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.

Download date: 09. Apr. 2024
Synthesis of Optically Pure 3-[(1n*)-(1S,6R)-Bicyclo[4.4.0]decane-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)-methoxyxymethylene)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]decane-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 polarization in the chemiluminescence of 8a–d. The degree of polarization (g) 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]decane-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 enantiomeric chromophores, as shown in Figure 1 for 1, R*, 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) 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 dissymmetry factor in absorption (g = OD/OD): in fact, the resultant enantiomeric excess (ee) equals gₐ/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 1,5-diketone 2*. 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 τ) due to 1n* energy transfer. In the absence of energy transfer, the circular polarization, as measured in these experiments, equals gₐgₐ/2. Energy transfer reduces the ee, and thus the CPL signal, by a factor of (2kₑτ + 1)⁻¹.

Since in photoselection experiments the ee is governed by gₐ (which, for the n→n* band of ketones, will give an ee of at least 10%), a major improvement of selectivity has been foreseen by using chemiexcitation to produce R*,S, potentially with an ee of 100%. 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.

2,4-adamantane-1,3-dione (4*) has been prepared by the thermolysis of the corresponding optically active 1,2-dioxetanes. 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).

In this paper we describe the synthesis and the circular polarization of the chemiluminescence of optically pure 3-([nπ*]- (1S,6R)-bicyclo[4.4.0]decane-3,8-dione (1*)), a diketone in which both carbonyls are more remote. The synthetic route is based on our previous work for the chemiexcitation of 4. 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-dimethoxynaphthalene (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]decan-3-one (6) using in the last step the HLADH-reduction of 1 as pioneered by Jones et al.1 The conversion of 6 into (1S,6R)-3-(E,Z)-methoxymethylene)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-(methoxymethylene)bicyclo[4.4.0]dec-8-yl acetate in a 1:1 ratio in 25% yield. Photodissociation of the acetyl group with LiOH and a pyridinium salt of the four-membered rings is 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).

Figure 2. 1H NMR analysis of the decomposition at 60 °C in toluene-\(\text{d}_8\) 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).

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 \(^1\)H NMR spectroscopy. First-order rate constants of \(k_1 = 9.6 \times 10^{-4} \text{s}^{-1}\) and \(k_2 = 6.5 \times 10^{-4} \text{s}^{-1}\) for two pairs of 1,2-dioxetanes are estimated from kinetic studies at 60 °C in toluene-\(\text{d}_8\) (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 \(\lambda_{\text{max}} = 295 \text{ nm}\).

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, \(^1\)nπ* species formed in the decomposition reaction are effectively quenched under the experimental conditions used.
Collecting the emission at 430 nm, we observe for 8a-d a dissymmetry factor of chemiluminescence \( g_{e} = (1.5 \pm 0.3) \times 10^{-3} \). 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 'nπ*' 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 ketone 6, \( g_{e} \), should be similar to \( g_{	ext{Chem}} \) of the chemiluminescent diketone 'nπ*'.

The fact that the dissymmetry factor in the excited state in a high enantiomeric excess, equally to the optical activity of this molecule is evidenced by the nonvanishing circular anisotropy in emission of the hydroxy ketone 6, \( g_{e} = -0.9 \pm 0.2 \times 10^{-3} \) at the same wavelength) implies that racemization due to energy transfer is relatively small: \( k_{ET} \leq 10^{3} \text{ s}^{-1} \), calculated with \( \tau = 2 \text{ ns} \). This result for the 1,6-diketone 1 is in line with the available data on the energy transfer for ketones 2-4. The distance between both carbonyl carbons in 1, \( R_{ab} \), as found from X-ray analysis,\(^{13}\) amounts to 5.25 Å (Figure 5).\(^{14}\) For the 1,7-diketone 2, energy transfer is relatively slow \( (k_{ET} \leq 10^{3} \text{ s}^{-1}) \) for an estimated \( R_{ab} \) of 6.95 Å PM3 calculation\(^{15} \)), while for the 1,5-diketone 3 and the 1,3-diketone 4, having estimated \( R_{ab} \) values of 4.47 and 2.50 Å, respectively, the energy transfer is fast \( (k_{ET} \geq 10^{10} \text{ s}^{-1}) \).

The chiroptical results indicate that the value of \( g_{	ext{Chem}} \) 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 \( 'n\pi* \)-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-('nπ*')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 \( (k_{ET} \leq 10^{3} \text{ s}^{-1}) \) 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 polarized laser.

**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 trans-bicyclo[4.4.0]decane-3,8-dione (1), showing the distance \( R_{ab} \) 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; 16 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 spectroscopy was recorded on a Perkin-Elmer 2400 spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 apparatus. Optical rotations were measured on a Optical Activity Ltd. AA10 polarimeter. Proton, deuterium, and carbon-13 NMR spectra were recorded on a Bruker AM-400 spectrometer using tetramethylsilane (TMS, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytics 8200 instrument with FID detection (25 m x 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. 11 The measurements were performed on ~0.05 M solutions in spectrometric grade CH2Cl2 for 6 and bis(2-methylthio) ether for 1b. 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 performed on a Kieselgel 60, 230–400 mesh as the stationary phase. Elemental analyses were performed on a Perkin-Elmer 2400 apparatus. Optical rotations were measured on a Optical Activity Ltd. AA10 polarimeter. Proton, deuterium, and carbon-13 NMR spectra were recorded on a Bruker AM-400 spectrometer using tetramethylsilane (TMS, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytics 8200 instrument with FID detection (25 m x 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. 11 The measurements were performed on ~0.05 M solutions in spectrometric grade CH2Cl2 for 6 and bis(2-methylthio) ether for 1b. 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 performed on a Kieselgel 60, 230–400 mesh as the stationary phase. Elemental analyses were performed on a Perkin-Elmer 2400 apparatus. Optical rotations were measured on a Optical Activity Ltd. AA10 polarimeter. Proton, deuterium, and carbon-13 NMR spectra were recorded on a Bruker AM-400 spectrometer using tetramethylsilane (TMS, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytics 8200 instrument with FID detection (25 m x 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. 11 The measurements were performed on ~0.05 M solutions in spectrometric grade CH2Cl2 for 6 and bis(2-methylthio) ether for 1b. 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 performed on a Kieselgel 60, 230–400 mesh as the stationary phase. Elemental analyses were performed on a Perkin-Elmer 2400 apparatus. Optical rotations were measured on a Optical Activity Ltd. AA10 polarimeter. Proton, deuterium, and carbon-13 NMR spectra were recorded on a Bruker AM-400 spectrometer using tetramethylsilane (TMS, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytics 8200 instrument with FID detection (25 m x 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. 11 The measurements were performed on ~0.05 M solutions in spectrometric grade CH2Cl2 for 6 and bis(2-methylthio) ether for 1b. 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 performed on a Kieselgel 60, 230–400 mesh as the stationary phase. Elemental analyses were performed on a Perkin-Elmer 2400 apparatus. Optical rotations were measured on a Optical Activity Ltd. AA10 polarimeter. Proton, deuterium, and carbon-13 NMR spectra were recorded on a Bruker AM-400 spectrometer using tetramethylsilane (TMS, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytics 8200 instrument with FID detection (25 m x 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. 11 The measurements were performed on ~0.05 M solutions in spectrometric grade CH2Cl2 for 6 and bis(2-methylthio) ether for 1b. 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 performed on a Kieselgel 60, 230–400 mesh as the stationary phase. Elemental analyses were performed on a Perkin-Elmer 2400 apparatus. Optical rotations were measured on a Optical Activity Ltd. AA10 polarimeter. Proton, deuterium, and carbon-13 NMR spectra were recorded on a Bruker AM-400 spectrometer using tetramethylsilane (TMS, 0 ppm) as internal standard. GC analyses were carried out on a Kipp Analytics 8200 instrument with FID detection (25 m x 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.
Optically Pure 3-((π*)-(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-d₄. 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 ¹H and ¹³C NMR spectra, an aliquot of the dioxetane solution was concentrated at 0 °C. During evaporation, cold CDCl₃ or toluene-d₄ 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. ¹H NMR (toluene-d₄, T = 25 °C): δ 5.26, 5.22, 5.20, 5.18 (4 × 1H, s, H₁₁), 3.28, 3.26 (2 × 3H, s, OCH₃), 3.16 (6H, s, OCH₃), 2.7-0.7 (envelope). ¹³C NMR (CDCl₃, T = -20 °C): δ 21 1.28, 21 1.08 (s, 2 × C₁), 109.60, 109.44 (d, 2 × C₁₁), 89.54, 89.51, 89.43, 89.34 (s, 4 × C₃), 56.04, 55.99, 55.69, 55.62 (q, 4 × OCH₃), 47.98, 47.25, 46.91, 46.74 (t, 4 × C₇), 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.