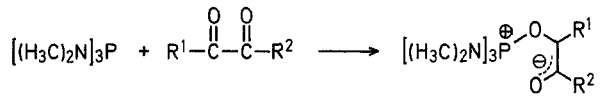
A Convenient Synthesis of Polysubstituted Cyclopropanes

H. FAUDUET, R. BURGADA

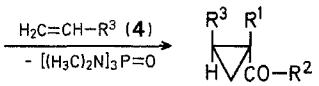
Laboratoire des Organo-Eléments ERA 825, Université P. et M. Curie, 4 place Jussieu, F-75230 Paris Cédex 05, France

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[1]. This method fails with methyl acrylate.

We now wish to describe a general method for the preparation of polysubstituted cyclopropanes **5** by condensing activated unsaturated systems **4** with the 1:1 adducts **3**, derived from hexamethylphosphorous triamide (**1**) and 1,2-dicarbonyl compounds **2**.



1 **2** **3**



5a-e

The resulting cyclopropanes **5** can be obtained in good yields under very mild conditions without isolation of the phosphonium betaine intermediates **3** (Table 1). Their structure is confirmed by I.R., ^{1}H- and ^{13}C-N.M.R. spectra. These results are compiled in Table 2.

This reaction is not stereospecific. The hexamethylphosphoric triamide formed is easily removed by washing with water. The condensation reaction is slightly exothermic, when hexamethylphosphorous triamide **1** 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 α-haloenolates with α,β-unsaturated esters[3,4]: the reaction proceeds by a nucleophilic attack of the carbanionic form of the betaine **3** on the more electrophilic carbon atom of the olefin **4** followed by a cyclisation with elimination of hexamethylphosphoric triamide[2].

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

Methyl acrylate (**4**; $R^3 = H_3COOC$; 4.5 g, 0.052 mol) is added with stirring to a solution of betaine **3b**[8] ($R^1 = R^2 = C_6H_5$; 18.65 g, 0.05 mol) freshly prepared *in situ* in dichloromethane (50 ml) under ni-

0039-7881/80/0832-0642 $ 03.00 © 1980 Georg Thieme Verlag · Stuttgart · New York

Downloaded by: Chinese University of Hong Kong. Copyrighted material.

Table 1. Polysubstituted Cyclopropanes **5a–e**

Product No.	R^1	R^2	R^3	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr	n_D^{20} (Lit. value)	Molecular formula[b] or Lit. m.p. [°C] or b.p. [°C]/torr	I.R. (KBr or CCl_4) ν [cm^{-1}]
5a	$COOC_2H_5$	OC_2H_5	$COOCH_3$	78	84–85°/0.01	1.4458	$C_{11}H_{16}O_6$ (244.2)	1732 (COO); 1721
5b	$COOC_2H_5$	OC_2H_5	$CO—CH_3$	70	76°/0.02	1.4498 (1.4486)[6]	154°/18[5]; 92°/0.08[6]	1735 (COO); 1715 (C=O); 1024
5c	$COOC_2H_5$	OC_2H_5	—CN	73	98–100°/0.1	1.4515 (1.4482)[7]	159°/15[5]; 117°/0.7[7]	2250 (C≡N); 1736 (COO); 1019
5d	C_6H_5	C_6H_5	$COOCH_3$	67[c]	97° *(cis)*	—	$C_{18}H_{16}O_3$ (280.3)	*cis:* 1724 (COO); 1675 (C=O); 1012 *trans:* —
5e	C_6H_5	OCH_3	$COOCH_3$	60[d]	95° *(trans)* 98°/0.01 *(cis)*	1.5140 *(cis)* (1.5150)[5]	96° *(trans)*[5] 125°/0.6 *(cis)*[5]	*cis:* 1739 (COO); 1025 *trans:* 1730 (C=O); 1025

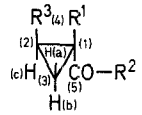
[a] Yield referred to 1,2-dicarbonyl compound **2**.

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

[c] *trans* COR^2/R^3 25%, *cis* COR^2/R^3 43%.

[d] *trans* COR^2/R^3 24%, *cis* COR^2/R^3 36%.

Table 2. N.M.R. Data for Compounds **5a–e**



Product	^{1}H-N.M.R. ($CDCl_3$/TMS)[a] δ [ppm]	^{13}C-N.M.R. ($CDCl_3$/TMS)[b] δ [ppm]				
		cyclopropane ring C-1	C-2	C-3	Substituent at C-1	Substituent at C-2
5a	1.27 (t, 6H, J=7.7 Hz, $H_3C—CH_2O$); 1.64 [dd, 1H, H(b)]; 1.93 [dd, 1H, H(a)]; 2.57 [dd, 1H, H(c)]; 4.19 (q, 4H, $H_3C—CH_2O$, J=7.7 Hz); $J_{H(a),H(b)}$=4.9 Hz; $J_{H(a),H(c)}$=6.6 Hz; $J_{H(b),H(c)}$=9.5 Hz	37.304	27.668	19.466	170.182–169.072 (COO); 62.630–61.843 (OCH_2CH_3); 14.193 (OCH_2CH_3)	165.947 (COO); 52.473 (OCH_3)
5b	1.30–1.33 (2 t, 6H, J=7.7 Hz, $H_3C—CH_2O$); 1.63 [dd, 1H, H(b)]; 2.03 [dd, 1H, H(a)]; 2.43 (s, 3H, $H_3C—CO$); 2.90 [dd, 1H, H(c)]; 4.32–4.37 (2 q, 4H, $H_3C—CH_2$, J=7.7 Hz); $J_{H(a),H(b)}$=4.7 Hz; $J_{H(a),H(c)}$=7.3 Hz, $J_{H(b),H(c)}$=9.2 Hz	39.062	33.984	19.856	169.202–166.015 (COO); 62.369–61.588 (OCH_2CH_3); 14.067 (OCH_2CH_3)	202.926 (C=O); 31.314 (CH_3)
5c	1.29–1.35 (2 t, 6H, $H_3C—CH_2O$, J=7.7 Hz); 1.72 [dd, 1H, H(b)]; 2.04 [dd, 1H, H(a)]; 2.51 [dd, 1H, H(c)]; 4.28–4.33 (2 q, 4H, $H_3C—CH_2O$, J=7.7 Hz); $J_{H(a),H(b)}$=5.6 Hz; $J_{H(a),H(c)}$=7.4 Hz; $J_{H(b),H(c)}$=10.2 Hz	—	—	—	—	—
cis-**5d**[c]	1.68 [dd, 1H, H(b)]; 2.25 [dd, 1H, H(a)]; 2.63 [dd, 1H, H(c)]; 3.46 (s, 3H, H_3COOC); 7.65 (m, 10H_{arom}); $J_{H(a),H(b)}$=5.5 Hz; $J_{H(a),H(c)}$=6.7 Hz; $J_{H(b),H(c)}$=8.9 Hz	42.578	27.799	19.986	194.859 (C=O); 138.541, 135.936, 133.202, 130.728, 129.556, 129.228, 128.645, 127.796, 126.624 (C_6H_5, 9 signals)	171.416 (COO); 53.388 (CH_3)
trans-**5d**[c]	1.67 [dd, 1H, H(b)]; 2.41 [dd, 1H, H(a)]; 3.11 [dd, 1H, H(c)]; 3.36 (s, 3H, H_3COOC); 7.5 (m, 10H_{arom}); $J_{H(a),H(b)}$=5.1 Hz; $J_{H(a),H(c)}$=6.7 Hz; $J_{H(b),H(c)}$=9.3 Hz					
cis-**5e**[c]	1.53 [dd, 1H, H(b)]; 2.12 [dd, 1H, H(a)]; 2.26 [dd, 1H, H(c)]; 3.61 (s, 3H, H_3COOC); 3.70 (s, 3H, H_3COOC); 7.36 (m, 5H_{arom}); $J_{H(a),H(b)}$=4.5 Hz; $J_{H(a),H(c)}$=7.2 Hz; $J_{H(b),H(c)}$=8.6 Hz	39.062	27.734	19.010	171.354 (COO); 138.475, 129.489, 128.968, 125.845 (C_6H_5, 4 signals); 52.473 (OCH_3)	170.312 (COO); 52.083 (OCH_3)
trans-**5e**[c]	1.87 [dd, 1H, H(b)]; 2.00 [dd, 1H, H(a)]; 2.75 [dd, 1H, H(c)]; 3.39 (s, 3H, H_3COOC); 3.60 (s, 3H, H_3COOC); 7.23 (m, 5H_{arom})	36.653	29.492	19.400	172.916 (COO); 135.026, 130.791, 128.317, 127.994 (C_6H_5, 4 signals)	169.530 (COO); 51.822 (OCH_3)

[a] 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 COR^1/R^2 groups.

Downloaded by: Chinese University of Hong Kong. Copyrighted material.

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**; $R^3 = H_3COOC$; 4.5 g, 0.052 mol) and methyl phenylglyoxalate (**2**; $R^1 = C_6H_5$, $R^2 = H_3CO$; 8.2 g, 0.05 mol) in dichloromethane (20 ml) is added dropwise to a solution of hexamethylphosphorous triamide (**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 hexamethylphosphoric triamide 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. Cahiez for the ^{13}C-N.M.R. spectra.

Received: January 24, 1980

[1] A. Foucaud, E. Corre, *J. Chem. Soc. Chem. Commun.* **1973**, 570; *Bull. Soc. Chim. Fr.* **1971**, 1514.
[2] (a) H. Fauduet, R. Burgada, *Nouv. J. Chim.* **3**, 555 (1979).
(b) H. Fauduet, R. Burgada, *Nouv. J. Chim.* **4**, 113 (1980).
[3] L. L. McCoy, *J. Am. Chem. Soc.* **84**, 2246 (1962).
[4] J. Villieras, J. R. Disnar, J. F. Normant, *J. Organometal. Chem.* **81**, 295 (1974).
H. Normant, *J. Organometal. Chem.* **100**, 189 (1975).
[5] G. Bonavent, M. Causse, M. Guitard, R. Fraisse-Julien, *Bull. Soc. Chim. Fr.* **1964**, 2462.
[6] D. T. Warner, *J. Org. Chem.* **24**, 1536 (1959).
[7] P. Madsen, F. Preston, S. O. Lawesson, *Ark. Kemi* **28**, 395 (1967).
[8] R. Burgada, *C. R. Acad. Sci. Paris Ser. C* **258**, 4789 (1964).

0039-7881/80/0832-0644 $ 03.00 © 1980 Georg Thieme Verlag · Stuttgart · New York

Downloaded by: Chinese University of Hong Kong. Copyrighted material.