Chiroptical properties of the ketene and diazo chromophores. Part 2.[1] Dissymmetric perturbing influence of α-alkyl substituents on the n–π* transitions in cyclic dialkylketenes and 2-diazoalkanes *vs.* cyclic ketones

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The relationship between the n–π* optical activity and the molecular geometry has been studied for structurally related ketones, ketenes, and diazoalkanes by theoretical and experimental methods. Ketones (**4a**–**e**), ketenes (**5a**–**e**), and diazoalkanes (**6a**–**e**) have a rigid bicyclo[2.2.1]heptane skeleton while ketenes (**7a**,**b**) have the less rigid cyclohexyl framework. Geometries were optimized at the B3LYP/6-31G* level and chiroptical properties were calculated by the CIS/6-31+G* method. The theoretical signs of the n–π* Cotton effects are in agreement with available experimental measurements: ketones **4a**–**e** (literature data), ketenes **5d**,**e** (this work), and diazoalkanes **6d**,**e** (this work). All signs are correctly predicted from additive torsional dependencies of the n–π* optical rotational strengths $\{[R]^{n-\pi^*}(\varphi)$ models$\}$. The models reflect the dissymmetric perturbing influence of α-alkyl substituents while taking some account of the relative strain of the C_α–C_β bonds. Analysis of the chiroptical properties of (2*S*,6*S*)-(2,6-dimethylcyclohexylidene)methanone **7b** by means of the ketene $[R]^{n-\pi^*}(\varphi)$ model and of the *ab initio* calculations show that this compound exists preferentially in the form of a chair conformer, for which a fast degenerate ring conversion is typical.

Introduction

Ketenes[2] and diazoalkanes[3] are very reactive species, which have great potential as reagents for asymmetric synthesis based on stereochemical and stereoelectronic models.[4] For creation of such models, knowledge of the stereochemistry of at least the initial reactants under the reaction conditions is necessary. For optically active compounds, this information can be extracted from CD spectra if a connection of the Cotton effect (CE) signs with the stereochemistry of the molecule has been established.

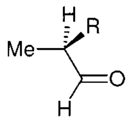
According to their local symmetry (C_{2v}) and the n–π*-like origin of the lowest electron transitions, the ketene and diazo chromophores can be regarded as analogs of the carbonyl chromophore, for which the CE sign of the n–π* transition obeys an octant rule.[5]

In a previous paper,[1] we have studied the perturbing influence of an α-alkyl group on the optically active n–π* transitions in the simple ketenes **2a**–**c** and diazoalkanes **3a**–**c** *versus* the analogous carbonyl compounds—aldehydes **1a**–**c**.

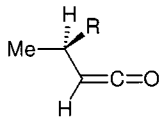
Examination of the dependencies of the optical rotational strengths ($[R]^{n-\pi^*}$) of the n–π* transitions on the dihedral angle C_β–C_α–C=X (φ) in **1a**, **2a**, and **3a** (Fig. 1) showed that the ketenes and diazoalkanes are very similar to each other in their chiroptical properties but are different from the aldehydes. The signs of $[R]^{n-\pi^*}$ of the ketene and diazo chromophores are opposite to the $[R]^{n-\pi^*}$ signs of the carbonyl chromophore over most of the range of the dihedral angle φ. For all three chromophores, the maximum of the perturbing influence of the α-alkyl group is observed at φ = 75–120°, but in this range, the ketene and diazo chromophores exhibit anti-octant behavior.

The torsional functions $[R]^{n-\pi^*}(\varphi)$ shown in Fig. 1 are based on *ab initio* calculations of the rotatory strengths of model systems, propanal **1a**, but-1-en-1-one **2a** and 1-diazopropane **3a**. They could, in principle, be used for the assignment of the absolute configuration and conformational analysis of *α-monosubstituted* ketenes and diazoalkanes.

Here we have studied the possibility of application of the models $[R]^{n-\pi^*}(\varphi)$ to C,C-dialkyl-substituted ketenes and 2-diazoalkanes which are analogs of ketones rather than aldehydes. Such compounds are encountered in synthetic organic chemistry[2,3] much more often than aldehyde analogs like **2a**–**c** and **3a**–**c**. (1*R*)-Bicyclo[2.2.1]heptane derivatives, ketenes **5a**–**e** and diazoalkanes **6a**–**e** were chosen because their relatively rigid skeleton simplifies analysis of the relationship between the n–π* CE sign and the spatial environment of the chromophore. As in the previous work,[1] the corresponding carbonyl compounds **4a**–**e** were also studied. The following methodology was employed. Molecular geometries of **4a**–**e**, **5a**–**e**, and **6a**–**e** were fully optimized at the B3LYP hybrid functional theoretical level and $[R]^{n-\pi^*}$ of these compounds were calculated by a CI-Singles



1a-c



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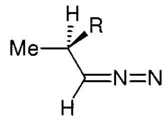
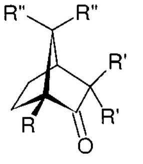
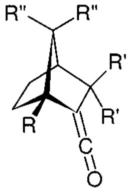


3a-c

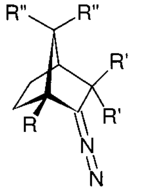
a R = H, **b** R = Me, **c** R = Et



4a-e

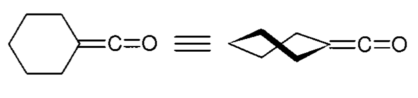


5a-e

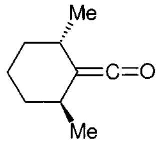


6a-e

a R = R' = R'' = H; **b** R = Me, R' = R'' = H; **c** R = R' = H, R'' = Me; **d** R = R'' = Me, R' = H; **e** R = R' = Me, R'' = H



7a



7b

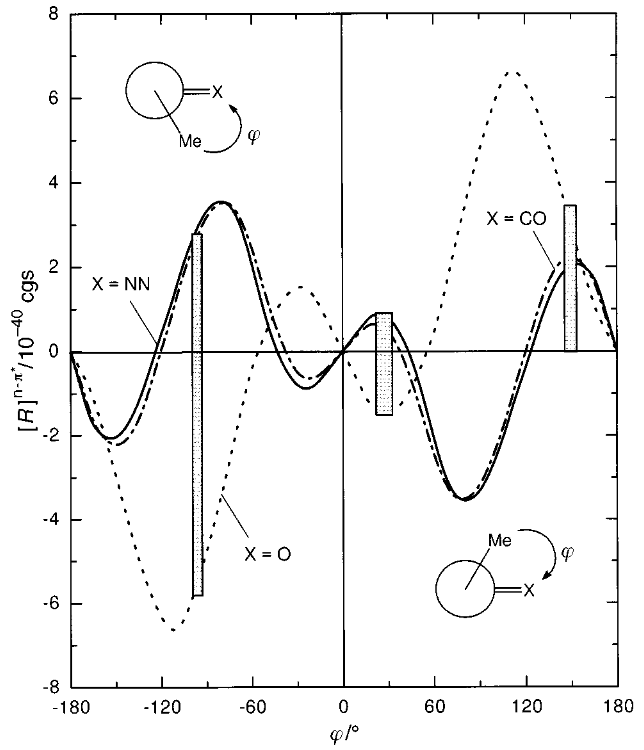


Fig. 1 Carbonyl, ketene and diazoalkane torsional $[R]^{n-\pi^*}(\varphi)$ functions derived with *ab initio* calculations.[1] The gray rectangles stand for rotational strengths estimated from calculated ranges of the C6C1C2X (−100° to −110°), C_{Me}C1C2X (16°–28°) and C7C1C2X dihedral angles (145°–155°) for bicycles **4a**–**e**, **5a**–**e** and **6a**–**e**.

method using the B3LYP geometries. The obtained theoretical data were verified by experimental CD spectra, which have been published[6] for ketones **4a**–**e** and were measured in the present work for ketenes **5d**,**e** and diazoalkanes **6d**,**e**.† Then the calculated dihedral angles φ and the $[R]^{n-\pi^*}(\varphi)$ functions (Fig. 1) were used for estimation of contributions of α-substituents in the n–π* CE of bicycles **4a**–**e**, **5a**–**e**, and **6a**–**e**. Comparison of the predicted n–π* CE signs with the theoretical and experimental ones gave an indication of the applicability of the $[R]^{n-\pi^*}(\varphi)$ models.

The predictive usefulness of the $[R]^{n-\pi^*}(\varphi)$ model for ketenes was also examined for the unstrained conformationally labile ketene (2*S*,6*S*)-(2,6-dimethylcyclohexylidene)methanone (**7b**). For this compound, an experimental CD spectrum was measured and the *ab initio* calculations (geometry optimization, n–π* electronic transition) of the chair and twist conformers were carried out. The contribution of the ring chirality in the n–π* CE of twist-**7b** was estimated from the calculated value of $[R]^{n-\pi^*}$ of the parent (cyclohexylidene)methanone (**7a**) in the twist conformation.

Computational methods

Geometries of the stationary structures of compounds **4a**–**e**, **5a**–**e**, **6a**–**e**, and **7a**,**b** were fully optimized at the B3LYP hybrid density functional theory level with the internal 6-31G* basis set, using procedures implemented in the GAUSSIAN94 system of programs.[7] For conformers of **7b**, harmonic frequency analysis was used to provide an estimate of the zero-point vibrational energy corrections, which were scaled by a factor 0.98.

Chiroptical properties were calculated by single point all-singles configuration interaction (CIS) calculation[7] with the 6-31+G* basis set at the B3LYP geometries. The use of diffuse s and p functions designated by the "+" is desired for a more accurate description of the excited states. The CIS calculation is carried out for a specific number of electronic states, and values of electric and magnetic dipole transition moments are calculated. The magnetic dipole transition moments as produced by the GAUSSIAN programs are for a ground- to excited-state transition and must be reversed in sign when used to calculate optical rotational strengths.

Experimental

CD spectra were recorded on a JASCO J-715 spectropolarimeter, UV spectra on a Varian Cary 219 spectrophotometer. GC-MS data were obtained on a Hewlett-Packard Model 5890 gas chromatograph equipped with an HP 5971A EI mass selective detector. A 12.5 m × 0.2 mm (id) DB-1 column was used. High resolution MS (HRMS) data were obtained on a Kratos MS-80 instrument. NMR spectra were measured on Bruker ACE-200 and AM-400 spectrometers, *J* in Hz, d = doublet, t = triplet, q = quartet; for ^{13}C NMR, q = quaternary, with multiplicities determined from DEPT 90 and 135 sequences. Infrared spectra were measured on a Mattson model 4030 FT instrument.

Preparation of ketenes 5d,e, 7b

The ketenes were prepared in each case from α-bromo carboxylic acid chlorides. The bromine atom stereochemistry was unimportant since in those cases where an epimeric product mixture was used, both epimers reacted to give the ketene.

(1*R*)-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)methanone 5d. *exo*-Bornane-2-carboxylic acid was prepared from (1*R*)-(+)-camphor as previously described.[8] This acid (100 mg, 0.55 mmol) was converted to the acid chloride [δ_H (200 MHz, $CDCl_3$) 0.92 (6 H), 1.13 (3 H), 3.17 (1 H, ddd, *J* 10.5, 6, 2), remaining peaks are overlapped; δ_C 62.6, 46.8, 44.7, 33.5, 29.8, 27.7, 19.1, 18.6, 15.1, 9.0] by treating with four equivalents of thionyl chloride at 62 °C for 1.5 h. This acid chloride was brominated using the method of Harpp *et al.*,[9] employing four equivalents of NBS (380 mg) and 48% aqueous HBr (5 μL) in CCl_4 (10 mL) at reflux for 5 h. The solution was washed with water, saturated aqueous $NaHCO_3$, water, and dried over $MgSO_4$ (the acid chloride is resistant to hydrolysis). Evaporation of the solvent gave 120 mg (79%) of semi-solid α-bromo acid chloride, which by NMR contains a dominant stereoisomer; δ_H (400 MHz, $CDCl_3$) 1.18, 1.00, 0.81 (3 H each), multiplets centered at 3.13 (1 H), 2.38 (1 H), 1.93 (1 H), 1.75 (3H), 1.34 (1 H); δ_C 170.1 (q), 80.4 (q), 56.9 (q), 47.8 (q), 46.7 (CH), 44.2 (CH2), 37.3 (CH2), 26.8 (CH2), 21.2 (Me), 21.0 (Me), 13.3 (Me); HRMS, found: 199.0884. $C_{11}H_{16}OBr^{35}Cl$ − Br requires 199.0890.

Ketene **5d** was prepared *in situ* by treating the above acid chloride (0.013 g, 0.046 mmol) with activated zinc[10] (15 mg) in THF (3 mL) with stirring at 20 °C. GC-MS analysis of the THF solution shows a single peak with a large parent ion, *m*/*z* 164 (M^+, 95%), 149 (60), 121 (100), 107 (35), 93 (65). This solution was immediately used to measure the CD spectrum.

(1*R*)-(1,3,3-Trimethylbicyclo[2.2.1]heptan-2-ylidene)methanone 5e. This ketene has been reported previously,[11] using the

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† Bicyclic ketenes **5d**,**e** and diazoalkenes **6d**,**e** were obtained from optically pure (1*R*)-camphor and (1*R*)-fenchone and can be considered as optically pure compounds because the chiral centers of the bicyclo-[2.2.1]heptane skeleton are not involved in the transformations of the functional groups. Ketene **7b** is the only enantiomerically enriched compound studied in our paper. But the conclusions that were made from the experimental and theoretical studies of this compound are based on the CE signs and not on the CE intensity. It was not necessary to try to synthesize the optically pure ketene **7b** for the purposes of the present paper. An ee of **7b** was not determined, but is should be close to the ee (45%) of the precursor, the corresponding α-bromo acid, because in this case the chiral carbon atoms also are not involved in the conversions of the carboxylic function into the ketene group. The values of [*R*] and Δε were established with this assumption.

acid chloride–triethylamine procedure, but we employed the same general preparative route described for ketene **5d**. An epimeric mixture (*ca.* 3:2) of 1,3,3-trimethyl-2-bromobicyclo-[2.2.1]heptane-2-carboxylic acid chlorides was prepared as an oil (72% yield) from the corresponding acid chloride and NBS, as described for **5d**. δ_H (400 MHz, $CDCl_3$) (a partial spectrum) 1.26, 1.36, 1.37 (Me's of major isomer), 1.35, 1.40, 1.43 (Me's of minor isomer); δ_C 171.6 (q), 168.5 (q), 93.5 (q), 57.6 (q), 50.5 (CH), 50.1 (CH), 45.2 (q), 44.6 (q), 43.5 (CH_2), 40.8 (CH_2), 38.7 (CH_2), 32.8 (CH_2), 29.9 (Me), 27.5 (CH_2), 27.4 (CH_2), 26.2 (Me), 26.1 (Me), 24.0 (Me), 21.6 (Me), 17.7 (Me); HRMS, found: 280.0031. $C_{11}H_{16}O^{79}Br^{35}Cl$ requires 280.0058. Ketene **5e** [ν_{max} (THF)/cm^{-1} 2100 (C=O of ketene); *m*/*z* 164 (M^+, 85%), 149 (80), 135 (80), 121 (100), 107 (40); single peak on GC analysis] was prepared *in situ* as described for **5d** from the α-bromo acid chloride mixture (5.9 mg, 0.021 mmol) and activated zinc (7 mg) in THF (4 mL), 2 h reaction time.

Enantiomerically enriched (2*S*,6*S*)-1-bromo-2,6-dimethylcyclohexane-1-carboxylic acid

Enantiomerically enriched (2*S*,6*S*)-2,6-dimethylcyclohexanone, together with about 30% of the *meso*-isomer was prepared as described.[12] The reported ee is 83%, but since our continuing route involves steps in which some racemization could occur, we deferred an ee determination. The mixture of ketones (2.0 g, 16 mmol) was converted to the corresponding crude methoxymethylene derivative using the general procedure of Corey and Tius.[13] This complex mixture of stereo- and regio-isomers in ether was directly brominated using a two-fold excess of Br_2 (stirring 1 h at 20 °C), washing with 10% aqueous $NaHSO_3$, saturated aqueous $NaHCO_3$, brine. The resulting crude product was then directly oxidized with excess Jones reagent at 5 °C. After 1 h, propan-2-ol was added, followed by water, and the mixture extracted 3× with ether. The ether layer was extracted with 10% aqueous Na_2CO_3 solution, and the latter was washed 2× with ether before neutralization with 6 M HCl. After re-extraction with ether, a crude carboxylic acid product (1.1 g, 30%) was isolated, from which a crystalline material was obtained by flash chromatography (2:1 hexane–ether), mp 139–140 °C (HRMS, found: 155.1072. $C_9H_{15}O_2Br - Br$ requires 155.1081); δ_H (400 MHz, $CDCl_3$) (a partial spectrum) 1.07 (3 H, d, *J* 6, Me) and 1.095 (3 H, d, *J* 6, Me); δ_C 175.1 (q), 76.5 (q), 39.4 (CH), 33.2 (CH), 30.9 (CH_2), 28.2 (CH_2), 20.0 (Me), 19.4 (CH_2) and 16.1 (Me). This product can be assigned to a *trans*-2,6-dimethyl configuration because of non-equivalent Me signals in the ^1H and ^{13}C NMR spectra.

(*S*)-(+)-Methyl mandelate (10.7 mg, 0.064 mmol), the above α-bromo acid (15 mg, 0.064 mmol), DCC (13.4 mg, 0.065 mmol), and DMAP (1 mg) in CH_2Cl_2 (3 mL) were stirred overnight, the mixture filtered, and the solvent removed. Preparative TLC was used to isolate the diastereomeric esters as a single material. In C_6D_6, the benzylic hydrogen at δ 6.19 ppm was resolved in the two diastereomers, $\Delta\delta = 8.6 \times 10^{-3}$ ppm (3.4 Hz), giving an ee of 45%. This assignment was confirmed using racemic α-bromo acid.

Enantiomerically enriched (2*S*,6*S*)-(2,6-dimethylcyclohexylidene)methanone 7b

The above acid (15 mg, 0.064 mmol) was converted to the acid chloride with excess of thionyl chloride, and after evaporation of thionyl chloride, the acid chloride in CH_2Cl_2 (0.5 mL) (CD_2Cl_2 for NMR measurements) was added by a syringe to a solution of $(Ph_3P{=})_2N^+$ $Cr(CO)_4NO^-$ (50 mg, 0.068 mmol) in CH_2Cl_2 contained at −78 °C in a small Schlenk tube.[14] After 10 min, pentane (4 mL) was added and stirring continued for 10 min. This mixture was filtered and the resulting solution was used for the CD measurement. The ketene **7b** was characterized by IR, NMR, and GC-MS; ν_{max} (CH_2Cl_2)/cm^{-1} 2106 (C=O); δ_H (400 MHz, CD_2Cl_2) 2.5, 1.66 and 1.3 (2 H each, m), 1.1 (6 H, d, *J* 7, 2,6-Me_2); δ_C 207.0 (CO), 38.2 (q), 33.3 (CH_2), 25.1 (CH), 20.2 (CH_2), 19.4 (Me); *m*/*z* 138 (M^+, 70%), 123 (100), 95 (75).

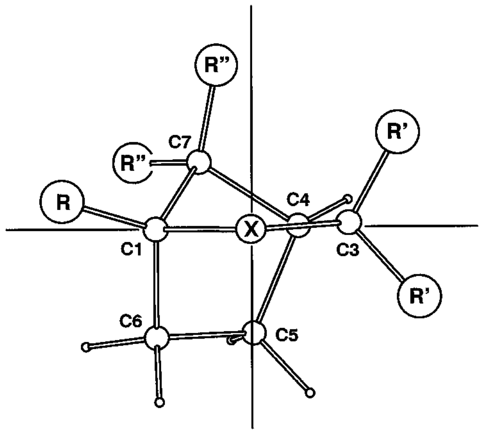


Fig. 2 An octant projection of the molecular framework of bicyclic compounds **4a–e** (X = O), **5a–e** (X = CO), and **6a–e** (X = NN).

Preparation of diazoalkanes 6d,e

(1*R*)-Camphor hydrazone [mp 54–55 °C (lit.,[15] mp 55 °C)] and (1*R*)-fenchone hydrazone [mp 57–58 °C (lit.,[16] mp 54–56 °C)] were prepared according to the procedures of Barton *et al.*[15] and Perera *et al.*,[16] respectively.

A mixture of the hydrazone (0.141 g, 0.85 mmol) and CaO (0.095 g, 1.7 mmol) in heptane (8.5 ml) was stirred at −60 °C and nickel peroxide[17] (0.485 g) was added. The stirring was continued for 45 min at −10 °C and the reaction mixture was centrifuged. The clear red solution was diluted with heptane and used for CD and UV measurement.

(1*R*)-1,7,7-Trimethyl-2-diazobicyclo[2.2.1]heptane (diazocamphane) 6d. λ_{max} (Heptane)/nm (ε/dm^3 mol^{-1} cm^{-1}) 512 (4.7), 235 (16400); λ_{max} (heptane)/nm ($\Delta\varepsilon$/dm^3 mol^{-1} cm^{-1}) 526 (+0.37), 515 (+0.37), 300 (+0.37), 237 (−3.15).

(1*R*)-1,3,3-Trimethyl-2-diazobicyclo[2.2.1]heptane (diazofenchane) 6e. λ_{max} (Heptane)/nm (ε/dm^3 mol^{-1} cm^{-1}) 506 (4.8), 238 (13300) [lit.,[18] 506 (4.2)]; λ_{max} (heptane)/nm ($\Delta\varepsilon$/dm^3 mol^{-1} cm^{-1}) 515 (+0.15), 291sh (−0.17), 244 (−1.65), 218 (−1.54).

Results and discussion

An octant projection of the bicyclo[2.2.1]heptane framework of **4a–e**, **5a–e**, and **6a–e** along the C=X bond is shown in Fig. 2. Groups 1-R, C6H_2, and C7R_2'' lie out of the nodal planes and should be principal contributors to the optical activity. Since all three groups are α-substituents with respect to the C=X chromophore, the relatively rigid skeleton makes these compounds suitable for testing the $[R]^{n-\pi^*}(\varphi)$ models (Fig. 1). The more remote C4 and C5 atoms lie in the nodal planes and therefore the C4H and C5H_2 groups should exert a minor influence at best on the n–π* transition. Contributions of the closer R′ substituents, should almost annihilate each other because these substituents form with the C=X bond dihedral angles which are almost equal in value but opposite in sign.

Ketones 4a–e

The CIS method with the B3LYP optimized geometries predicts properly the n–π* CE signs of the bicyclic ketones **4a–e** (Table 1). Agreement of the theoretical values of $[R]^{n-\pi^*}$ with the experimental ones varies from excellent (norcamphor **4a**, fenchone **4e**) to good (α-fenchocamphorone **4c**, camphor **4d**). The reproduction of the experimental data for the ketones **4a–e** can be considered as a testimony of reliability of the chosen theoretical methods.

Table 1 Calculated parameters[a] for the first (n–π*) electronic transition of (1*R*)-bicyclo[2.2.1]heptan-2-one (**4a**) and its derivatives **4b**–**e** along with selected calculated geometrical parameters[b] and experimental CD spectra[c]

Parameter	**4a**	**4b**	**4c**	**4d**	**4e**
φ(C6C1C2O)	−105.4	−107.1	−107.3	−110.2	−108.2
φ(C7C1C2O)	149.5	149.2	146.1	144.7	148.2
φ(C_{Me}C1C2O)		19.9		15.6	19.0
C2=O	1.211	1.212	1.211	1.212	1.214
oop[d]	0.9	0.2	0.8	0.6	0.2
ΔE	5.06	5.07	5.07	5.09	5.03
λ	245	245	245	244	246
[R]	+1.24	−0.62	+4.03	+2.69	−1.90
f	0.0002	0.0001	0.0002	0.0001	0.0000
Experimental[c]					
λ_{max}	306		304	303	291
$\Delta\varepsilon$	+0.55	−0.25[e]	+1.97	+1.69	−0.76
[R][f]	+1.3		+6.3	+4.5	−2.2

[a] CIS(fc)/6-31+G*//B3LYP/6-31G*; the transition energies (ΔE) are given in eV, the wavelengths (λ) in nm, the rotational strengths ([R]) in cgs × 10^{-40}, the oscillator strengths (f) in cgs. [b] B3LYP/6-31G* optimized geometries; the dihedral angles in degrees, the bond lengths in Å. [c] Ref. 6; measured in cyclohexane; λ_{max} in nm, $\Delta\varepsilon$ in $dm^3\ mol^{-1}\ cm^{-1}$, and [R] in cgs × 10^{-40}; $\Delta\varepsilon = -0.55$, -1.97, and $+0.76$ were measured[6] for **4a**, **4c**, and **4e**, respectively, with the opposite absolute configuration. [d] The out-of-plane angle between the C2=O bond and the plane of three atoms C1C2C3. [e] An estimate[22] from an ORD spectrum.[6b] [f] Ref. 21.

Several earlier attempts to reproduce theoretically the n–π* CE signs for the parent compound **4a**[19–21] and its derivatives[21] were unsuccessful. In each case, the predicted signs were opposite to the experimental ones apparently because of poor-quality wavefunctions and the use of non-optimized molecular geometries. Tokiwa and Kamiya[22] attained agreement with the experiment for **4a**, **4c**–**e** but only after imposing a substantial out-of-plane deformation of the carbonyl group. For example, the experimental sign and value of $[R]^{n-\pi^*}$ of fenchone **4e** could be obtained if the oxygen of the carbonyl group was forcibly distorted out-of-plane by 9.3°. Certainly, the asymmetry of the framework dictates that the carbonyl group in bicyclo[2.2.1]heptanones **4a**–**e** will not be precisely planar. However, in the fully optimized B3LYP structures of **4a**–**e**, this deviation is negligibly small: the calculated out-of-plane (oop) angles are within the narrow range of 0.2–0.9° (Table 1). Nevertheless, the calculated signs and values of $[R]^{n-\pi^*}$ are in perfect agreement with the experimental data.

Kirk[23] has suggested another kind of molecular deformation which can influence $[R]^{n-\pi^*}$ in bicyclo[2.2.1]heptanones. This is a chiral twisting distortion of the skeleton (*M* or *P* helicity).[23] We have analyzed the calculated C1C2C3C4 and C1C6C5C4 dihedral angles for all compounds and do not find any chiral distortion of this kind.

Thus, the α-substituents 1-R, $C6H_2$, and $C7R_2''$ remain the main sources of the dissymmetric perturbation of the n–π* transition in bicyclic ketones **4a**–**e**. (1*R*)-Norcamphor **4a** is the simplest case. In this compound, only the $C6H_2$, and $C7H_2$ groups can make noticeable contributions to the n–π* CE. These contributions have to be opposite each other in sign because the $C6H_2$ and $C7H_2$ groups form the dihedral angles φ with opposite signs (Table 1). Both the *ab initio* calculation and experiment give a positive n–π* CE for **4a** (Table 1). However, from the carbonyl $[R]^{n-\pi^*}(\varphi)$ model (Fig. 1), one might expect a net negative n–π* CE for (1*R*)-**4a** because the contribution to $[R]^{n-\pi^*}$ arising from the C6C1C2O dihedral angle (−105°) should be larger than the value estimated from the C7C1C2O angle (+150°). Apparently, as suggested by Kirk,[5b,23] the strain of the bridging C1–C7 bond in bicyclo[2.2.1]heptanones induces a dominant role for the $C7H_2$ group in the dissymmetric perturbation of the n–π* transition. This role is considerably strengthened in α-fenchocamphorone **4c** because of the two methyl groups at the C7 atom. As a result the positive $[R]^{n-\pi^*}$ is notably increased (Table 1).

In 1-methylnorcamphor **4b**, the methyl group at C1 forms an angle φ of *ca.* 20° and in accordance with the $[R]^{n-\pi^*}(\varphi)$ model (Fig. 1) has to make a negative contribution to the n–π* CE. The combined negative contributions from the 1-methyl and $C6H_2$ groups evidently outweigh the positive contribution of the $C7H_2$ group because **4b** has a small negative n–π* CE. The same situation is apparently realized in fenchone **4e**, which also is characterized by a negative n–π* CE. On the other hand, in the case of camphor **4d**, strengthening of the C7 positive perturbation by the two methyl groups suppresses the total negative perturbation from the 1-methyl and $C6H_2$ groups and provides the positive n–π* CE.

Fig. 3 summarizes the picture of the relative contributions of the α-substituents 1-R (methyl group), $C6H_2$, and $C7R_2''$ to the n–π* CE in bicyclic ketones **4a**–**e** derived with the carbonyl $[R]^{n-\pi^*}(\varphi)$ model (Fig. 1).

Ketenes 5a–e, 7a,b and diazoalkanes 6a–e

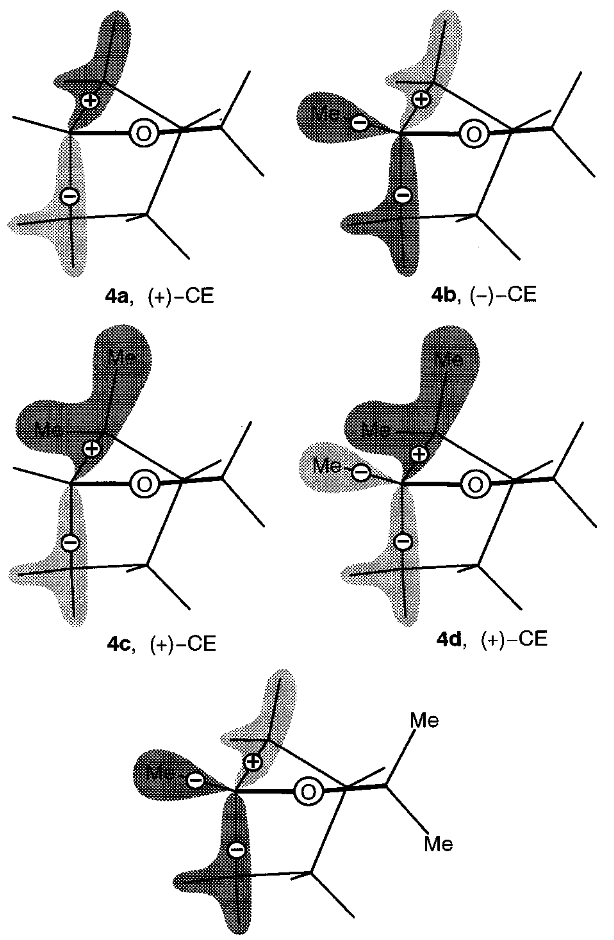
As in the case of ketones **4a**–**e**, conformity between the theoretical and experimental n–π* CE signs is observed for ketenes **5d**,**e** and diazoalkanes **6d**,**e** (Tables 2, 3). The CIS calculations give positive signs of $[R]^{n-\pi^*}$ for all compounds **5a**–**e** and **6a**–**e**. Positive signs are also predicted by the ketene and diazoalkane $[R]^{n-\pi^*}(\varphi)$ models (Fig. 1) based on the dihedral angles φ formed by the 1-Me, $C6H_2$, and $C7R_2''$ groups. According to these models, all three α-substituents fall in the region of positive contributions to the n–π* CE of **5a**–**e** and **6a**–**e** (Figs. 1 and 4). This is especially evident in the case of the 1-methylnorcamphane and fenchane derivatives **5b**, **6b** and **5e**, **6e** which have oppositely signed n–π* CE from their carbonyl analogs **4b**,**e** (Tables 2, 3). The difference is consistent with the behavior of the ketene and diazoalkane $[R]^{n-\pi^*}(\varphi)$ functions, which have signs opposite to the signs of the carbonyl $[R]^{n-\pi^*}(\varphi)$ function within the range of the C_{Me}C1C2X (20–30°) and C6C1C2X dihedral angles (−100 to −108°) but the same sign in the case of C7C1C2X (145–150°). Correspondingly, the dissymmetric perturbations of the n–π* transition from the 1-Me and $C6H_2$ groups in the ketene and diazo chromophores are opposite to those in the carbonyl chromophore.

It is of interest to apply the ketene $[R]^{n-\pi^*}(\varphi)$ model to the case of a non-strained conformationally labile ketene, **7b**, the experimental CD spectrum of which contains a negative n–π* CE ($\lambda_{max} = 373$ nm, $\Delta\varepsilon = -0.07\ dm^3\ mol^{-1}\ cm^{-1}$, $[R] = -0.23$). This compound can exist in the form of two equivalent chair-conformers and two diastereomeric C_2-symmetric twist-conformers.

Table 2 Calculated parameters[a] for the first (n–π*) electronic transition of (1*R*)-(bicyclo[2.2.1]heptan-2-ylidene)methanone (**5a**) and its derivatives **5b–e** along with selected calculated geometrical parameters[b] and experimental CD spectra[c]

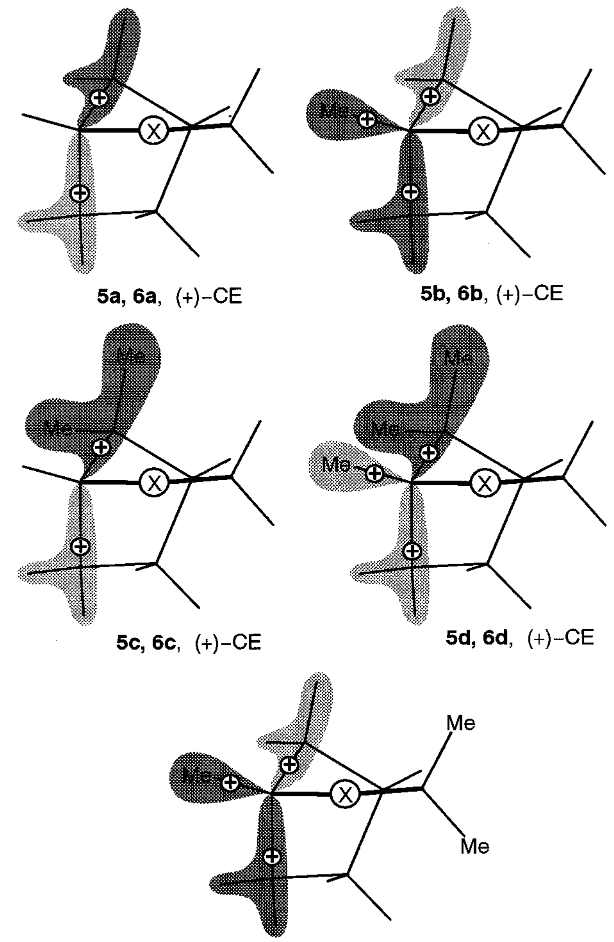
Parameter	5a	5b	5c	5d	5e
$\varphi(C6C1C2C_{exo})$	−108.0	−106.8	−105.5	−103.3	−107.8
$\varphi(C7C1C2C_{exo})$	146.8	149.4	147.7	151.6	148.3
$\varphi(C_{Me}C1C2C_{exo})$		22.6		24.3	21.6
$C2{=}C_{exo}$	1.310	1.310	1.309	1.310	1.310
$C_{exo}{=}O$	1.179	1.179	1.179	1.180	1.180
ΔE	3.64	3.63	3.64	3.63	3.63
λ	340	342	340	342	342
[*R*]	+1.94	+1.23	+2.82	+2.16	+1.05
f	0.0000	0.0000	0.0000	0.0000	0.0000
Experimental[c]					
λ_{max}				398	395
$\Delta\varepsilon$				+0.48	+0.15
[*R*]				+1.64	+0.50

[a,b] See the corresponding footnotes to Table 1. [c] This work; measured in tetrahydrofuran; λ_{max} in nm, $\Delta\varepsilon$ in dm^3 mol^{-1} cm^{-1}, [*R*] in cgs × 10^{-40}.



4a, (+)-CE **4b**, (–)-CE **4c**, (+)-CE **4d**, (+)-CE **4e**, (–)-CE

Fig. 3 A qualitative estimate of relative contributions of the α-substituents to the n–π* CE of the carbonyl chromophore in ketones **4a–e**, derived with the carbonyl $[R]^{n-\pi^*}(\varphi)$ function[1] (Fig. 1). The dark gray fields stand for the major contributions and the light gray ones for the minor contributions.



5a, 6a, (+)-CE **5b, 6b**, (+)-CE **5c, 6c**, (+)-CE **5d, 6d**, (+)-CE **5e, 6e**, (+)-CE

Fig. 4 A qualitative estimate of relative contributions of the α-substituents to the n–π* CE of the ketene/diazo chromophore in ketenes **5a–e** (X = CO) and diazoalkanes **6a–e** (X = NN), derived with the ketene and diazoalkane $[R]^{n-\pi^*}(\varphi)$ functions[1] (Fig. 1). The dark gray fields stand for the major contributions and the light gray ones for the minor contributions.

The optimized structure of ketene **7b** is the chair conformation. Only the axial methyl group should provide a dissymmetric perturbation to the n–π* transition (Fig. 5). The equatorial methyl group lies close to the C2C1C6 plane and the molecular framework is almost symmetrical. Therefore, their influence can be neglected. According to the ketene $[R]^{n-\pi^*}(\varphi)$ function (Fig. 1), the sign and value corresponding to the dihedral angle φ formed by the axial methyl group in chair-**7b** is negative. The same sign is predicted by the CIS calculation for this conformer (Table 4).

In the C_2 symmetric conformers, ee-twist-**7b** and aa-twist-**7b**, the ring chirality is expected to make a substantial contribution to the n–π* CE. Indeed, the CIS calculation of the parent (cyclohexylidene)methanone **7a** in the *S*-twist conformation gives a substantial value of $[R]^{n-\pi^*}$ (Table 4). The calculated

Table 3 Calculated parameters[a] for the first (n–π*) electronic transition of (1*R*)-2-diazobicyclo[2.2.1]heptane (**6a**) and its derivatives **6b**–**e** along with selected calculated geometrical parameters[b] and experimental CD spectra[c]

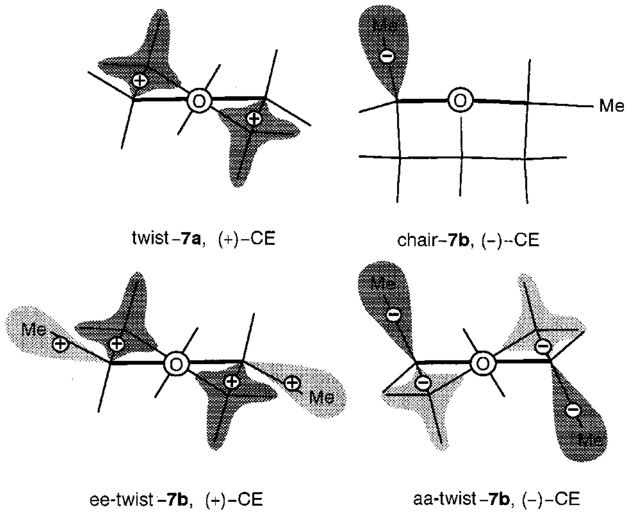
Parameter	**6a**	**6b**	**6c**	**6d**	**6e**
φ(C6C1C2N)	−105.8	−102.7	−100.4	−1005.	−102.8
φ(C7C1C2N)	149.3	154.0	153.1	154.7	153.7
φ(C_{Me}C1C2N)		27.2		27.5	27.1
C2=N	1.284	1.284	1.284	1.284	1.284
N=N	1.156	1.156	1.155	1.156	1.156
ΔE	2.53	2.52	2.53	2.52	2.51
λ	491	493	490	492	494
[*R*]	+1.88	+1.37	+2.72	+2.26	+1.42
f	0.0000	0.0000	0.0000	0.0000	0.0000
Experimental[c]					
λ_{max}				526	515
$\Delta\varepsilon$				+0.37	+0.15
[*R*]				+1.50	+0.58

[a,b] See the corresponding footnotes to Table 1. [c] This work; measured in heptane; λ_{max} in nm, $\Delta\varepsilon$ in $dm^3\ mol^{-1}\ cm^{-1}$, [*R*] in cgs × 10^{-40}.

Table 4 Calculated parameters[a] for the first (n–π*) electronic transition of (*S*)-twist-(cyclohexylidene)methanone (**7a**) and (2*S*,6*S*)-(2,6-dimethylcyclohexylidene)methanone (**7b**) along with selected geometrical parameters[b] and relative energies[c] of the chair, ee-twist, and aa-twist conformers of **7b**

Parameter	**7a**	chair-**7b**	ee-twist-**7b**	aa-twist-**7b**
φ(C3C2C1C_{exo})	150.8	−128.1	151.3	−153.1
φ(C5C6C1C_{exo})	150.8	127.2	151.3	−153.1
φ(C_{Me}C2C1C_{exo})		106.9	27.2	81.5
φ(C_{Me}C6C1C_{exo})		2.2	27.2	81.5
C1=C_{exo}	1.314	1.315	1.316	1.315
C_{exo}=O	1.178	1.178	1.178	1.178
ΔE	3.75	3.88	3.78	3.78
λ	331	320	328	328
[*R*]	+4.98	−0.71		−4.37
f	0.0001	0.0000	0.0000	0.0000
E_{rel}		0.0	15.5	27.6

[a,b] See the corresponding footnotes to Table 1. [c] In kJ mol^{-1}.



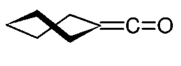
twist-**7a**, (+)-CE

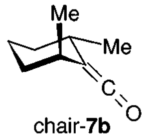
chair-**7b**, (−)-CE

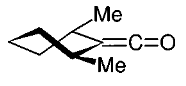
ee-twist-**7b**, (+)-CE

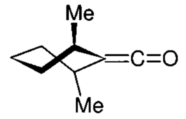
aa-twist-**7b**, (−)-CE

Fig. 5 A qualitative estimate of relative contributions of the α-substituents to the n–π* CE of the ketene chromophore in ketenes, **7a**,**b**, derived with the ketene $[R]^{n-\pi^*}(\varphi)$ function[1] (Fig. 1). The dark gray fields stand for the major contributions and the light gray ones for the minor contributions.


S-twist-**7a**

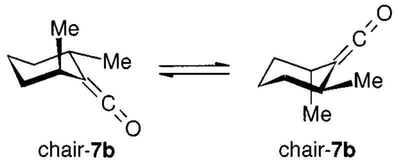

chair-**7b**


ee-twist-**7b**


aa-twist-**7b**

sign of $[R]^{n-\pi^*}$ for **7a** agrees with the sign (Fig. 5) predicted by the ketene $[R]^{n-\pi^*}(\varphi)$ model (Fig. 1) from the dihedral angles φ (+151°). Conformers ee-twist-**7b** and aa-twist-**7b** possess opposite ring chiralities. This chirality is left-handed in the diequatorial isomer and right-handed in the diaxial one. On the base of the data on **7a** and the ketene $[R]^{n-\pi^*}(\varphi)$ model, one can assume that both the left-handed ring chirality and the equatorial methyl groups in ee-twist-**7b** will bear a positive perturbation to the n–π* transition and the right-handed ring chirality together with the axial methyl groups in aa-twist-**7b** will bear a negative perturbation (Fig. 5). Therefore, the diequatorial isomer has to have a positive n–π* CE and the diaxial isomer a negative one. This conclusion is supported by the calculated data (Table 4).

The negative experimental n–π* CE of **7b** presupposes a preferential population of conformers, chair-**7b** and/or aa-twist-**7b**, with negative $[R]^{n-\pi^*}$ in the equilibrium mixture. According to the B3LYP calculations, the latter isomer is 15.5 kJ mol^{-1} less stable than the former one (Table 4). Hence one can assume that ketene **7b** exists mainly in the form of chair-**7b**. Apparently, the



Scheme 1

degenerate chair interconversion (Scheme 1) is facile because the methyl groups and the ring CH_2 (CH) groups are observed to be magnetically equivalent in ^1H and ^{13}C NMR spectra of the ketene **7b** even at low temperatures (−40 °C).

Summary

The Cotton effect signs of the n–π* electronic transitions in ketenes, diazoalkanes, and carbonyl compounds are reliably reproduced by the CIS/6-31+G* method for calculations of the singlet excited states, using B3LYP/6-31G* optimized geometries of the ground states. The previously derived[1] torsional dependencies of the n–π* rotational strengths on the dissymmetric perturbing influence of α-alkyl substituents work well for mono- and bicyclic dialkylsubstituted ketenes, 2-diazoalkanes, and ketones, and can be used for stereochemical analysis of these classes of organic compounds on the base of their CD spectra. In the case of derivatives with a strained molecular framework, it is necessary to take into account the relative strain of the C_α–C_β bonds of the skeleton. The more strained bond makes a greater contribution to the Cotton effect of the n–π* transition in the absence of additional substitution.

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