# Reaction of Enaminothiones with Diphenylcyclopropenone. Synthesis of 4,5-Dimethylenecyclopentenone Derivatives

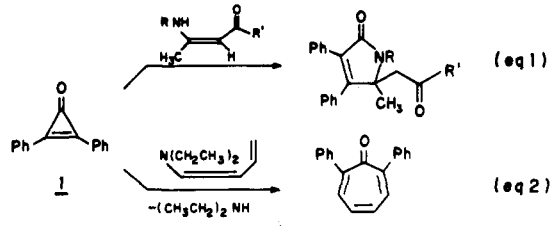
Albert Kascheres,* Concetta Kascheres, and A. C. Herrera Braga

*Universidade Estadual de Campinas, Instituto de Química, CP 6154, 13081 Campinas, SP, Brazil*

*Received September 30, 1992*

Diphenylcyclopropenone (1) reacts with enaminothiones 2 to afford 4,5-dimethylenecyclopentenone derivatives 3. The results of AM1 calculations performed on both geometrically optimized 2a and the oxygen analog in the *Z*,s-cis-configuration favor a mechanism in which the sulfur atom of 2 acts as a nucleophile at the phenyl-C of 1.

Cycloaddition reactions involving diphenylcyclopropenone (1) continue to reveal the diversified reactivity of this system.[1] Previously, we reported the reaction of primary and secondary enaminones with 1 which provided a convenient route to 5-functionalized 1,5-dihydropyrrol-2-ones (eq 1),[2] envisioned as occurring via cycloaddition

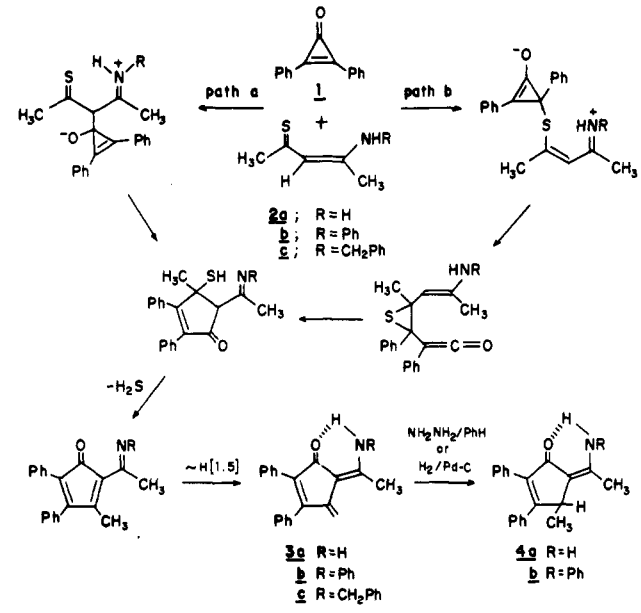



of 1 at the $C_\beta$,N positions of the enaminone. In this case, the enaminone would act as a nucleophilic species through nitrogen. The chemistry of enaminothiones, i.e., 2, has received considerable attention in recent literature.[3] The principal differences in reactivity between this system and the oxygen analog reside in the observed heterodiene character of the former in Diels-Alder reactions with electron-deficient olefins,[4] as well as behavior as a nucleophile almost exclusively through sulfur.[3] The observed participation of 1 as a dienophile on reaction with (diethylamino)butadiene (eq 2)[5] prompted us to examine the reactivity of 1 with enamines 2, wherein the effect of a $\beta$-thione substituent might be compared with that of the $\beta$-keto and $\beta$-vinyl derivatives previously studied.

## Results and Discussion

Reaction of 1 with 2a–c occurred slowly in refluxing benzene to afford 4-methylenecyclopentenones 3a–c in good yield. The structure assignment was based on the appearance, in the mass spectra, of molecular ions (100% relative intensity) corresponding to the incorporation of both reagents less $H_2S$ (confirmed by elemental analysis) and the presence, in the $^1H$ NMR spectra, of a terminal methylene ($\delta$ 5.1–5.25 and 5.45–5.65; $\delta$ 109–110 in the $^{13}C$ NMR spectra) in addition to a low-field exchangeable hydrogen ($\delta$ 9.4–12.8, intramolecular hydrogen bonding). Ozonolysis of 3b yielded acetanilide (1 equiv) as the only

**Scheme I**

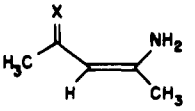



characterizable product, the formation of which is consistent with the previously reported behavior of $\beta$-enamino ketones.[6] The most straightforward mechanistic interpretation of the formation of 3 is represented in Scheme I (path a). It may be seen that this route involves initial nucleophilic attack of 2 at $C_1$ of 1 through $C_\alpha$, with subsequent ring expansion to the thione carbon. The problem here is that enaminothiones are not known to react as nucleophiles through $C_\alpha$.[3] With the objective of gaining further insight into the electronic distribution in 2, an AM1 calculation[7] as implemented in the AMPAC package[8] was performed on geometrically optimized 2a in the *Z*,s-cis-configuration. For the purpose of comparison, a similar calculation was performed on the oxygen analog. The results are presented in Table I. The frontier orbital treatment calls attention to the importance of the HOMO of 2a in reactions of this system as a nucleophile. This HOMO is essentially a nonbonding orbital on sulfur. In contrast, the corresponding orbital of the oxygen analog involves the $\pi$-system with largest coefficients at $C_\alpha$ and N. Interestingly, the chemical behavior of these derivatives toward electrophiles reflects exactly these differences. Thus, as mentioned above, enaminothiones react through

(1) Musicki, B. *J. Org. Chem.* **1991**, *56*, 110.
(2) Kascheres, A.; Kascheres, C.; Pilli, P. S. *J. Org. Chem.* **1980**, *45*, 5340.
(3) For a recent review see: Pulst, M.; Greif, D.; Kleinpeter, E. *Z. Chem.* **1988**, *28*, 345.
(4) Baruah, P. D.; Mukherjee, S.; Mahajan, M. P. *Tetrahedron* **1990**, *46*, 1951.
(5) Ciabattoni, J.; Berchtold, G. A. *J. Org. Chem.* **1966**, *31*, 1336.
(6) Eicher, T.; Weber, J. L.; Chatila, G. *Liebigs Ann. Chem.* **1978**, 1203.
(7) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.
(8) Dewar, M. J. A. Research Group, *QCPE Bull.*, 1986, Program No. 506.

0022-3263/93/1958-1702$04.00/0 

**Table I. Frontier Orbital Coefficients and Energies by the AM1 Method**




| | coefficients | | | | | |
|---|---|---|---|---|---|---|
| orbital | X | $C_{\alpha x}$ | $C_\alpha$ | $C_\beta$ | N | energy (eV) |
| LUMO (S, pz) | −0.470 | 0.593 | | −0.530 | 0.317 | −0.593 |
| (O, pz) | 0.368 | −0.452 | −0.324 | 0.639 | −0.307 | 0.466 |
| HOMO (S, py) | −0.933 | | −0.102 | | | −8.215 |
| (O, pz) | 0.299 | −0.064 | −0.711 | −0.299 | 0.542 | −8.717 |
| 2° HOMO (S, pz) | 0.586 | 0.028 | −0.622 | −0.284 | 0.420 | −8.498 |
| (O, py) | 0.722 | −0.231 | 0.261 | −0.119 | | −10.083 |
| 3° HOMO (S, pz) | 0.555 | 0.473 | 0.311 | −0.060 | −0.405 | −10.916 |
| (O, pz) | −0.428 | −0.212 | 0.125 | 0.342 | 0.613 | −12.110 |

sulfur, while enaminones react through $C_\alpha$ or N.[9] An alternative mechanism for the formation of **3** wherein the nucleophilic site is sulfur, is presented as path b in Scheme I. While more round-about, this pathway is more coherent with regard to the expected behavior of **2**.

In as much as path b requires reaction at phenyl-C in **1**, the LUMO coefficients for this system were obtained using the AM1 approach. The results of this calculation, 0.455 for phenyl-C versus 0.0001 for $C_{CO}$, provide additional support for path b, while, at the same time, suggesting that such a route should be favorable in reactions of "soft" nucleophiles in general. We believe that previous reactions of **1**, including that of eq 1, should be reexamined mechanistically within this framework.

To the best of our knowledge, the formation of **3** represents the first reaction of an enaminothione with an electrophilic reagent where sulfur is not incorporated into the final product. Treatment of **3** with hydrazine in benzene (a procedure[10] typically employed to transform enaminones into pyrazoles), or exposure to conditions of catalytic hydrogenation (Pd/C), resulted in reduction of the terminal methylene with quantitative formation of **4**.

The results of the present study complement the above-mentioned behavior of **1** toward other enamine derivatives and, at the same time, furnish a convenient route to derivatives of the previously unreported 4,5-dimethylenecyclopentenone system. Many examples exist of biologically active cyclopentenones bearing 5-alkylidene substituents,[11] suggesting various future synthetic applications for this newly uncovered reaction sequence.

## Experimental Section

NMR spectra were recorded with a Varian T-60 or Varian XL-100-15-FT spectrometer using TMS as internal reference. Infrared spectra were obtained with a Perkin-Elmer 337 spectrometer and mass spectra with a Varian Mat 311A spectrometer. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were performed by UNICAMP-Instituto de Química. Enaminothiones **2a–c** were prepared according to known procedures.[12]

**Reaction of Diphenylcyclopropenone (1) with Enaminothiones 2a–c.** A solution of **1** (10 mmol) and **2** (10 mmol) in benzene (50 mL) was heated at reflux for 48 h (**2a**), 179 h (**2b**), or 105 h (**2c**). The solvent was evaporated, and the residues containing **3** were purified as follows.

**3a.** Trituration of the crude reaction product with hexanes afforded **3a** (97%) as colorless crystals: mp 171–173 °C; IR (KBr) 3370, 1625 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.37 (3 H, s), 5.13 (1 H, br s), 5.47 (1 H, br s), 7.00–7.53 (11 H, m, 10 H with $D_2O$), 9.33 (1 H, br, disappears with $D_2O$); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.08 (q), 101.23 (s), 109.12 (t), 127.10–129.79 (aromatic C-H), 131.97 (s), 133.94 (s), 138.64 (s), 145.14 (s), 152.17 (s), 157.26 (s), 192.39 (s); MS *m/e* (relative intensity) 287 ($M^+$, 100). Anal. Calcd for $C_{20}H_{17}NO$: C, 83.60; H, 5.96; N, 4.87. Found: C, 84.00; H, 6.30; N, 4.90.

**3b.** Purification of the residue by column chromatography (Florisil, hexanes–ether (1:1)) afforded **3b** (55%) as colorless crystals: mp 184.5–186.5 °C; IR (KBr) 3200, 1620 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.47 (3 H, s), 5.25 (1 H, br s), 5.65 (1 H, br s), 6.83–7.73 (15 H, m), 12.77 (1 H, br, disappears with $D_2O$); $^{13}$C NMR ($CDCl_3$) $\delta$ 17.60 (q), 103.01 (s), 110.16 (t), 123.86–129.87 (aromatics), 131.78 (s), 133.87 (s), 138.03 (s), 145.28 (s), 1521 (s), 155.87 (s), 192.14 (s); MS *m/e* (relative intensity) 363 ($M^+$, 100), 348 (11.3), 93 (10.3), 77 (11.6). Anal. Calcd for $C_{26}H_{21}NO$: C, 85.92; H, 5.82; N, 3.85. Found: C, 85.63; H, 5.74; N, 3.92.

**3c.** Purification of the residue by column chromatography (Florisil, hexanes–ether (1:1)) afforded **3c** (34%) as colorless crystals: mp 145–148 °C; IR (KBr) 3400, 1620 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.33 (3 H, s), 4.57 (2 H, d, $J$ = 4.1 Hz, collapses to singlet with $D_2O$), 5.10 (1 H, br s), 5.47 (1 H, br s), 6.90–7.60 (15 H, m), 11.50 (1 H, br, disappears with $D_2O$); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.80 (q), 46.55 (t), 101.30 (s), 109.17 (t), 126.74–129.97 (aromatics), 132.03 (s), 134.08 (s), 137.72 (s), 138.31 (s), 145.58 (s), 159.35 (s), 191.72 (s); MS *m/e* (relative intensity) 377 ($M^+$, 100), 286 (28), 91 (62). Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.99; H, 5.79; N, 3.61.

**Reduction of 3 upon Treatment with Hydrazine.** A mixture of **3a** or **3b** (0.18 mmol) and hydrazine hydrate (95%, 0.62 mmol) in benzene (3 mL) was allowed to stand at room temperature for 6 days. The solvent was evaporated and the residue triturated with hexanes to afford **4a** or **4b** in quantitative yield.

**4a** (from **3a** and hydrazine) as colorless crystals: mp 164–166 °C; IR (KBr) 3460, 1630 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.14 (3 H, d, $J$ = 8.0 Hz), 2.10 (3 H, s), 3.84 (1 H, q, $J$ = 8.0 Hz), 7.25 (11 H, br s, 10 H with $D_2O$), 9.75 (1 H, br, disappears with $D_2O$); MS *m/e* (relative intensity) 289 ($M^+$, 100), 274 (25.9), 260 (11.5), 246 (19.0). Anal. Calcd for $C_{20}H_{19}NO$: C, 83.01; H, 6.62; N, 4.84. Found: C, 82.83; H, 6.73; N, 4.71.

**4b** (from **3b** and hydrazine) as colorless crystals: mp 160–162 °C; IR (KBr) 3200, 1640 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.18 (3 H, d, $J$ = 7.0 Hz), 2.20 (3 H, s), 3.83 (1 H, q, $J$ = 7.0 Hz), 7.23 (15 H, s), 12.18 (1 H, br, disappears with $D_2O$); MS *m/e* (relative intensity) 365 ($M^+$, 91.3), 350 (21.7), 118 (100), 77 (36.2). Anal. Calcd for $C_{26}H_{23}NO$: C, 85.45; H, 6.34; N, 3.83. Found: C, 85.21; H, 6.43; N, 4.01.

(9) Eberlin, M. N.; Kascheres, C. *J. Org. Chem.* **1988**, *53*, 2084.
(10) Plath, P.; Rohr, W. *Synthesis* **1982**, 318.
(11) Stone, G. B.; Liebeskind, L. S. *J. Org. Chem.* **1990**, *55*, 4614.
(12) (a) Duguay, G.; Metayer, C.; Quiniou, H. *Bull. Soc. Chim. Fr.* **1974**, 2507. (b) Walter, W.; Proll, T. *Synthesis* **1979**, 941. (c) Shabana, R. Rasmussen, J. B.; Olesen, S. O.; Lawesson, S. O. *Tetrahedron* **1980**, *36*, 3047.