Short Synthesis of a New Cyclopentene-1,3-dione Derivative Isolated from *Piper carniconnectivum*

Luiz C. Dias*, Simone B. Shimokomaki and Robson T. Shiota

Instituto de Química, Universidade Estadual de Campinas, CP 6154, 13083-970 Campinas - SP, Brazil

The total synthesis of cyclopentene-1,3-dione (1), a new natural cyclopentenedione derivative isolated from the roots of *Piper carniconnectivum*, is described in 8 steps and 11% overall yield from 2-acetylfuran, giving a 57:43 mixture of the two possible geometric isomers 1a and 1b.

Keywords: aldol reaction, allylic alcohol oxidation, cyclopentenedione derivative, *Piper carniconnectivum*

Introduction

The cyclopentenedione (1a/1b) (Figure 1) is a new natural cyclopentenedione derivative that was isolated recently by Braz-Filho and coworkers\(^1\) from the roots of a specimen of *Piper carniconnectivum*, collected in Porto Velho, Rondônia, in the northern part of Brazil. This specimen belongs to the tropical *Piperaceae* family, that comprises many important plants, very useful in folk medicine as bioproducers of essential oils.\(^2,3\) The structure of cyclopentenedione derivative (1) was established by spectroscopic data, mainly 1D and 2D NMR as well as by Electron Impact Mass Spectrometry (EI MS).\(^1\) According to the authors,\(^1\) the isolated cyclopentenedione derivative may have structure 1a or 1b or even exist as an equilibrium mixture between these two enol forms showing average \(^1\)H and \(^13\)C NMR spectra due to a proposed rapid interconversion between 1a and 1b.

![Figure 1. Enol forms of cyclopentenedione derivative (1).](image)

In connection with our interest in the total synthesis of natural products isolated from Brazilian sources, we became interested in the synthesis of the cyclopentenedione derivative (1). An efficient and flexible synthesis of this very interesting natural product is important to provide further material for biological studies, along with access to novel analogues, as well as to prove the assignment given by Braz-Filho and coworkers.\(^1\) The approach described here to the cyclopentenedione derivative (1) might give access to additional derivatives with potential relevance to biological studies.

Results and Discussion

Theoretical calculations

At the beginning, we were intrigued by the proposed equilibrium between enol forms 1a and 1b, and by the fact that this rapid equilibrium would lead to average \(^1\)H and \(^13\)C NMR spectra. At first we decided to evaluate the thermodynamic stability of enol forms 1a-d when compared to triketone 1e (Scheme 1). The heat of formation (\(\Delta H_f\)) obtained by AM1 semiempirical calculations (using PC Spartan Plus) of compound 1e was compared with those of possible enols 1a-d and is outlined in Scheme 1.

The calculated heats of formation confirmed that the enol forms 1a and 1b, and not the enol forms 1c and 1d, were the thermodynamically favorable structures. We believe that the antiaromatic electronic structure of the
cycles in enol forms 1c and 1d explains the absence of these tautomers in solution, as proposed by Braz-Filho and coworkers.\(^1\) The difference in the heats of formation for enol forms 1a and 1b is very small. We first suspected of structure 1a as being the natural product in view of the larger calculated dipole moment for 1b (1.51 D) in comparison with that of 1a (0.85 D). It is also interesting to observe that the most stable enol forms 1a (C9-C10, Z) and 1b (C9-C10, E) are more stable than triketone 1e by 3.69 and 3.77 kcal mol\(^{-1}\), respectively.\(^4\) We believe that these differences are too large to allow a rapid interconversion between enol forms 1a (Z isomer) and 1b (E isomer) at room temperature. Based on these results we believed that the geometric C9-C10 isomers 1a and 1b should not be present in a rapid equilibrium, the \(^1\)H and \(^13\)C NMR spectra should not be an average of these two forms, and that Braz-Filho and coworkers had isolated one of the two isomeric compounds, 1a or 1b.

**Synthetic results**

Our approach to cyclopentenedione derivative (1) started with the preparation of furylmethylcarbinol (3) by the reduction of commercially available 2-acetylfuran (2) with NaBH\(_4\) (Scheme 2).\(^6\) Compound 3 was isolated in 98% yield and transformed into 4-hydroxy-5-methylcyclopenten-2-one (4) in 90% yield after treatment with ZnCl\(_2\)-HCl (pH = 6) under reflux in dioxane-H\(_2\)O for 48 h.\(^6\) Upon treatment of 4-hydroxy-5-methylcyclopenten-2-one (4) with phosphate buffer (pH = 8.0) in refluxing dioxane for 24 h, 4-hydroxy-2-methylcyclopenten-2-one (5) was obtained in 65% yield.\(^7\) By using this strategy we were able to prepare up to gram quantities of hydroxyketone 5.

Diketone 6 was obtained in almost quantitative yield by the smooth oxidation of hydroxyketone 5 with MnO\(_2\) (Scheme 3).\(^8,9\) At this point, all that remained was to carry out the necessary acylation coupling. It was with some gratification that we observed that the reaction between lithium enolate of diketone 6 and cinnamic anhydride 7 gave a 57.43 mixture of cyclopentenediones 1a/1b in 22% yield, after purification by flash column chromatography, together with starting material and by-products arising from O-acylation (Scheme 3).

In order to try to improve the yields for formation of 1a/1b, we tested a new synthetic route (Scheme 4). Protection of the OH-functionality in 5 with TESCl and imidazole at room temperature gave ketone 8 in 85% yield. Treatment of 8 with LDA in THF at \(-78\) °C, followed by slow addition of cinnamaldehyde, gave aldol adduct 9 as a mixture of diastereoisomers. Oxidation of the OH-function at C9 in allylic alcohol 9 under standard Swern conditions followed by removal of the TES protecting group with TBAF in THF led to diol 10 in 60% overall yield. The last step involved treatment of diol 10 under standard Swern oxidation conditions, to give a 59:41 mixture of 1a/1b in 79% yield.\(^11\)

The spectroscopic and physical data [\(^1\)H and \(^13\)C NMR, IR, MP (Table 1)] for the major component of the 59:41
mixture present in the synthetic material were identical in all respects with the published data for natural cyclopentenedione derivative. In the synthetic material, we were able to observe additional new signals corresponding to the possible geometric isomer.1

In fact, both isomers, 1a (C9-C10, E) and 1b (C9-C10, Z) revealed very similar 1H and 13C NMR spectra. This result is in agreement with the small difference in the heats of formation for enol forms 1a and 1b.

We observed two doublets for the CH₃ groups at C12, at 2.12 and 2.11 ppm, respectively, both with coupling constants equal to 1.6 Hz (Figure 2). The doublet in 2.12 corresponds to the methyl group found in the natural product, as described by Braz-Filho and coworkers.1

Other noteworthy observations from this spectrum are two quartets at 6.70 and 6.61 ppm, with coupling constants equal to 1.6 Hz (Figure 3). The quartet at 6.70 ppm corresponds to the quartet found in the natural product.

We were also able to observe two different broad signals at 12.11 and 11.99 ppm, corresponding to the hydrogens

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* A signal marked with (*) corresponds to the minor isomer.

Table 1. Comparison of ¹H and ¹³C NMR data (CDCl₃) for synthetic and authentic cyclopentenedione 1a/1b¹

Figure 2. Expansion of the methyl resonances (δ 2.11 and 2.12) for synthetic 1a/1b.

Figure 3. Expansion of the vinylic resonances (δ 6.70 and 6.61) for synthetic 1a/1b.
bonded to the OH in enol forms 1a and 1b (Figure 4). These new signals at 2.11, 6.61 and 112.99 ppm are strong evidence in favor of the presence of the other geometric isomer. The chemical shift for the signals at 11.99 and 12.11 ppm do not change with dilution or with temperature.

![Figure 4. Expansion of the OH resonance (δ 11.99 and 12.11) for synthetic 1a/1b.](image)

Looking carefully at the 1H NMR spectra of compound 1a/1b, kindly sent by Braz-Filho and coworkers, we were able to confirm that exactly the same signals at 2.11 and 6.61 ppm, as very small peaks, are present in the original spectra of the natural product (Figures 5 and 6). This lead to the conclusion that the natural product was isolated as a >95:5 mixture of the two isomers.

![Figure 5. Expansion of the methyl resonance (δ 2.11 and 2.12) for natural 1a/1b.](image)

We have acquired 1H and 13C NMR spectra of a CDCl₃ solution of a 57:43 mixture of 1a/1b at 25 °C as well as at 60 °C and observed that these spectra did not change with time, with the NMR being identical even after 30 days in the NMR tube. Acquisition of the 1H NMR spectra in DMF-d6 at room temperature and at 140 °C proved to be very interesting. At 25 °C, we have observed two signals related to the vinylic hydrogens of both isomers at 6.9 and 7.2 ppm. At 140 °C, these signals coalesce to a single broad signal at 7.0 ppm, showing that only at high temperature we can observe an average NMR spectrum.

On the other hand, we have tried to separate the two isomers in order to get a crystal of one of them to carry out an X-ray crystallographic analysis but, unfortunately, that was not possible, since they are not separable by flash column chromatography. However, we were able to isolate a fraction enriched with one isomer in a 34:66 ratio. This is shown in Figures 7-9 with expansions taken from a sample of this mixture.

![Figure 6. Expansion of the vinylic resonance (δ 6.70 and 6.61) for natural 1a/1b.](image)

We have acquired the 1H NMR of this sample again after two days and have observed that this changed to the same 57:33 ratios observed before (Figures 2 to 4). In acidic CDCl₃, an equilibrium exists between these enol forms and this equilibrium favors the natural product. Based on these results, we strongly believe that Braz-Filho and coworkers isolated one isomer, and that the minor signals in their NMR spectra correspond to the unnatural isomer, and that the NMR in acidic CDCl₃ shows the other isomer being formed in small amounts. We believe that even in the case of the natural product a long exposition in the NMR tube with CDCl₃ as solvent would lead to the same 57:33 equilibrium ratio.
The correct structure for the natural product was confirmed as being 1a by the heteronuclear long-range coupling (\(J_{\text{CH}}\) n = 2,3,4) obtained by HMBC experiments in CDCl\(_3\) as solvent. Heteronuclear long-range coupling of C11 (\(\delta_C 201.3\)) with H13 (\(\delta_H 6.70, J_{\text{CH}} 3\)) and H15 (\(\delta_H 2.12, J_{\text{CH}} 3\)) for 1a, together with the long-range coupling of C14 (\(\delta_C 191.8\)) with H13 (\(\delta_H 6.70, J_{\text{CH}} 2\)) and H15 (\(\delta_H 2.12, J_{\text{CH}} 3\)) for 1a, unambiguously established the correct structure as being 1a (Figure 10).

Conclusions

Our approach required 8 steps from commercially available 2-acetylfuran and produced the desired product in 11% overall yield. The results of extensive application of 2D NMR spectral techniques were used to determine the correct structure for the natural product as being 1a. This synthesis confirms the assignment of Braz-Filho and coworkers\(^1\) and, as a result, the route to cyclopentenedione derivative (1) presented here is, in principle, readily applicable for the preparation of additional analogs with potential relevance to biological studies.\(^{1,2}\) Studies are underway in order to further improve the synthesis of cyclopentenedione (1) and the results will be described in due course.

Experimetal

All reactions were carried out under an atmosphere of argon or nitrogen in flame-dried glassware with magnetic stirring. Dichloromethane was distilled from CaH\(_2\), THF, diethyl ether and toluene were distilled from sodium/benzophenone ketyl. Cynnamaldehyde was distilled immediately prior to use. iPrOH was distilled from Mg(PrO)\(_2\). TLC plates were obtained of silica gel 60 and GF (5-40\(\mu\)m thickness) and visualization was accomplished with either a UV lamp or I\(_2\) staining. Chromatography on silica-gel (Aldrich, 230-400 mesh) was performed using a forced-flow of the indicated solvent system (flash chromatography). Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain or phosphomolybdic acid followed by heating or I\(_2\) staining.

1H NMR spectra were recorded on either a Varian Gemini 300 (300 MHz) or a Varian Inova 500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl\(_3\) at 7.26 ppm or C\(_6\)D\(_6\) at 7.15 ppm) unless otherwise indicated. Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, st = sextet, ap t = apparent triplet, m = multiplet, b = broad, br s = broad singlet, br d = broad
doublet, dd = doublet of doublets, coupling constant(s) in Hz; integration. Proton-decoupled $^{13}$C NMR spectra were recorded on either a Varian Gemini 300 (75 MHz) or Bruker AC 300/P (75 MHz) spectrometers and are recorded in ppm using solvent as an internal standard (CDCl$_3$ at 77.0 ppm or CD$_2$D at 128 ppm) unless otherwise indicated. Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. Mass spectra were recorded on GC/MS HP-5988-A.

2-Furylmethylcarbinol (3)

Procedure 1. Furan (2.7 mL, 37 mmol) was measured into a dry round-bottom flask equipped with a magnetic stirrer and containing freshly distilled ether (20 mL) under argon atmosphere. The flask was cooled to –25 °C, and n-BuLi in hexanes (7.9 mL, 0.5 mol L$^{-1}$, 18 mmol) was added dropwise from a syringe. The flask was allowed to warm to 0 °C, the cold bath was removed, and the reaction mixture was stirred 4 h at room temperature. The reaction mixture was cooled back to –25 °C, and acetaldehyde (4 mL, 73 mmol) was added dropwise via syringe. After being allowed to warm to room temperature over a period of 3 h, the reaction mixture was neutralized with cold saturated NH$_4$Cl solution (5 mL). The organic layer was separated, and aqueous layer was extracted with ether (2 x 5 mL). The combined organic phase was dried (MgSO$_4$) and passed through a silica gel plug to remove polar impurities, after which TLC analysis showed the presence of a single component. The solution was concentrated and dried in vacuo to give 1.7 g (84%) of 2-furylmethylcarbinol (3) as an orange liquid (used without further purification).

Procedure 2. To a solution of 2-acetyl furan (2) (1.0 g, 9.09 mmol) in ethanol (20 mL), at 0 °C, was slowly added NaBH$_4$ (0.19 g, 5.0 mmol). The reaction mixture was let to stir at room temperature for 2 h and the solvent was removed under reduced pressure. After filtration in a plug of silica, 2-furylmethylcarbinol (3) (1.036 g, 98%) was isolated as an orange liquid (used without further purification). R$_f$ 0.25 (20% EtOAc/hexanes); IR (film) $\nu_{\text{max}}$/cm$^{-1}$: 3352, 2982, 2927, 1703, 1684, 1380, 1251; $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.20 (m, 1H), 4.94 (m, 1H), 2.80 (dd, J 18.7, 6.0 Hz, 1H), 2.31 (br s, 1H), 2.30 (dd, J 18.7, 1.8 Hz, 1H), 1.80 (t, J 1.6 Hz, 3H); $^{13}$C-NMR (75 MHz, CDCl$_3$) $\delta$ 206.3, 156.6, 143.5, 68.4, 44.5, 10.0.

4-Methyl-4-cyclopentene-1,3-dione (6)

To a solution of 4-hydroxy-2-methylcyclopentenone (5) (0.5 g, 4.45 mmol) in CH$_2$Cl$_2$ (20 mL) was added MnO$_2$ (7.75 g, 89 mmol) at room temperature. The resulting mixture was stirred at room temperature for 1 h, passed through a celite plug and concentrated. Purification by silica gel column chromatography (10% EtOAc in hexane) gave 4.5 g (92%) of cyclopentenedione (6) as a yellow solid. R$_f$ 0.36 (40% EtOAc/hexane); IR (film) $\nu_{\text{max}}$/cm$^{-1}$: 3430, 3081, 2927, 1703, 1684, 1380, 1251; $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.01 (q, J 1.8 Hz, 1H), 2.90 (s, 2H), 2.12 (d, J 1.4 Hz, 3H); $^{13}$C-NMR (75 MHz, CDCl$_3$) $\delta$ 201.0, 199.2, 162.3, 146.0, 41.7, 11.3.

2-Methyl-4-(triethylsilyloxy)cyclopent-2-ene (8)

To a stirred solution of hydroxy ketone 5 (0.127 g, 1.0 mmol) in CH$_2$Cl$_2$ (4 mL) at –5 °C was added imidazole (0.086 g, 1.31 mmol), triethylsilylchloride (0.166 g, 1.1 mmol) and catalytic amounts of N,N-dimethylaminopyridine and stirring was continued for 1 h. The reaction mixture was partitioned between EtOAc (5 mL) and H$_2$O (5 mL) then the organic layer was washed with
brine, dried over anhydrous MgSO4, filtered and evaporated. Purification of the crude product on silica gel with 5% EtOAc:hexanes as eluant gave the silyl ether 8 (0.192 g, 85%) as a colorless oil. Rf 0.32 (5% EtOAc/ hexane); IR (film) ν_max/cm⁻¹: 3478, 3414, 2961, 2917, 2873, 1723, 1646, 1461, 1413; ¹H NMR (300 MHz, C6D6) δ 6.63 (m, 1H), 4.36 (dd, J 17.9, 5.9, Hz, 1H), 2.21 (dd, J 17.9, 2.2 Hz, 1H), 1.64 (t, J 1.5 Hz, 3H), 0.98 (t, J 8.0 Hz, 3H), 0.54 (q, J 8.0 Hz, 6H); ¹³C NMR (75 MHz, C6D6) δ 204.2, 156.4, 128.0, 69.0, 45.4, 7.2, 5.3, 0.3.

2-[1-Hydroxy-3-phenyl-(Z,2E)-2-propenylidene]-4-methyl-4-cyclopentene-1,3-dione (1)

From diketone (6). A solution of diisopropylamine (0.31 mL, 2.2 mmol) in 4 mL of THF was cooled under argon in an ice bath, and n-butyl lithium 2.56 mol L⁻¹ (0.86 mL, 2.2 mmol) in hexane was added. The resulting solution was stirred at 0 °C for 15 min, cooled to −78 °C, and a solution of ketone 6 (0.22 g, 2.0 mmol) in 1 mL of THF was added dropwise. After 45 minutes at −78 °C, a solution of cinnamic anhydride (7) (0.441 g, 3.0 mmol) in 2 mL of THF was added dropwise. The resulting mixture was stirred at −78 °C for 45 min, poured into aqueous NH4Cl, and extracted with ether (2 x 10 mL). The combined organic extracts were washed with 20 mL of brine, dried over anhydrous Na2SO4, and concentrated in vacuo. 1H NMR spectroscopy of the unpurified diketone 10 in 2 mL of CH2Cl2 was added forming a cloudy white mixture. This was stirred for 15 min at −78 °C then 0.22 mL (1.62 mmol) of triethylamine was added. The reaction was stirred at −78 °C for 40 min then quenched by the addition of 5 mL of saturated aqueous NH4Cl. The mixture was allowed to warm to ambient temperature then diluted with 10 mL of CH2Cl2. The layers were separated and the aqueous phase was extracted with two 10 mL portions of CH2Cl2. The combined organic extracts were washed with 10 mL of brine, dried over anhydrous MgSO4, and concentrated in vacuo. ¹H NMR spectroscopy of the unpurified diketone was very clean. To a solution of the previously prepared diketone in 2 mL of THF, at ambient temperature was added 2.5 mL (2.5 mmol) of a 1.0 mol L⁻¹ solution of TBAF in THF. The reaction mixture was stirred at ambient temperature for 16 h then concentrated in vacuo. The crude product was purified by flash chromatography (EtOAc:hexanes 25%) as eluant to give diketone 10 (0.078 g, 60% over two steps) as a yellow oil. To a solution of 0.07 mL (1.0 mmol) of DMSO in 3 mL of CH2Cl2, at −78 °C was added 0.07 mL (0.78 mmol) of oxalyl chloride (gas evolution). After 10 min, a solution of 0.078 g (0.324 mmol) of alcohol 10 in 2 mL of CH2Cl2 was added forming a cloudy white mixture. This was stirred for 15 min at −78 °C then warmed to ambient temperature then diluted with 5 mL of CH2Cl2. The layers were separated and the aqueous phase was extracted with two 5 mL portions of CH2Cl2. The combined organic extracts were washed with 5 mL of brine, dried over anhydrous MgSO4, and concentrated in vacuo to give 0.062 g (0.26 mmol, 79%) of the cyclopentenedione derivative (1) as a yellow solid.

From Ketone (8). A solution of diisopropylamine (0.155 mL, 1.1 mmol) in 3 mL of THF was cooled under argon in an ice bath, and n-butyl lithium 2.56 mol L⁻¹ (0.43 mL, 1.1 mmol) in hexane was added. The resulting solution was stirred at 0 °C for 15 min, cooled to −78 °C, and a solution of ketone 8 (0.226 g, 1.0 mmol) in 1 mL of THF was added dropwise. After 45 minutes at −78 °C, a solution of cinnamaldehyde (0.38 mL, 3.0 mmol) in 1 mL of THF was added dropwise. The resulting mixture was stirred at −78 °C for 45 min, poured into aqueous NH4Cl, and extracted with ether (2 x 10 mL). The combined organic extracts were washed with 10 mL of brine, dried over anhydrous Na2SO4, and concentrated in vacuo to give a yellow oil which was purified by silica gel column chromatography (10% EtOAc in hexane) to provide 0.106 g (0.44 mmol, 22%) of the cyclopentenedione derivative (1) as a yellow solid.

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References

4. The numbering of (1) as well as of each intermediate follows that suggested in reference 1.
5. West, F. G.; Gunawardena, G. U.; J. Org. Chem. 1993, 58, 2402. Furfurylcarbinol (5) could also be obtained by the reaction of 2-lithium furan with acetaldehyde in 84% yield.
12. New compounds and the additional isolated intermediates gave satisfactory \(^1\)H and \(^13\)C NMR, IR, HRMS and analytical data. Yields refer to chromatographically and spectroscopically homogeneous materials.

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