A Convenient Synthesis of Polysubstituted Cyclopropanes

H. Fauduet, R. Burgada

Laboratoire des Organo-Éléments ERA 825, Université P. et M. Curie, 4 place Jussieu, F-75230 Paris Cédex 05, France

Foucaud and Corre have described the synthesis of cyclopropanes by the reaction of 4,5-dimethyl-2,2,2-trimethoxy-1,3,2-dioxaphospholene with electrophilic olefins, carrying several electron-withdrawing substituents. This method fails with methyl acrylate.

We now wish to describe a general method for the preparation of polysubstituted cyclopropanes by condensing activated unsaturated systems with the 1:1 adducts derived from hexamethylphosphorous triamide (1) and 1,2-dicarbonyl compounds.

\[
\begin{align*}
[\text{H}_2\text{C}=\text{N}]_3\text{P} + \text{R}^1\text{C}\equiv\text{C}-\text{R}^2 & \rightarrow [\text{H}_2\text{C}=\text{N}]_3\text{P} + \text{R}^1\text{C}\equiv\text{C}-\text{R}^2 \\
1 & 2 & 3 \\
\text{H}_2\text{C}=\text{CH}=\text{R}^3 (41) & \rightarrow \text{H}_2\text{C}=\text{CH}=\text{R}^3 (5a-e) \\
& - [\text{H}_2\text{C}=\text{N}]_3\text{P} = 0 \\
& \text{H}_2\text{C}=\text{CH}=\text{R}^3 (41) & \text{H}_2\text{C}=\text{CH}=\text{R}^3 (5a-e)
\end{align*}
\]

The resulting cyclopropanes can be obtained in good yields under very mild conditions without isolation of the phosphonium betaine intermediates (Table 1). Their structure is confirmed by I.R., 'H- and 13C-N.M.R. spectra. These results are compiled in Table 2.

This reaction is not stereospecific. The hexamethylphosphoronic triamide formed is easily removed by washing with water. The condensation reaction is slightly exothermic, when hexamethylphosphorous triamide is used, but it fails in when cyclic aminophosphines are used instead of 1. This phenomenon may be attributed to the facts that the spirophosphoranes are not in equilibrium with their open dipolar form, and they do not possess good leaving groups as compared with hexamethylphosphorous triamide.

We assume that this cyclopropane formation can be explained by the mechanism given for the similar condensation of \( \alpha \)-haloenoates with \( \alpha,\beta \)-unsaturated esters: the reaction proceeds by a nucleophilic attack of the carbanionic form of the betaine on the more electrophilic carbon atom of the olefin followed by a cyclisation with elimination of hexamethylphosphorous triamide.

1-Benzoyl-2-methoxycarbonyl-1-phenylecyclopropane (5d); Typical Procedure:

Methyl acrylate (4; \( \text{R}^1 = \text{H}, \text{COOC} ) 4.5 g, 0.052 mol) is added with stirring to a solution of betaine 3b (\( \text{R}^1 = \text{R}^2 = \text{C}_2\text{H}_5, 18.65 g, 0.05 mol) freshly prepared in situ in dichloromethane (50 ml) under ni-
### Table 1. Polysubstituted Cyclopropanes 5a-e

<table>
<thead>
<tr>
<th>Product No. R¹ R² R³</th>
<th>Yield* [%]</th>
<th>m.p. [°C] or b.p. [°C]/torr</th>
<th>nD²⁵ (Lit. value)</th>
<th>Molecular formula* or L.R. (KBr or CCl₄) [°C] or b.p. [°C]/torr</th>
<th>I.R. (KBr or CCl₄) [cm⁻¹]</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a COOC₂H₅OC₂H₅</td>
<td>78</td>
<td>84-85°/0.01</td>
<td>1.4458</td>
<td>C₁₁H₁₄O₄</td>
<td>1732 (COO); 1721</td>
</tr>
<tr>
<td>5b COOC₂H₅OC₂H₅</td>
<td>70</td>
<td>76°/0.02</td>
<td>1.4498</td>
<td>C₁₁H₁₄O₄</td>
<td>1735 (COO); 1715 (C O); 1024</td>
</tr>
<tr>
<td>5c COOC₂H₅OC₂H₅</td>
<td>73</td>
<td>98-100°/0.1</td>
<td>1.4515</td>
<td>C₁₁H₁₄O₄</td>
<td>2250 (C N); 1736 (COO); 1019</td>
</tr>
<tr>
<td>5d C₄H₉</td>
<td>67°</td>
<td>97°</td>
<td>1.5140</td>
<td>C₄H₉O₂</td>
<td>cis: 1724 (COO); 1675 (C O); 1012</td>
</tr>
<tr>
<td>5e C₄H₉</td>
<td>60°</td>
<td>97°</td>
<td>1.5150</td>
<td>C₄H₉O₂</td>
<td>trans: 1739 (COO); 1025</td>
</tr>
</tbody>
</table>

* Yield referred to 1,2-dicarbonyl compound 2.

The microanalyses of all products were in satisfactory agreement with the calculated values (C ± 0.29, H ± 0.21); exception 5a: H +0.72%.

trans COR²/R³ 25%, cis COR²/R³ 43%.

d trans COR²/R³ 24%, cis COR²/R³ 36%.

### Table 2. N.M.R. Data for Compounds 5a-e

<table>
<thead>
<tr>
<th>Product (trans)</th>
<th>¹H-N.M.R. ([CDCl₃/TMS]°) δ [ppm]</th>
<th>¹³C-N.M.R. ([CDCl₃/TMS]° δ [ppm])</th>
<th>Substituent at C-1</th>
<th>Substituent at C-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>1.27 (t, 6 H, J = 7.7 Hz, H₂C–CH₂O); 1.64 (dd, 1 H, H(b)); 1.93 (dd, 1 H, H(a)); 2.57 (dd, 1 H, H(c)); 4.19 (q, 4 H, H₂C–CH₂O, J = 7.7 Hz); J₉₁₂₅₁₆₆₆₆ = 4.9 Hz; J₉₁₂₅₁₇₁₇ = 6.6 Hz; J₆₁₅₁₆₆₆₆ = 9.5 Hz</td>
<td>37.304 27.668 19.466</td>
<td>170.182-169.072 (COO); 62.630-61.843 (OCH₂CH₂); 14.193 (OCH₂CH₂)</td>
<td>165.947 (COO); 52.473 (OCH₂CH₂)</td>
</tr>
<tr>
<td>5b</td>
<td>1.30-1.33 (2 t, 6 H, J = 7.7 Hz, H₂C–CH₂O); 1.63 (dd, 1 H, H(b)); 2.03 (dd, 1 H, H(a)); 2.43 (s, 2 H, H₂C–CO); 2.90 (dd, 1 H, H(c)); 4.32-4.37 (2 q, 4 H, H₂C–CH₂O, J = 7.7 Hz); J₉₁₂₅₁₆₆₆₆ = 4.7 Hz; J₉₁₂₅₁₇₁₇ = 7.3 Hz; J₆₁₅₁₆₆₆₆ = 9.2 Hz</td>
<td>39.062 33.984 19.856</td>
<td>169.202-166.015 (COO); 62.369-61.588 (OCH₂CH₂); 14.067 (OCH₂CH₂)</td>
<td>202.926 (COO); 31.314 (CH₂)</td>
</tr>
<tr>
<td>5c</td>
<td>1.29-1.35 (2 t, 6 H, H₂C–CH₂O, J = 7.7 Hz); 1.72 (dd, 1 H, H(b)); 2.04 (dd, 1 H, H(a)); 2.51 (dd, 1 H, H(c)); 4.28-4.33 (2 q, 4 H, H₂C–CH₂O, J = 7.7 Hz); J₉₁₂₅₁₆₆₆₆ = 7.4 Hz; J₉₁₂₅₁₇₁₇ = 10.2 Hz</td>
<td>42.578 27.799 19.986</td>
<td>194.859 (COO); 135.936, 133.202, 130.728, 129.556, 129.228, 128.645, 127.796, 126.624 (C₆H₉, 9 signals)</td>
<td>171.416 (COO); 53.388 (CH₂)</td>
</tr>
<tr>
<td>cis-5d*</td>
<td>1.68 (dd, 1 H, H(b)); 2.25 (dd, 1 H, H(a)); 2.63 (dd, 1 H, H(c)); 3.46 (s, 3 H, H₂COOC); 7.65 (m, 10 Hₓᵧₚₛₜₛₚₛₚₛ); J₉₁₂₅₁₆₆₆₆ = 5.5 Hz; J₉₁₂₅₁₇₁₇ = 6.7 Hz; J₆₁₅₁₆₆₆₆ = 8.9 Hz</td>
<td>37.062 27.734 19.010</td>
<td>171.354 (COO); 138.475, 129.489, 128.968, 125.845 (CH₃, 4 signals); 52.473 (OCH₃)</td>
<td>170.312 (COO); 52.083 (OCH₃)</td>
</tr>
<tr>
<td>trans-5d*</td>
<td>1.67 (dd, 1 H, H(b)); 2.41 (dd, 1 H, H(a)); 3.11 (dd, 1 H, H(c)); 3.36 (s, 3 H, H₂COOC); 7.5 (m, 10 Hₓᵧₚₛₚₛₚₛ); J₉₁₂₅₁₆₆₆₆ = 5.1 Hz; J₉₁₂₅₁₇₁₇ = 6.7 Hz; J₆₁₅₁₆₆₆₆ = 9.3 Hz</td>
<td>37.062 27.734 19.010</td>
<td>171.354 (COO); 138.475, 129.489, 128.968, 125.845 (CH₃, 4 signals); 52.473 (OCH₃)</td>
<td>170.312 (COO); 52.083 (OCH₃)</td>
</tr>
<tr>
<td>cis-5e*</td>
<td>1.53 (dd, 1 H, H(b)); 2.12 (dd, 1 H, H(a)); 2.26 (dd, 1 H, H(c)); 3.61 (s, 3 H, H₂COOC); 3.70 (s, 3 H, H₂COOC); 7.36 (m, 5 Hₓᵧₚₛₚₛₚₛ); J₉₁₂₅₁₆₆₆₆ = 4.5 Hz; J₉₁₂₅₁₇₁₇ = 7.2 Hz; J₆₁₅₁₆₆₆₆ = 8.6 Hz</td>
<td>37.062 27.734 19.010</td>
<td>171.354 (COO); 138.475, 129.489, 128.968, 125.845 (CH₃, 4 signals); 52.473 (OCH₃)</td>
<td>170.312 (COO); 52.083 (OCH₃)</td>
</tr>
<tr>
<td>trans-5e*</td>
<td>1.87 (dd, 1 H, H(b)); 2.00 (dd, 1 H, H(a)); 2.75 (dd, 1 H, H(c)); 3.39 (s, 3 H, H₂COOC); 3.60 (s, 3 H, H₂COOC); 7.23 (m, 5 Hₓᵧₚₛₚₛₚₛ)</td>
<td>36.653 29.492 19.400</td>
<td>172.916 (COO); 135.026, 130.791, 128.317, 127.994 (C₆H₉, 4 signals)</td>
<td>169.530 (COO); 51.822 (OCH₃)</td>
</tr>
</tbody>
</table>

* Recorded on a Jeol MH 100 instrument at 100 MHz.

b Recorded on a Jeol JNM-FX 60Q instrument at 15 MHz.

c Stereochemistry of COR²/R³ groups.
trogen at room temperature. The mixture is stirred for 20 h and then washed with water (3 × 10 ml). The organic phase is dried with anhydrous sodium sulfate and evaporated in vacuo. Treatment of the residue with cold ether/petroleum ether (1:3; 40 ml) gives a solid mixture containing 36% of trans-isomer and 64% of cis-isomer; yield: 9.40 g (67%). The predominant isomer can be isolated by fractional crystallization from benzene/petroleum ether (1:2).

1,2-Dimethoxycarbonyl-1-phenylcyclopropane (5e):
A solution of methyl acrylate (4; R' = H, COOC: 4.5 g, 0.052 mol) and methyl phenylglyoxalate (2; R' = C₆H₅, R' = H, CO: 8.2 g, 0.05 mol) in dichloromethane (20 ml) is added dropwise to a solution of hexamethylphosphorotriamide (1; 8.15 g, 0.05 mol) in dichloromethane (50 ml) at −45 °C in a nitrogen atmosphere. This mixture is stirred for 20 min at −40 °C and then allowed to warm slowly to room temperature. The hexamethylphosphorotriamide formed is removed by several washings with water (3 × 10 ml). The organic phase is dried with anhydrous sodium sulfate, the solvent is evaporated in vacuo, and the residue obtained is purified by distillation. The trans-isomer crystallizes and is selectively removed by filtration, after dilution with methanol. The filtrate contains only the cis-isomer.

We are indebted to Dr. G. Cabiez for the ¹³C-N.M.R. spectra.

Received: January 24, 1980

   (b) H. Fauduet, R. Burgada, Nouv. J. Chim. 4, 113 (1980).