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Diastereoselective Synthesis and Conformation of *trans*-2,3-Dibenzoyl-1,4-dithiacycloheptane

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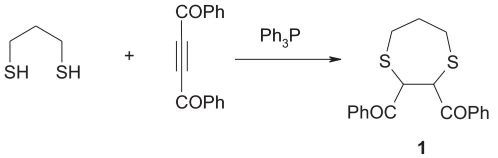
The reaction of dibenzoylacetylene and propane-1,3-dithiol in the presence of triphenylphosphine leads to diastereoselective synthesis of the mesocyclic dithioether *trans*-2,3-dibenzoyl-1,4-dithiacycloheptane in 70 % yield. The results of *ab initio* calculations at HF/6-31G* level show that the *trans* isomer is 31.3 kJ mol^{-1} more stable than the *cis* geometry.

INTRUDUCTION

Mesocyclic polythioethers have been employed as bidentate ligands in coordination chemistry.[1] The gas phase conformation of 1,4-dithiacycloheptane is deduced from the correlation of the observed helium I photoelectron spectra with semi-empirical MO calculations.[2] The axial symmetrical twist-chair conformation in the gas phase is the same as that observed in the solid state.[3] In continuation of our interest in sulfur-containing heterocycles,[4] we wish to report a new and operationally convenient approach to the diastereoselective synthesis of *trans*-2,3-dibenzoyl-1,4-dithiacycloheptane (**1**) based on the reaction between propane-1,3-dithiol and dibenzoylacetylene in the presence of triphenylphosphine (Ph_3P) (Scheme 1). The results of *ab initio* calculations at the HF/6-31G* level are reported for the most stable conformation of *trans*-**1** and *cis*-**1**.



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Scheme 1.

RESULTS AND DISCUSSION

The reaction of dibenzoylacetylene with propane-1,3-dithiol in the presence of Ph_3P was carried out in CH_2Cl_2 at 0 °C. The white powder separated from the reaction mixture was identified as *trans*-2,3-dibenzoyl-1,4-dithiacycloheptane (**1**). The structure of **1** was deduced from its elemental analyses and IR, ^1H NMR and ^{13}C NMR spectral data. The mass spectrum of **1** displayed a molecular ion peak at m/z = 342.

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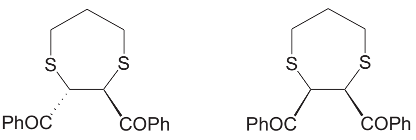
The ^1H NMR spectrum of **1** exhibited a quintet (for C–CH_2–C group, $\delta = 2.30$ ppm), an ABX_2 system (for the two –SCH_2– groups, $\delta = 3.00$ ppm), and a singlet (for methine protons, $\delta = 5.20$ ppm). The phenyl residues gave rise to characteristic signals in the aromatic region ($\delta = 7.48$–8.01 ppm) of the spectrum. The proton decoupled ^{13}C NMR spectrum of **1** showed eight distinct resonances, as expected for the 2,3-dibenzoyl-1,4-dithiacycloheptane structure. Partial assignment of these resonances is given in the Experimental section. The structural assignment of compound **1** made on the basis of the ^1H NMR and ^{13}C NMR spectra was supported by its IR spectrum, which in the carbonyl region displayed two distinct absorption bands for the symmetric and antisymmetric stretchings of the two C=O groups.

When the reaction between dibenzoylacetylene and propan-1,3-dithiol was carried out in the EtOH/EtONa solution,[5] a complex reaction mixture was obtained. The ^1H NMR spectrum of this mixture was consistent with the presence of about 10 % of **1**. No further work was done on this mixture.

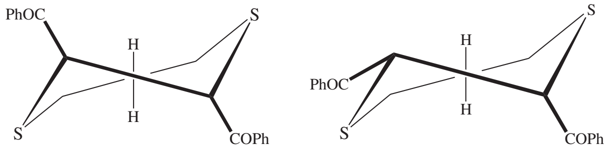


trans-**1** *cis*-**1**

Scheme 2.

The stereochemical relationship between the two benzoyl groups in **1** (see Scheme 2) was established by selective irradiation of the –SCH_2– protons. Thus, the multiplet arising from the C–CH_2–C protons appears as a singlet upon irradiation of the –SCH_2– multiplet. This result is consistent with the presence of the C_2-symmetric *trans*-isomer. If the two benzoyl groups were *cis*, then an AB quartet would be expected for the diastereotopic C–CH_2–C protons upon irradiation of the –SCH_2– multiplet.

The *trans* geometry of **1** is corroborated by the results of *ab initio* calculations at the HF/6-31G* level. The results of these calculations are shown in Table I and Figure 1. The X-ray structural parameters[3] obtained for 1,4-dithiacycloheptane[3] are also given in Table I. The most stable conformation for both *cis*-**1** and *trans*-**1** is the twist-chair (TC) geometry, similar to that obtained for 1,4-dithiacycloheptane. The calculated strain energy for the TC conformation of *trans*-**1** is 31.3 kJ mol^{-1} lower than that calculated for the *cis* isomer.



TC (*trans*-**1**), C_2
0.0 kJ mol^{-1}

TC (*cis*-**1**), C_1
31.3 kJ mol^{-1}

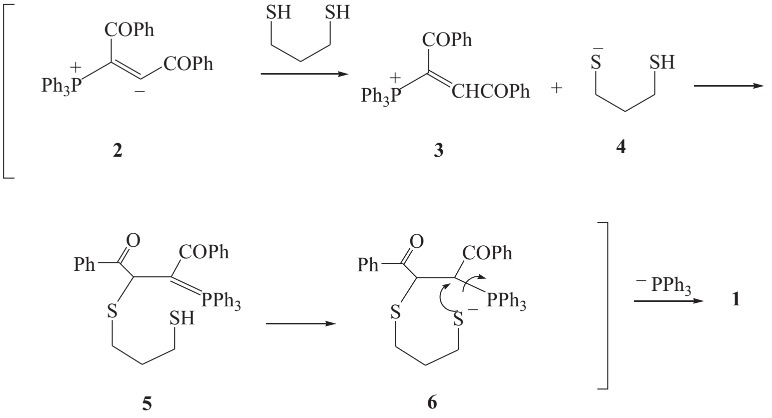
Figure 1. Energy of the TC (*trans*-**1**) conformation with respect to the TC (*cis*-**1**) geometry from HF/6-31G* calculations.

Table I. Calculated heats of formation: total and zero-point vibrational energies[(a)], relative energy[(b)] and structural parameters[(c)] for TC conformation of *trans*- and *cis*-2,3-dibenzoyl-1,4-dithiepane (**1**)

	TC (*trans*-**1**), C_2	TC (*cis*-**1**), C_1
HF/6-31G* / hartree	–1674.735618	–1674.722915
ZPE / hartree	0.155857	0.155012
E_{rel} / KJ mol^{-1}	0.0	31.32
Bond lengths / Å		
S–C_2	1.848 (1.801)[(d)]	1.828
C_2–C_3	1.529 (1.829)	1.542
C_3–S	1.848 (1.811)	1.831
S–C_5	1.822 (1.818)	1.822
C_5–C_6	1.519 (1.530)	1.528
C_6–C_7	1.519 (1.529)	1.530
C_7–S	1.822 (1.815)	1.819
Bond angles / deg		
S–C2–C3	113.3 (116.7)	120.3
C_2–C_3–S	113.3 (115.7)	115.6
C_3–S–C_5	103.0 (101.8)	104.1
S–C_5–C_6	115.6 (115.9)	115.1
C_5–C_6–C_7	115.2 (115.8)	115.5
C_6–C_7–S	115.63 (115.1)	115.2
C_7–S–C_2	103.0 (101.0)	100.3
Dihedral angles / deg		
S–C_2–C_3–S	66.8 (65.7)	57.9
C_2–C_3–S–C_5	–76.2 (–73.1)	–65.3
C_3–S–C_5–C_6	93.4 (91.2)	92.5
S–C_5–C_6–C_7	–44.5 (–47.4)	–49.0
C_5–C_6–C_7–S	–44.5 (–44.2)	–44.8
C_6–C_7–S–C_1	93.4 (92.9)	92.8
C_7–S–C_2–C_3	–76.2 (–74.1)	–72.3
CO–C_2–C_3–CO	–57.0	–63.4
H–C_2–C_3–H	–175.6	–50.9

[(a)] Zero-point vibrational energy is scaled by a factor of 0.9135 to eliminate known systematic errors in calculations.
[(b)] Including zero-point energy.
[(c)] Experimental values are given in parentheses.
[(d)] X-ray structure analysis, Ref. 3.

Although the mechanism of the reaction between Ph_3P and dibenzoylacetylene in the presence of propane-1,3-dithiol has not yet been established in an experimental



Scheme 3.

manner, a possible explanation is proposed in Scheme 3. On the basis of the well established chemistry of trivalent phosphorous nucleophiles,[6–8] it is reasonable to assume that compound **1** results from the initial addition of triphenylphosphine to dibenzoylacetylene and subsequent protonation of the reactive 1:1 adduct by propan-1,3-dithiol. Then, the conjugate base of the SH-acid attacks the positively charged ion. The product is presumably produced by elimination of Ph_3P.

In conclusion, we have found that the reaction of propane-1,3-dithiol with dibenzoylacetylene in the presence of Ph_3P leads to stereoselective synthesis of the mesocyclic dithioether *trans*-2,3-dibenzoyl-1,4-dithiacycloheptane in moderate yield. According to *ab initio* calculations at the HF/6-31G* level, the twist-chair conformation of *trans*-**1** is 31.3 kJ mol^{-1} more stable than the twist-chair geometry of the *cis*-isomer.

EXPERIMENTAL

Triphenylphosphine and propane-1,3-dithiol were obtained from Fluka and were used without further purification. Dibenzoylacetylene was prepared by a known method.[9,10] Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C and H were performed using a Leco 600 instrument. The NMR spectra were recorded at 300 (^{1}H) and 75.5 (^{13}C) MHz on a Brucker 300-AVANCE FT-NMR instrument with $CDCl_3$ as solvent. Chemical shifts (δ) are reported relative to TMS as the internal standard. IR spectra were recorded on a Bomem MB-100 IR spectrometer. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Analytical thin layer chromatography was performed on glass plates prepared with silica gel. Column chromatography was performed using 230–400 mesh Merck silica gel and mixtures of hexane and EtOAc were used as eluents.

Preparation of trans-*2,3-Dibenzoyl-1,4-dithiacycloheptane (1)*

To a stirred solution of Ph_3P (0.52 g, 2 mmol) and propane-1,3-dithiol (0.22 g, 2 mmol) in CH_2Cl_2 (15 mL), a mixture of dibenzoylacetylene (0.45 g, 2 mmol) in CH_2Cl_2 (15 mL) was added dropwise for 5 min at –10 °C. The reaction mixture was then allowed to warm up to 0 °C and was stirred for 14 h. The solvent was removed under reduced pressure and the viscous residue was purified by preparative TLC on silica gel (Merck silica gel DC-Fertigplatten 60/Kieselgur F_{254}) 20×20 cm plates using n-hexane-EtOAc (1:1) as eluent. Zones were detected by quenching of indicator fluorescence upon exposure to 366 nm UV light. The product was obtained by extraction of silica gel with CH_2Cl_2 to produce compound **1** as white powder, yield: 0.47 g (70 %), m.p. 136–138 °C. IR(KBr) ν_{max}/cm^{-1}: 1673 and 1652 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 2.30 (dd, 2 H, $^3J_{HH}$ = 6.3 Hz, $^3J_{HH}$ = 7.4 Hz, CH_2), 3.00 (ABX_2 system, 4 H, J_{AB} = 18.0 Hz, $^3J_{AX}$ = 6.3 Hz, $^3J_{BX}$ = 7.4 Hz, $\Delta\upsilon_{AB}$ = 43 Hz, 2 S–CH_2), 5.25 (2 H, s, 2 CH), 7.48 (t, 2 H, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.51 (t, 1 H, $^3J_{HH}$ = 7.5 Hz, CH), 8.01 (d, 2 H, $^3J_{HH}$ = 7.5 Hz, 2 CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ/ppm: 32.7 (CH_2), 35.3 (2 CH_2), 52.8 (2 CH), 129.5 (2 CH), 129.9 (2 CH), 133.9 (CH), 136.1 (C), 198.2 (2 C=O). MS (EI, 70 eV) *m/z*: = 342 (M^+, 4 %), 325 (3), 237 (26). 105 (100). 77 (92). 51 (46).

Anal. Calcd. for $C_{19}H_{18}S_2O_2$ (M_r = 342.2): C, 66.68; H, 5.30. Found: C, 66.72; H, 5.33.

CALCULATIONS

Ab initio molecular orbital calculations were carried out using the GAUSSIAN 98 program.[1] Geometries for all structures were fully optimized by means of analytical energy gradients using the Berny optimizer with no geometrical constraints.[12] The restricted Hartree-Fock calculations with the split-valence 6-31G* basis set, which include a set of d-type polarization functions on all non-hydrogen atoms, were used in the calculations.[13]

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SAŽETAK

Dijastereoselektivna sinteza i konformacija *trans*-2,3-dibenzoil-1,4-ditiacikloheptana

Issa Yavari, Rahebeh Amiri i Mina Haghdadi

Dijastereoselektivnom reakcijom dibenzoilacetilena i propan-1,3-ditiola uz prisutnost trifenilfosfina dobiven je u 70 postotnom iskorištenju mezociklički ditioeter *trans*-2,3-dibenzoil-1,4-ditiacikloheptan. Uporabom *ab initio* HF/6-31G* računske metode izračunato je da je *trans*-izomer za 31,3 kJ mol^{-1} stabilniji od *cis*-izomera.