to the reaction mixture and liquid products were immediately analyzed by GLC.

Treatment of 11′ under catalytic cyclocarbonylation conditions was carried out analogously.

Registry No. **1a**, 21040-45-9; **1b**, 26146-77-0; **2**, 830-81-9; **3a**, 65693-16-5; **3b**, 115117-74-3; **3c**, 77134-00-0; **3d**, 115117-75-4; **4a**, 76605-37-3; **4b**, 115117-79-8; **4c**, 62521-66-8; **4d**, 115117-80-1; **5a**, 115117-76-5; **5b**, 115117-77-6; **5c**, 115117-78-7; **6a**, 115117-81-2; **6b**, 115117-83-4; **6c**, 115117-84-5; **7a**, 115117-82-3; **7b**, 82265-46-1; **7c**, 115117-85-6; **8**, 115117-86-7; **9**, 115117-87-8; **11**, 115117-89-0; **11′**, 115117-92-5; **12**, 115117-91-4; **13**, 115117-90-3; $PdCl_2(PPh_3)_2$, 13965-03-2; $Pd(CO)(PPh_3)_3$, 24670-32-4; $Pd(PPh_3)_4$, 14221-01-3; $PdCl_2(PMePh_2)_2$, 52611-08-2; $PdCl_2(PMe_2Ph)_2$, 29484-74-0; $PdCl_2(PMe_3)_2$, 25892-38-0; $PdCl_2(PCy_3)_2$, 29934-17-6; $PtCl_2(PPh_3)_3$, 10199-34-5; $NiBr_2(PPh_3)_2$, 14126-37-5; $Ru_3(CO)_{12}$, 15243-33-1; $Pt(CO)(PPh_3)_3$, 15376-99-5; 3-methyl-1-naphthol, 13615-40-2; menadione, 58-27-5; *cis*-cinnamyl bromide, 115117-88-9.

Stereoselectivity Differences in Wittig Reactions of Semistabilized Ylides

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The Wittig reactions of phosphorane **1** with various benzaldehydes **3** (series A) and the phosphoranes **4** with salicylaldehyde **6** (series B) have been studied. The *Z*:*E* stilbene ratio in series B is enhanced relative to that in series A. This difference in the stereochemical outcome between the two series is rationalized in terms of steric factors mainly imposed by the *o*-methoxymethoxy group in ylide **1** and aldehyde **6**, whereas electronic and possibly steric effects due to the para substituents in aldehydes **3** and ylides **4** seem to be relatively unimportant. Oxaphosphetanes that may collapse to olefins or decompose to Li^+-stabilized betaine complexes are postulated as the important intermediates.

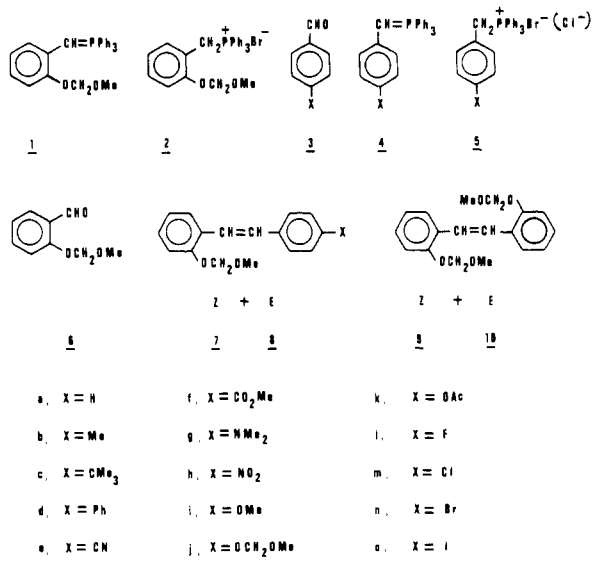
The significance and generality of the Wittig carbonyl olefination process in synthetic organic chemistry have prompted several investigators to consider this reaction from the mechanistic point of view.[1] Efforts have been primarily focused on reactive ylides in salt-free solutions, and relatively little attention has been devoted to semistabilized ylides.[1a,b,g,2] Mechanistically,[1a,b] free betaine,[2a-c] ion-stabilized betaine,[2e,f] and oxaphosphetane[2d,f] intermediates have been entertained.

Herein we report the results of a study concerning the Wittig reactions of [*o*-(methoxymethoxy)benzylidene]triphenylphosphorane (**1**), generated from the corresponding phosphonium salt **2**, with various para-substituted benzaldehydes **3** (series A) on one hand and the para-substituted benzylidenetriphenylphosphoranes **4**, resulting from phosphonium salts **5**, with *O*-(methoxymethyl)salicylaldehyde (**6**) (series B) on the other hand, i.e., interchanging the ylide and the aldehyde substituents. Such a systematic investigation is lacking, particularly in evaluating the effect of steric crowding imposed by a bulky group in the ortho position of the benzylidene group of an ylide,[3] and also in benzaldehyde, from the final *Z*:*E* (7:8) stilbene ratios (Chart I). We have also carried out the Wittig reaction between phosphorane **1** and aldehyde **6** to obtain the isomeric stilbenes **9** and **10**.

The reactions were carried out in benzene, at 25 °C, with *n*-butyllithium as the base as previously described.[4] The lithium salts were not excluded. Product composition was determined by analytical GC with internal standards to correct the GC areas (Table I).

Structural assignments were based on the physical and spectroscopic properties of the products. In the UV spectra (see paragraph at the end of paper about supplementary material) the (*E*)-stilbenes exhibit a bathochromic shift (λ_{max} 311–361 nm) and a hyperchromic effect (ϵ 17 000–37 000) relative to the *Z* (λ_{max} 274–332 nm, ϵ 7000–17 500) in accord with the literature.[4,5a,b] The IR

Chart I



spectra of the (*E*)-stilbenes show an absorption in the region 957–970 (s–m) cm^{-1}, characteristic of *E*-disubsti-

† NRCPS "Demokritos".

‡ University of Thessaloniki.

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0022-3263/88/1953-3838$01.50/0

Table I. Absolute Yields (%) of Stilbenes 7 and 8 from Wittig Reactions of 1 with 3 and 4 with 6[a]

			series A (1 + 3)					series B (4 + 6)				
entry[b]	X	IS[c]	min	7	8	total	7:8	min	7	8	total	7:8
1			30	27	33	60	45:55	15	52	44	96	54:46
	H	$C_{22}H_{46}$										
2			120	34	52	86	40:60					
3	Me	$C_{23}H_{48}$	120	30	51 (46)[d]	81	37:63	15	38	29	67	57:43
4			30	19	35	54	35:65	15	42	48	90	47:53
	CMe_3	$C_{22}H_{46}$										
5			120	28	43	71	39:61					
6	Ph[e]	$C_{24}H_{50}$	30	16	36	52	31:69	30	54	46	100	54:46
7			90	27	53	80	34:66					
	CN	$C_{21}H_{44}$										
8			1140	35	52	85	39:61	900	13	10	23	57:43
9			15	26	34	60	44:56	30	24	14	38	64:36
	CO_2Me[e]	$C_{22}H_{46}$										
10			60	33	45	78	42:58	900	23	18	41	56:44
11			20	3	45	48	6:94	20	5	24	29	17:83
	NMe_2	$C_{22}H_{46}$										
12			240	0	100 (68)[f]	100	0:100					
13			15	32	46	78	41:59	20	14	7	21	67:33
	NO_2[e]	$C_{24}H_{50}$										
14			120	27	50 (50)[d]	77	35:65					
15			60	33	65	98	33:67	15	77	22	99	78:22
	OMe	$C_{22}H_{46}$										
16			120	23	59 (59)[d]	82	27:73					
17			15	18	38	56	32:68	15	23	19	42	55:45
	OCH_2OMe[e]	$C_{25}H_{52}$										
18			720	27	49	76	35:65					
19	OAc[e]	$C_{26}H_{54}$	30	30	44 (33)[f]	74	41:59					
20			30	26	54	80	33:67	15	57	39	96	59:41
	F	$C_{22}H_{46}$										
21			120	28	64	92	31:69					
22			15	21	49	70	30:70	15	54	25	79	68:32
	Cl	$C_{23}H_{48}$										
23			120	26	57 (57)[d]	83	32:68					
24			15	26	46	72	36:64	15	51	32	83	62:38
	Br	$C_{22}H_{46}$										
25			120	27	57 (57)[d]	84	33:67					
26	I	$C_{23}H_{48}$	15	27	50 (54)[f]	77	35:65					

[a] See Table II for reagents used (supplementary material). [b] Correspond to those of Table II. [c] GC internal standards: *n*-alkanes. [d] Isolated by fractional crystallization on a preparative scale; this work. [e] Column chromatography preceded GC analysis in both series. [f] Isolated by fractional crystallization on a preparative scale; ref 4.

tuted olefins,[4,5] which is absent in the *Z* isomers. Mass spectrometry indicated the correct molecular ion, whereas the elemental analyses were satisfactory (≤±0.30%). Finally, cleavage of the (*E*)-stilbene–acetals with 10% HCl in MeOH afforded the corresponding stilbenols with the same melting point and IR characteristics as those previously reported.[4]

From Table I, stereoselectivity is low within either series as expected for reactions of semistabilized ylides with aryl aldehydes in the presence of lithium salts.[1a,b] The predominant feature, however, of our results is the difference in stereoselectivity between the two sets. In series A the (*E*)-stilbene is the major product (55–70%), whereas in series B the *Z* isomer is obtained in a greater proportion (54–78%). Even though the energy differences between the two sets are small, they are nevertheless characteristic of the differences in reactivity. On the basis of previous electronic considerations,[1a,b,2a,b] an electron donor on the ylide (series A) or on benzaldehyde (series B) is expected to increase the *Z* proportion in series A and to decrease it in series B for X = electron-withdrawing. These predictions notwithstanding, however, the electronic effect appears to be insignificant in determining the stereochemical outcome in both series. We attribute the differences in stereoselectivity between series A and B mainly to steric crowding exerted by the OCH_2OMe group placed in the ortho position of ylide **1** or aldehyde **6**, whereas the para substituents in aldehydes **3** or ylides **4** seem to play only a secondary steric role.

Even though a conclusive mechanistic rationale is not necessitated by the results, nevertheless we have adopted a scheme that adequately explains our observations. The analogies are drawn from the arsenal of reactive ylides, more specifically, from the important work of the Vedejs, Maryanoff, and Schlosser teams. A traditional free betaine mechanism[1a,b] or the Bestmann zwitterion rationale[1c] seem unlikely, since they are both heavily based on substituent electronic effects. On one hand, these potential intermediates have never been observed in Wittig reactions, albeit the possible fleeting intervension of free dipolar betaines,[1d,g,6] and on the other hand, had they played a decisive role, the (*Z*)-stilbene proportion would have been increased in series A and decreased in series B for X = electron-withdrawing. What in fact is observed in Table I is exactly the reverse.

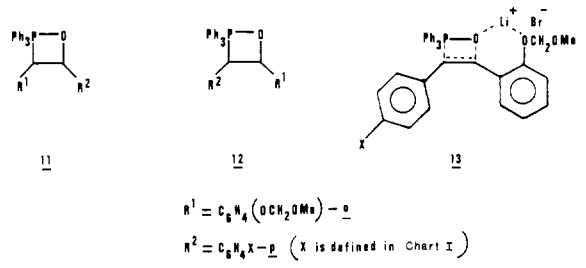
(3) Some results on reactive ylides with ortho-substituted P ligands have appeared recently: Schaub, B.; Jeganathan, S.; Schlosser, M. *Chimia* **1986**, *40*, 246.

(4) Mylona, A.; Nikokavouras, J.; Takakis, I. M. *J. Chem. Res.* **1986**, (S) 433, (M) 3514.

(5) (a) Silverstein, R. M.; Bassler, G. C. *Spectrometric Identification of Organic Compounds*, 2nd ed.; Wiley: New York, 1963. (b) Wheeler, O. H.; Battle D. Pabon, H. N. *J. Org. Chem.* **1965**, *30*, 1473. (c) Bellamy, L. T. *The Infrared Spectra of Complex Molecules*, 3rd ed.; Chapman and Hall: London, 1975; Vol. 1.

(6) Piskala, A.; Rehan, A. H.; Schlosser, M. *Collect. Czech. Chem. Commun.* **1983**, *48*, 3539.

Chart II



Our results can best be accommodated by postulating a rationale involving oxaphosphetanes and betaine–lithium halide complexes as the important intermediates. Vedejs[1d,7] was the first to show the involvement of oxaphosphetanes in Wittig reactions of reactive ylides, whereas betaine–lithium salt adducts have been known to exist much earlier.[1d,8] Semiquantitative partial rate constants were, for the first time, measured recently by Maryanoff.[1g,9]

The final isomeric ratio may be controlled by initial oxaphosphetane formation[1d,g] and by oxaphosphetane collapse to olefin, or Li^+-catalyzed decomposition to the betaine–lithium halide complex. Oxaphosphetane reversibility[1g] may not be significant in the present study, as it was shown in the past that there is ≤2% reversal in the formation of the parent stilbene compound under similar conditions.[10] An asynchronous cycloaddition with nonparallel ylide and aldehyde π-bonds[1d,g,f] leads to *cis*- and *trans*-oxaphosphetanes **11** and **12**, shown in Chart II. The transition state leading to oxaphosphetane **11**-*cis* would be destabilized more that the one leading to **12**-*cis*, on steric grounds. Consequently, the latter will be formed to a greater extent than **11**-*cis*, affording a greater amount of *Z* olefin in series B.

In a nonpolar medium such as benzene, Li^+ is not solvated and hence free to coordinate with oxaphosphetane and catalyze its irreversible decomposition to betaine–lithium halide adduct.[11] Indeed, upon addition of the aldehyde to the ylide during our reactions, we observed undissolved solids that dissolved in water during workup. The transition state for Li^+-catalyzed decomposition of oxaphosphetane **12**-*cis* to the corresponding betaine–lithium halide adduct would be stabilized slightly more than the analogous transformation of **11**-*cis*. This is because **12**-*cis* is capable of forming a bidentate linkage with Li^+ through a six-membered transition state as depicted in structure **13** (Chart II). An analogous transition state with **11**-*cis* and Li^+ across the four-membered ring would be prevented by strong steric repulsions. According to this, the rate of collapse of oxaphosphetane **12**-*cis* to the corresponding betaine–lithium halide complex (and hence to *Z* olefin) would be faster than that for the analogous decomposition of **11**-*cis*, thus obtaining a greater proportion of *Z* olefin in series B. Similarly, oxaphosphetanes[2d,f] and Li^+-stabilized betaine complexes[2e,f] have been proposed by Allen in his work on semistabilized ylides with benzaldehyde.

It is interesting to note that ylide **1** and aldehyde **6** afforded the two geometrical isomers **9** and **10** in an 1:1 ratio, even though an even smaller (*Z*)-stilbene proportion was expected than that in series A, on account of the steric factors discussed above. Perhaps the group that matters most is the one on the ylide, and not on the aldehyde.[1a,b] However, more work is needed with ortho-substituted benzaldehydes to clarify this.

Given the above mechanistic considerations, Maryanoff[1g] did not find any evidence for an itermediate by NMR in Wittig reactions of semistabilized (or stabilized) ylides. However, very recently, Vedejs[12] observed an oxaphosphetane (by NMR) in the reaction of a semistabilized ylide with an aldehyde. Clearly, more work is needed to clarify whether oxaphoshetanes or other intermediates are involved in Wittig reactions of moderated ylides.

Experimental Section

General. Much of the general experimental details has been described elsewhere[4] (also see paragraph at the end of paper about supplementary material).

(*p*-Carbomethoxybenzyl)triphenylphosphonium Bromide (5f). A solution of *p*-carbomethoxybenzyl bromide (5.73 g, 25 mmol) and triphenylphosphine (6.61 g, 25.2 mmol) in benzene (62 mL) was heated at reflux for 4 h to furnish 9.12 g (74%) of phoshphonium salt **5f** as a white powder.

[*p*-(Dimethylamino)benzyl]triphenylphosphonium Chloride (5g). This was prepared by a procedure similar to that described in the literature.[14] Into a solution of *p*-(dimethylamino)benzyl alcohol (9.38 g, 62 mmol) and triphenylphosphine (16.3 g, 62.1 mmol) in acetonitrile (100 mL) kept at 0 °C was passed HCl gas until saturation. The mixture was heated at reflux for 60 h followed by removal of the solvent. The gummy precipitate was washed with ca. 500 mL of ether and dissolved in water, and 10% K_2CO_3 solution was added to pH ~9. Extraction with chloroform, drying, and concentration gave phosphonium salt **5g** as a pale yellow solid, which was washed with ether to obtain 24.2 g (90%).

[*p*-(Methoxymethoxy)benzyl]triphenylphosphonium Bromide (5j). This was prepared by a procedure identical with that described for the preparation of the ortho isomer.[4] *p*-(Methoxymethoxy)benzyl bromide (1.96 g, 8.5 mmol, 71%) was first prepared from the corresponding alcohol[15] (2.0 g, 11.9 mmol) and triphenylphosphine dibromide (5.01 g, 11.9 mmol) in dry dichloromethane (45 mL) containing pyridine (0.94 g, 11.9 mmol) at 0 °C: IR 1228 (s), 1217 (s), 1199 (s), 1172 (s), 1152 (s), 1077 (s), 997 (s), 920 (m), 590 (w) cm^{-1}. The crude bromide and triphenylphosphine (2.23 g, 8.5 mmol) in benzene (30 mL) was heated at reflux for 2 h to obtain phosphonium salt **5j** as a white powder (2.42 g, 58%).

(*p*-Iodobenzyl)triphenylphosphonium Bromide (5o). A solution of *p*-iodobenzyl bromide (4.06 g, 13.7 mmol) and triphenylphosphine (3.60 g, 13.7 mmol) in benzene (34 mL) was heated at reflux for 15 h to give phosphonium salt **5o** as a white powder, 6.56 g (86%).

General Wittig Carbonyl Olefination Procedure. Wittig reactions were carried out at 25 °C under argon as previously described.[4] To the phosphonium bromide **2** or **5** in benzene (25 mL, except that 50 mL was used for 5 and 10 mmol of phosphonium bromide **2** in series A) was added *n*-butyllithium (1.22 or 1.14 M in hexane, or 0.96 M in ether) and the mixture was stirred for 30 min. The reactions were followed by TLC until disappearance of the aldehyde. After workup and before column chromatography, solutions in ether were prepared at 20 ± 0.1 °C, and aliquots were withdrawn. A weighed quantity of the appropriate GC internal standard was added to each aliquot, and it was analyzed by GC. In a few cases, column chromatography preceded GC analysis to avoid interference of triphenylphosphine

(7) (a) Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778. (b) Vedejs, E.; Snoble, K. A. J.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 1178.

(8) (a) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1954**, *87*, 1318. (b) Schlosser, M.; Christmann, K. F. *Justus Liebigs Ann. Chem.* **1967**, *708*, 1.

(9) (a) Reitz, A. B.; Mutter, M. S.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1984**, *106*, 1873. (b) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr. *Ibid.* **1985**, *107*, 1068.

(10) Vedejs, E.; Fuchs, P. L. *J. Am. Chem. Soc.* **1973**, *95*, 822.

(11) An oxaphosphetane–betaine (LiBr) adduct equilibrium is probable with aromatic aldehydes,[1d] however unlikely, or shifted far toward the side of the latter species, under our reaction conditions (25 °C).

(12) Vedejs, E., private communication.

(13) Jones, R. G.; Gilman, H. *Org. React.* **1951**, *6*, 352.

(14) Marxer, A.; Leutert, T. *Helv. Chim. Acta* **1978**, *61*, 1708.

(15) Bohnsack, H.; Seibert, W. *Riechst. Aromen, Koerperpflegem.* **1965**, *15*, 321, 324, 407. Also see: *Chem. Abstr.* **1966**, *64*, 17349*g*, 17458*f*.

oxide with the peak due to the *E* isomer. The results (Table I) represent mean values of at least two experimental runs and at least two GC determinations with standard deviation: 2–3. The remainder of the solution was concentrated and subjected to column chromatography[4] using benzene or chloroform to elute the column. The major fraction containing both isomers was concentrated and the (*E*)-stilbene was isolated by fractional crystallization.[4] The *Z* isomer was subsequently isolated from the mother liquor by preparative GC. In the majority of cases separation by fractional crystallization failed; thus the two isomers were separated by preparative GC as white solids or viscous colorless liquids. Reagents and quantities used are listed in Table II (see paragraph at the end of the paper about supplementary material). All the *E* isomers thus isolated were cleaved to the corresponding stilbenols, which had similar melting points and IR characteristics with those previously obtained.[4] Exceptions to the above are noted.

Acknowledgment. We are indebted to G. Barbaratsas (Chemistry Department, University of Thessaloniki) for carrying out the elemental microanalyses.

Registry No. **1**, 115032-58-1; **2**, 110983-36-3; **3a**, 100-52-7; **3b**, 104-87-0; **3c**, 939-97-9; **3d**, 3218-36-8; **3e**, 105-07-7; **3f**, 1571-08-0; **3g**, 100-10-7; **3h**, 555-16-8; **3i**, 123-11-5; **3j**, 6515-21-5; **3k**, 878-00-2; **3l**, 459-57-4; **3m**, 104-88-1; **3n**, 1122-91-4; **3o**, 15164-44-0; **4a**, 16721-45-2; **4b**, 39110-21-9; **4c**, 115032-59-2; **4d**, 115032-60-5; **4e**, 59625-61-5; **4f**, 115032-61-6; **4g**, 115032-62-7; **4h**, 6933-17-1; **4i**, 21960-26-9; **4j**, 115032-63-8; **4l**, 59625-60-4; **4m**, 38897-99-3; **4n**, 59625-59-1; **5a**, 1449-46-3; **5b**, 2378-86-1; **5c**, 65413-33-4; **5d**, 36908-37-9; **5e**, 26104-68-7; **5f**, 1253-46-9; **5g**, 115032-56-9; **5h**, 2767-70-6; **5i**, 3462-97-3; **5j**, 115032-57-0; **5l**, 51044-11-2; **5m**, 1530-39-8; **5n**, 51044-13-4; **5o**, 61130-13-0; **6**, 5533-04-0; **7a**, 115032-31-0; **7b**, 115032-33-2; **7c**, 115032-35-4; **7d**, 115032-37-6; **7e**, 115032-39-8; **7f**, 115032-41-2; **7g**, 115032-42-3; **7h**, 115032-43-4; **7i**, 115032-45-6; **7j**, 115032-47-8; **7k**, 115032-48-9; **7l**, 115032-49-0; **7m**, 115032-51-4; **7n**, 115032-53-6; **7o**, 115032-55-8; **8a**, 115032-32-1; **8b**, 115032-34-3; **8c**, 115032-36-5; **8d**, 115032-38-7; **8e**, 115032-40-1; **8f**, 110983-46-5; **8g**, 110983-47-6; **8h**, 115032-44-5; **8i**, 115032-46-7; **8j**, 110983-48-7; **8k**, 110983-49-8; **8l**, 115032-50-3; **8m**, 115032-52-5; **8n**, 115032-54-7; **8o**, 110983-50-1; **9**, 115032-65-0; **10**, 115032-66-1; *p*-carbomethoxybenzyl bromide, 2417-72-3; *p*-(dimethylamino)-benzyl alcohol, 1703-46-4; *p*-(methoxymethoxy)benzyl bromide, 115032-64-9; *p*-iodobenzyl bromide, 16004-15-2.

Supplementary Material Available: General experimental, melting point, IR, NMR, and microanalytical data for phosphonium salts **5f,g,j,o**; table of reagents and conditions for the Wittig reactions (Table II); UV (Table III), melting point, IR, NMR, and microanalytical data for stilbenes **7a–o**, **8a–o**, **9**, and **10** (10 pages). Ordering information is given on any current masthead page.

Notes

Convenient Route to 1,3-Disubstituted Cyclobutanes: An Inexpensive Synthesis of 3-Oxocyclobutanecarboxylic Acid

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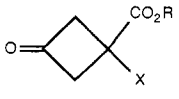
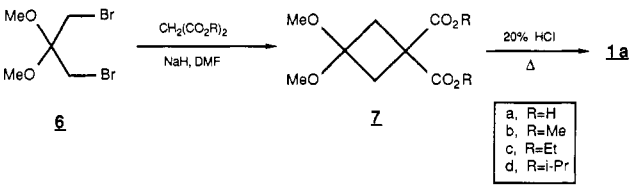
The formation of carbocycles is a common requirement in organic synthesis, and cyclobutanes are undoubtedly the most difficult of the small to medium sized rings to prepare. Although there are good procedures available for the preparation of cyclobutane,[1,2] methylenecyclobutane,[2] and 1,1-disubstituted cyclobutanes,[3,4] routes to 1,3-disubstituted derivatives with functionality amenable to further elaboration are not as plentiful. The title compound **1a** is a very useful precursor in the preparation of the substituted bicyclo[1.1.1]pentane skeleton[5] and is currently under investigation in these laboratories as an intermediate to higher bicyclo[*n*.1.1]alkanes. Other 1,3-disubstituted cyclobutanes have been found useful in the syntheses of thromboxane analogues.[6–9]



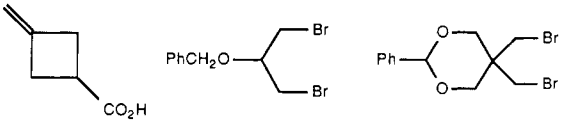
1, X=H
2, X=CO_2R

a, R=H
b, R=Me
c, R=Et
d, R=i-Pr

Scheme I



Previously **1a** has been prepared by the cycloaddition of allene and acrylonitrile[10,11] followed by hydrolysis to the carboxylic acid **3**[12] and subsequent oxidation of the alkene.[13] This is a useful route to **1** and is suited to large-scale preparations; however, it is not without limitation. The cycloaddition requires specialized equipment, and caution must be exercised with the potentially hazardous operation.[12,14] Furthermore, allene is expensive and not a commercially available feedstock in all localities.



3 **4** **5**

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