMR (CDCl₃): δ 5.82, 4.90 (s, 2 CH₃), 2.56–2.85 (14H, m), 1.00–2.40 (14H, m), 1.25–5.00 (SH, m), 0.25–1.25 (1H, m), 0.10–1.25 (1H, m). \(^1\) C NMR (CDCl₃): δ 21.52 (C₂), 20.10 (C₁), 170.08 (C=O), 69.13 (C₁₁), 47.99 (C₄), 46.42 (C₄), 40.75 (C₁, C₉), 30.08 (2H, C₆), 27.90, 27.85, 27.90, 27.90, 27.46, 21.12. IR (neat): ν 1711 (C=O stretch, saturated), 1715 (C=O stretch, saturated), 1300 (C₃=C₃ deformation), 1240 (C=C stretch, unsaturated). \(^1\) S, E. Mienes et al. J. Am. Chem. Soc. 1994, 5132, 5132.
Optically Pure 3-(\(\text{in}^\text{R}\))-(1S,6R)-Bicyclo[4.4.0]decane-3,8-dione blue (10 mg) were dissolved in 600 mL of dichloromethane and photooxygenated for 1 h at -80 °C. The irradiations were carried out with a Hanau TQ78 500-W medium-pressure mercury lamp through quartz, using a sheet of brownish polyimide (Kapton 500H, du Pont de Nemours) wrapped around the lamp compartment as short wavelength filter (cutoff 550 nm). Cooling of the lamp and primary cooling of the reaction vessel were accomplished by means of a closed circuit filled with methanol from a cryostat. The temperature of -80 °C was reached by extra external cooling baths of ethanol and liquid nitrogen. Column chromatography at -30 °C using dichloromethane/ethyl acetate, 60:40 elution, resulted in removal of the sensitizer, yielding a mixture of dioxetanes and allylic hydroperoxides in a ratio of 60:40. Pure dioxetane was obtained by concentrating 700 mL of the crude dioxetane solution to ~250 mL and subsequent column chromatography at -30 °C using dichloromethane/aceton, 96:4 as eluent. The relatively low-boiling solvents, dichloromethane, acetone, and ethyl acetate, were removed in the presence of an appropriate high-boiling solvent, bis(2-methoxyethyl) ether (diglyme) or toluene-d_8. CPL measurements were carried out using a concentrated dioxetane solution (a solution of 550 mL of 1,2-dioxetane was concentrated into 20 mL of diglyme). For recording \(\text{^1H} \) and \(\text{^13C} \) NMR spectra, an aliquot of the dioxetane solution was concentrated at 0 °C. During evaporation, cold CDCl_3 or toluene-d_8 was added in such a way that the 1,2-dioxetane was always present in solution. The 1,2-dioxetane was stored as a solution in dichloromethane below -20 °C. \(\text{^1H} \) NMR (toluene-d_8, \(T = 25 \) °C): \(\delta 5.26, 5.22, 5.20, 5.18 \times 4 (\text{H}, s, H_11), 3.28, 3.26 \times 2 \text{H}, s, OCH_3), 3.16 \times 6 \text{H}, s, OCH_2), 2.7-0.7 \text{(envelope)}. \) \(\text{^13C} \) NMR (CDCl_3, \(T = -20 \) °C): \(\delta 211.28, 211.08 \times 2 \text{C}, 109.60, 109.44 \times 2 \text{C}, 89.54, 89.51, 89.43, 89.34 \times 4 \text{C}, 56.04, 55.99, 55.69, 55.62 \times 4 \text{OCH_3), 47.98, 47.25, 46.91, 46.74 \times 4 \text{C}, 41.16, 40.92, 40.67, 40.52, 40.16, 40.92, 40.67, 40.06, 39.37, 38.02, 37.11, 35.70, 35.38, 34.94, 33.79, 33.52, 32.64, 32.44, 32.28, 30.23, 29.2, 28.04, 27.7, 26.27).