237. A Short Synthesis of Allene- and [3]Cumulenecarboxylates

by **Elisabeth Kohl-Mines**[1]) and **Hans-Jürgen Hansen**[2])*

Institut de chimie organique de l'Université, Pérolles, CH-1700 Fribourg

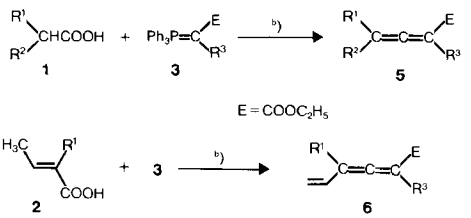
(7.X.85)

It is shown that carboxylic acids, in the presence of Bu_3N and 2-chloro-1-methylpyridinium iodide in toluene or CH_2Cl_2, react with [(alkoxycarbonyl)methylidene]phosphoranes to yield the corresponding esters of allene carboxylic acids *(cf. Scheme 1* and *Table 1)*. This procedure can also be applied to cinnamic acids which form [3]cumulenecarboxylates in low yield *(Table 3)*. Under the same conditions 4-methyl-2-pentynoic acid can be transformed into (2*E*)-4-chloro-2,6-dimethylhepta-2,4,5-trienoate *(Scheme 4)*.

About five years ago, we reported in this journal [1] on a simple method for the synthesis of allenecarboxylates by reacting [(alkoxycarbonyl)methylidene]phosphoranes or the corresponding phosphonium salts with acyl chlorides in the presence of 1 or 2 mol of Et_3N in CH_2Cl_2 or MeCN at room temperature (*cf.* [2]). Intermediates in this reaction are the corresponding acylphosphonium salts which are deprotonated by Et_3N in α-position to the acyl group. In the case of phosphoranes, which are unsubstituted at the ylide C-atom, there is good evidence that ketenes, generated from the acyl chlorides with Et_3N, are the key intermediates for the *Wittig* reaction (*cf.* the discussion in [1]). An efficient synthesis of allene carboxylic esters with alkoxycarbonylmethylidene phosphoranes, therefore, needs a suitable acylating agent or a good ketene generator.

From the numerous methods developed in the last decade for the activation of carboxylic acids (*cf.* [3]) that of *Mukaiyama* and coworkers [4] which utilizes 1-alkyl-2-halogenopyridinium salts and related compounds has found without doubt the broadest

Scheme 1[a])



[a]) R^1, R^2, R^3, see *Table 1*.

[b])  and 2 Bu_3N in toluene or CH_2Cl_2 (see *Table 1*).

[1]) Part of the Ph. D. thesis of *E. K.-M.*, No. 872, University of Fribourg, 1984.

[2]) Present address: Prof. Dr. *H.-J. Hansen*, Central Research Units, *F. Hoffmann-La Roche & Co., Ltd.*, CH-4002 Basle.

application (*cf.* [5]). Therefore, we were interested in testing whether 2-acyloxy-1-alkylpyridinium salts, generated *in situ* from the corresponding carboxylic acids and the appropriate 2-halogenopyridinium salt in the presence of a base, would be able to acylate [(alkoxycarbonyl)methylidene]phosphoranes or possibly even serve as a ketene source. The advantage of such a procedure would be the direct use of carboxylic acids for the synthesis of allenecarboxylates, thus avoiding the sometimes labile acyl chlorides.

Indeed, when we treated AcOH and related acids *(Scheme 1)* with 2-chloro-1-methylpyridinium iodide (**4**) in the presence of 2 mol of Bu_3N and [(ethoxycarbonyl)methylidene]phosphoranes (**3**) in boiling toluene or CH_2Cl_2, we observed the formation of the corresponding allenecarboxylates **5** *(Table 1)*.

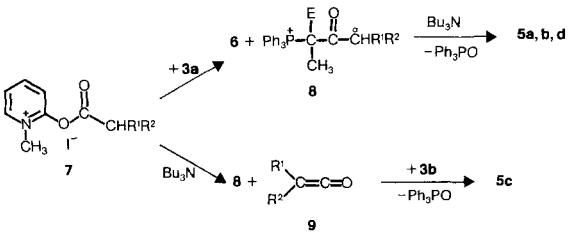
Table 1. *Allenecarboxylates Prepared According to* Scheme 1[a])

Acid			Phosphorane		Solvent	Allenic ester		
Nr.	R^1	R^2	Nr.	R^3		Nr.	Yield [%]	Ref.
1a	H	H	**3a**	CH_3	Toluene (110°/3 h)	**5a**	75	[1] [2]
1b	CH_3	H	**3a**	CH_3	Toluene (110°/3 h)	**5b**	51[b])	[1] [2]
1b	CH_3	H	**3b**	H	Toluene (110°/3 h)	**5c**	40	[1] [2]
1c	CH_3	CH_3	**3a**	CH_3	CH_2Cl_2 (40°/4 h)	**5d**	20	[1] [2]
2a	CH_3	–	**3a**	CH_3	Toluene (110°/3 h)	**6a**	18	[6]
2b	H	–	**3b**	H	Toluene (110°/1.5 h)	**6b**	16	[6]

[a]) See *Scheme 1*; 2 mol of Bu_3N were used in all experiments (*cf. Exper. Part*); none of the reactions were optimized. [b]) Dependence of the yield from the applied base, see *Table 2*.

It is of interest to note that propionic acid (**1b**) reacts also with phosphorane **3b**, known to give allenic esters only if ketenes are present in the reaction mixture (*cf.* [1] and the discussion therein). Similarly, tiglic and crotonic acid (**2a** and **2b**, resp.) yielded the corresponding γ-vinylallenecarboxylates **6a** and **6b**, respectively[3]). These observations indicate that 2-acyloxypyridinium ions (**7**) in the presence of bases may be just as good acyl-group-transfer reagents (→**8**) as they are sources for ketenes (→**9**; *cf. Scheme 2*).

Scheme 2



The yields given in *Table 1* are not optimized, especially with respect to the reactive γ-vinylallenecarboxylates **6a** and **6b**. However, we studied briefly the influence of bases *(Table 2)* and found that tertiary aliphatic bases give similar yields, whereas the yield drops distinctly when pyridine is used. This is in accordance with our earlier observation [1] that acylphosphonium salts of type **8** cannot be deprotonated at C(α) by pyridine in CH_2Cl_2 at room temperature.

[3]) Both esters can also be prepared from the corresponding acyl chlorides with Et_3N as base (*cf.* [6]).

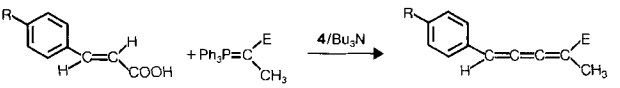
Table 2. *Influence of the Base on the Reaction of Propionic Acid* (**1b**) *with Phosphorane* **3a** *in the Presence of 2-Chloro-1-methylpyridinium Iodide* (**4**)[a]

Base (pK_a)[b]	Reaction time [h]	Yield of **5b** [%]
Bu_3N (10.77)	3	51
Et_3N (11.01)	3.5	53
1,4-Diazabicyclo[2.2.2]octane (8.82)	3–5	57
N-Methylpyrrolidine (10.32)	2.5	60
Pyridine (5.21)	24	15

[a]) In boiling toluene. [b]) pK_a values from [7].

To apply the *Wittig* reaction also to the synthesis of esters of [3]- and [4]cumulenecarboxylic acids (*cf.* [9–12]) we investigated the reaction of cinnamic acids **10a–c** with phosphorane **3a** in the presence of *Mukaiyama*'s reagent **4** *(Table 3)*. The formation of ethyl 2,3,4-pentatrienoates **11a–c** could be observed. However, the yields were reproducibly low. Nevertheless, our reaction represents a very short synthesis for δ-phenyl-substituted [3]cumulenecarboxylates[4]).

Table 3. *Synthesis of 5-Aryl-2,3,4-pentatrienoates* **11** *from Cinnamic Acids* **10** *and Phosphorane* **3a** *(E = COOEt) in the Presence of 2-Chloro-1-methylpyridinium Iodide* (**4**)



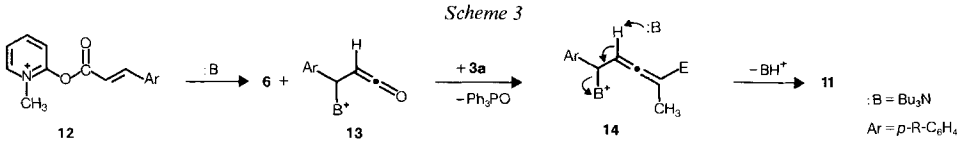
10 **3a** **11**[a])

Cinnamic acid		Solvent	2,3,4-Pentatrienoate	
Nr.	R		Nr.	Yield [%][b])
10a	H	toluene (110°/11 h)	**11a**	8
10b	Cl	CH_2Cl_2 (40°/11 h)	**11b**	6
10c	NO_2	CH_2Cl_2 (40°/9 h)	**11c**	9

[a]) The configuration of the esters was not determined. *p*-Methoxycinnamic acid gave no **11** (R = CH_3O).
[b]) Yields are not optimized.

Since there are no protons that can easily be abstracted in cinnamoylated phosphonium salts corresponding to **8** *(Scheme 2)*, we tentatively assume that the 2-cinnamoyloxy-pyridinium salts **12** react first with Bu_3N in a *Michael* addition followed by decomposition into **6** and the ammonio-ketene **13** *(Scheme 3)*. These intermediates can then undergo the *Wittig* reaction with **3a** to yield the allenic esters **14.** Such allenic esters should exhibit an enhanced acidity at the γ-proton (see [1]) so that elimination of the base and formation of **11** can easily occur.

Scheme 3

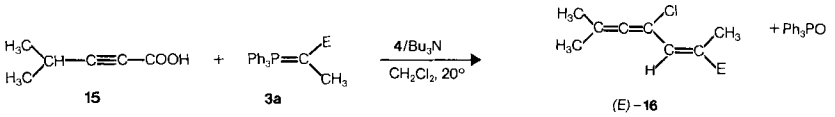


12 **13** **14**

[4]) The [3]cumulenecarboxylates are also formed from the corresponding cinnamoyl chlorides, **3a**, and Et_3N in CH_2Cl_2 [6] [8].

The reactions of phosphorane **3a** and **3b** with tiglic **(2a)** and crotonic acid **(2b)**, respectively *(Table 1)*, demonstrate that γ-deprotonation in the corresponding phosphonium salts (comparable with **8**) or acyloxypyridinium salts (comparable with **7**; *Scheme 2*) takes place as facile as α-deprotonation in **8**. Therefore, we were interested to know how an acetylenecarboxylic acid with an abstractable proton at C(γ) would behave under our reaction conditions. Such a reaction would principally open a short path to esters of [4]cumulenecarboxylic acids (*cf.* [9] [12]). In *Scheme 4*, the result of the reaction of 4-methyl-2-pentynoic acid (**15**) with phosphorane **3a** in the presence of pyridinium salt **4** at room temperature is shown. No doubt, the expected ethyl ester of 2,6-dimethylhepta-2,3,4,5-tetraenoic acid must have been formed in the *Wittig* reaction. However, incorporation of HCl led to the formation of (*E*)-**16** (*cf.* [13]). We were not able to repress this reaction[5]). The assignment of the (*E*)-configuration to **16** is based on the observed relatively large allylic coupling constant (^4J) between CH_3–C(2) and H–C(3) of 2.6 Hz in the ^{1}H-NMR spectrum (*cf.* [15]).

Scheme 4



15 3a (*E*)-16

In conclusion, the reaction of carboxylic acids with phosphoranes in the presence of 2-chloro-1-methylpyridinium salts represents a short access to the esters of allene- and [3]cumulenecarboxylic acids. The mechanism of these 'short-hand' reactions seems to be characterized by the same dichotomy as that found for the reactions with acyl chlorides [1] [6].

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Experimental Part

General. See [1] [16]. UV spectra on a *Perkin-Elmer* spectrophotometer (model *320*). Flash column chromatography (FCC) on silica gel *60 (Merck,* No. *9385)* (*cf.* [17]).

1. *General Procedure for the Preparation of the Allenecarboxylates* **5a–5d**, **6a**, *and* **6b**. To a suspension of 2-chloro-1-methylpyridinium iodide (**4**; 0.85 g, 3.31 mmol; *Fluka AG*) in toluene (5 ml) was added a mixture of phosphorane **3** (2.76 mmol)[6]), the carboxylic acid **1**, **2** (or **10**) (2.76 mmol), and Bu_3N (1.23 g, 6.62 mmol; *Fluka AG*) in toluene (15 ml). The combined mixtures were refluxed for several hours until **4** had been dissolved (dark red soln.). One half of the solvent was evaporated and the residue purified by FCC (hexane/Et_2O). All spectral data of the esters **5a–5d**, **6a**, and **6b** thus obtained were identical with those of the esters prepared from the corresponding acyl chlorides and **3** in the presence of Et_3N [1] [6].

2. *Syntheses of the [3]Cumulene Carboxylates*[7]). The general procedure was applied (see *1*). 2.1. *Ethyl 2-Methyl-5-phenylpenta-2,3,4-trienoate* (**11a**). The purified ester was distilled at 80°/0.1 Torr. UV (EtOH): λ_{max} 270 (4.09), 313 (sh, 3.58). IR (film): 1710 (COOR), 1640 (C=C=C=C). ^{1}H-NMR ($CDCl_3$): 7.70 (*q*, *J* = 1.5, H–C(5)); 7.4 (*m*, 5 arom. H); 4.28 (*q*, *J* = 7.2, CH_3CH_2O); 2.13 (*d*, *J* = 1.5, CH_3–C(2)); 1.37 (*t*, *J* = 7.2, CH_3CH_2O). ^{13}C-NMR ($CDCl_3$): 168.4 (*s*, C(1)); 138.4 (*d*, C(5)); 135.8 (*s*, C(2), C(3), C(4)); 129.5, 128.5, 128.1 (5 arom. C); 60.8 (*t*, CH_3CH_2O); 14.3, 14.0 (2*q*, CH_3CH_2O, CH_3–C(2)).

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[5]) In the presence of 1-ethyl-2-fluoropyridinium tetrafluoroborate (*cf.* [14]) no reaction of **15** and **3a** took place. The reaction was not further investigated.

[6]) Prepared according to published procedures [16] [18].

[7]) For spectral data of cumulenes, see [19].

2.2. *Ethyl 5-(4'-Chlorophenyl)-2-methylpenta-2,3,4-trienoate* (**11b**). UV (EtOH): λ_{max} 273 (4.26). IR (film): 1710 (COOR), 1640 (C=C=C=C). ^{1}H-NMR ($CDCl_3$): 7.60 (*q*, *J* = 1.5, H–C(5)); 7.35 (*m*, 4 arom. H); 4.27 (*q*, *J* = 7.2, CH_3CH_2O); 2.09 (*d*, *J* = 1.5, CH_3–C(2)); 1.33 (*t*, *J* = 7.2, CH_3CH_2O). ^{13}C-NMR ($CDCl_3$): 168.2 (*s*, C(1)); 137.1 (*d*, C(5)); 139.5, 136.9, 134.3, 134.0, 129.1 (5*s*, C(2), C(3), C(5), C(1'), C(4')); 130.7, 128.5 (2*d*, C(2'), C(3'), C(5'), C(6')); 60.9 (*t*, CH_3CH_2O); 14.3, 14.0 (2*q*, CH_3CH_2O, CH_3–C(2)).

2.3. *Ethyl 2-Methyl-5-(4'-nitrophenyl)penta-2,3,4-trienoate* (**11c**). The purified compound was recrystallized twice from pentane; yellow needles, m.p. 76.5–77.5°. UV (EtOH): λ_{max} 295 (4.21), 222 (sh, 4.03). IR ($CHCl_3$): 1700 (COOR), 1640 (C=C=C=C). ^{1}H-NMR ($CDCl_3$): 8.25 (*d*, *J* = 9, H–C(3'), H–C(5')); 7.70 (br. *s*, H–C(5)); 7.52 (*d*, *J* = 9, H–C(2'), H–C(6')), 4.32 (*q*, *J* = 7.2, CH_3CH_2O); 2.12 (*d*, *J* = 1.8, CH_3–C(2)); 1.37 (*t*, *J* = 7.2, CH_3CH_2O).

3. *Attempted Synthesis of Ethyl 2,6-Dimethylhepta-2,3,4,5-tetraenoate; Isolation of Ethyl (2E)-4-Chloro-2,6-dimethylhepta-2,4,5-trienoate* ((*E*)-**16**). *4-Methyl-2-pentynoic acid* (**15**; 0.31 g, 2.76 mmol)[8]) was reacted in CH_2Cl_2 at 5° with **3a** according to the general procedure (50 min). Workup and FCC (hexane/Et_2O 2:1) yielded 0.31 g (52%) of pure (*E*)-**16** as a yellow oil. IR (film): 1955 (C=C=C); 1720 (COOR); 1650, 1630 (C=C). ^{1}H-NMR ($CDCl_3$): 6.45 (*q*, *J*(CH_3–C(3),CH_3–C(2)) = 2.6, H–C(3)); 4.17 (*q*, *J* = 7.2, CH_3CH_2O); 1.93 (*s*, CH_3–C(6), 3 H–C(7)); 1.88 (*d*, *J*(CH_3–C(2), H–C(3)) = 2.6, CH_3–C(2)); 1.24 (*t*, *J* = 7.2, CH_3CH_2O). MS ($C_{11}H_{15}ClO_2$; 214.07): 215 (6, $M^+ + 1$)[9]), 214 (48, M^+)[9]), 179 (80, $M^+ - Cl$), 151 (62), 105 (100), 91 (55), 77 (45).

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[8]) Prepared in analogy to the procedure described in [20]. The spectral data were identical with those published [21].

[9]) The peaks showed the correct isotopic ratio of 3:1 for the presence of 1 Cl-atom.