238. Synthesis of Alkenyl-Substituted Allenecarboxylates[1])

by **Robert Werner Lang**[2]), **Elisabeth Kohl-Mines**, and **Hans-Jürgen Hansen**[3])*

Institut für Organische Chemie der Universität, Pérolles, CH–1700 Freiburg

(7.X.85)

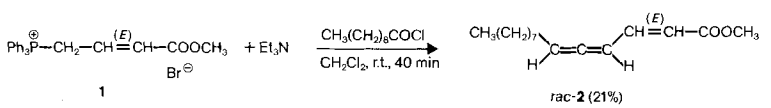
The *Wittig* olefination of decanoyl chloride by using the phosphonium salt **1** in the presence of two equivalents of Et_3N represents a one-step synthesis of the racemic form of the naturally occurring pheromone (–)-**2** which contains an alkenyl-substituted allenic moiety *(cf. Scheme 1)*. It is also shown, that unsaturated acyl chlorides which contain at least one γ-H-atom undergo the *Wittig* reaction with an appropriate phosphorane yielding γ-alkenyl-substituted α-allenic esters and α-allenic γ-lactones, respectively *(cf. Schemes 2* and *3)*.

Allenes containing unsaturated substituents which interact with the allene moiety are useful synthetic building blocks. Such functionalities[4]) may effectively be built up by utilizing the *Wittig* reaction for the construction of the allene skeleton whether by reacting a phosphorane with a ketene (or a ketene equivalent) or by coupling a phosphacumulene with an aldehyde or a ketone (*cf. Vol. 1* of [1]). In this context, our recent interest was focused especially on the preparation of α-allenic esters by reacting a resonance-stabilized phosphorane with an appropriate coupling partner [3] [4].

In the past, we reported on the synthesis of α-allenic esters containing alkyl and/or aryl substituents [4] [5]. Now, we would like to present the extension of this synthesis to allenic esters having a conjugated double bond either in between the ester and the allene functionality or simply as an additional γ-substituent. In contrast to numerous publications on the synthesis and reactions of vinyl-allenes (*cf. Chap. 4* in [2]), γ-vinyl-α-allenic esters have so far not been reported in the literature.

Methyl (–)-(*E*)-2,4,5-tetradecatrienoate (**2**), the sex pheromone produced by the male dried-bean beetle [6], has been synthesized in both racemic and optically active form in various multi-step transformations [1] [2]. While using the easily accessible phosphonium salt **1** [7], we could isolate the fairly stable allenic ester *rac*-**2** in 21% yield *(Scheme 1)*. Despite the fact of obtaining racemic **2** in low yield, our approach represents most likely the shortest access to the anticipated pheromone.

Scheme 1



1 *rac*-**2** (21%)

[1]) Parts of the Ph. D. thesis of *R.W.L.*, No. 817 (1980), and of *E.K.-M.*, No. 872 (1984), University of Fribourg.

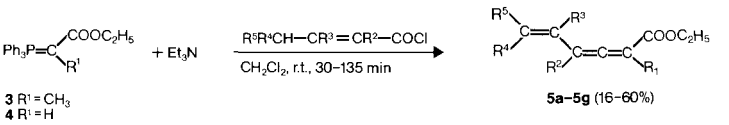
[2]) Present address: Dr. *Robert W. Lang*, Central Research Laboratories, *Ciba-Geigy AG*, CH–4002 Basle.

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

[4]) For recent reviews on the synthesis and reactions of allenes, see [1] [2].

In contrast to the mechanistic statement outlined for a related process [8], we do have good reasons for supposing *in situ* generated ketenes as the reactive intermediates in our synthesis of α-allenic esters (*cf.* [4a] and the discussion therein). As a matter of fact, we were interested to investigate whether vinyl ketenes would undergo such olefination reactions. According to the base-induced generation of ketenes from acyl chlorides, vinyl-ketenes should be accessible from α,β-unsaturated acyl chlorides having at least one γ-H-atom[5]). To apply the *Wittig* olefination to the synthesis of γ-vinyl-substituted α-allenic esters, we investigated the reaction of several α,β-unsaturated acyl chlorides with the phosphoranes **3** and **4** in the presence of Et_3N *(Scheme 2)*. In spite of having non-optimized reaction conditions, the *Table* documents the easy access to the anticipated alkenyl substituted allenic esters[6]). Still further elongation of unsaturation is demonstrated by base-induced ε-deprotonation and olefination of 2,4-hexadienoyl chloride (Entry **5g**).

Scheme 2[a])



3 $R^1 = CH_3$
4 $R^1 = H$

5a–5g (16–60%)

[a]) R^2 to R^5 see *Table 1.*

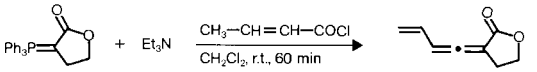
Table. *γ-Alkenyl-Substituted Allenic Esters Prepared According to* Scheme 2[a])

	Allenic ester					Phos-	Acyl chloride	Reaction	Yield
	R^1	R^2	R^3	R^4	R^5	phorane		conditions	[%]
5a	CH_3	H	CH_3	H	H	**3**	$(CH_3)_2C=CH-COCl$	r.t./45 min	60
5b	CH_3	H	H	H	H	**3**	$CH_3-CH=CH-COCl$	r.t./55 min	30
5c	CH_3	CH_3	H	H	H	**3**	$CH_3-CH=C(CH_3)-COCl$	40°/135 min	50
5d	CH_3	H	H	CH_3	H	**3**	$C_2H_5-CH=CH-COCl$	r.t./50 min	40
5e	H	CH_3	H	H	H	**4**	$CH_3-CH=C(CH_3)-COCl$	r.t./135 min	45
5f	H	H	H	H	H	**4**	$CH_3-CH=CH-COCl$	r.t./35 min	16
5g	CH_3	H	H	H	$CH=CH_2$	**3**	$CH_3-CH=CH-CH=CH-COCl$	r.t./30 min	16

[a]) All reactions were performed in CH_2Cl_2.

Based on the ketene-olefination methodology, we have recently published the first synthesis of α-allenic γ-lactones [5]. As it is outlined in *Scheme 3,* the preparation of the γ-vinyl-substituted α-allenic γ-lactone **7** from **6** further supports the above elongation of unsaturation following the principle of vinylology.

Scheme 3

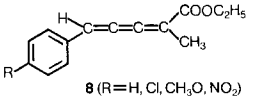


6 **7** (31%)

[5]) For recent papers dealing with the base-induced generation of vinyl-ketenes, see [9] [10].

[6]) The esters **5c** and **5e** react with dimethyl acetylenedicarboxylate in boiling benzene to yield the corresponding esters of (2,3-dimethoxycarbonylphenyl)acetic acid (*cf.* Ph. D. thesis of *E. K.-M.* cited in *Footnote 1*). Similarly, **5e** reacts with maleic anhydride.

The reaction of phosphorane **3** with α,β-unsaturated acyl chlorides which have no γ-H-atom, like cinnamoyl chloride for example, in the presence of Et_3N lead to a carbon framework with 3 cumulated double bonds (*e.g.* **8**). The yields of these reactions, which all were done for a qualitative survey only, are rather low (below 10%). From the mechanistic point of view, it seems very unlikely that cumulated ketenes should play a significant role as reactive intermediates for the synthesis of such cumulated systems. For a more detailed discussion of a very similar process, see [3].



8 (R=H, Cl, CH_3O, NO_2)

Finally, it is noteworthy that the *Wittig* reaction of a ketene (or ketene equivalent) with an appropriate phosphorane has become (at least at laboratory scale) the method of choice for the synthesis of molecules containing an allene skeleton. Our method represents an extension of this synthetic conception.

We thank Dr. *M. Cosandey* and Dr. *T.A. Jenny* for NMR spectra. The support of this work by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

General. See [4] [11]. All chemical yields refer to non-optimized reaction conditions. The phosphorane **3** was prepared according to [12]; **4** was purchased from *Fluka AG* (practical grade).

1. *[(E)-3-(Methoxycarbonyl)-2-propenyl]triphenylphosphonium Bromide* (**1**). Reaction of 5.56 g (21 mmol) of Ph_3P and 3.58 g (20 mmol) of methyl 4-bromocrotonate[7]), according to [7], yielded 8.35 g (95%) of colourless, crystalline **1**: m.p. 181–183° (dec.; [7]: 179–180°). ^{1}H-NMR (90 MHz, $CDCl_3$): 8.16–7.46 (*m*, 15 arom. H); 7.00–6.25 (*m*, 2 H–C(2), 2 H–C(3)); 5.27 (*dd*, J = 15.8, 7.2, 2 H–C(1)); 3.65 (*s*, CH_3O).

2. *Methyl (E)-2,4,5-Tetradecatrienoate* (**2**). To a soln. of 4.41 g (10 mmol) of **1** in CH_2Cl_2 (40 ml) were added, under N_2, 2.02 g (20 mmol) of Et_3N in CH_2Cl_2 (10 ml) at r.t. Thereafter, 1.90 g (10 mmol) of decanoyl chloride in CH_2Cl_2 (10 ml) were added at a rate that maintained the exothermic reaction near r.t. Stirring for another 30 min followed by standard workup [4] yielded after TLC separation (silica gel; hexane/Et_2O 9:1) 0.50 g (21%) of *rac*-**2** as an easily polymerizable yellowish oil. All spectral data of **2** were identical with those reported in [14].

3. *General Procedure for the Preparation of the γ-Alkenylated α-Allenic Esters* **5a–g.** To a soln. of **3** (1.00 g, 2.76 mmol) or **4** (1.00 g, 2.86 mmol) in CH_2Cl_2 (10 ml), 1 equiv. of Et_3N in CH_2Cl_2 (5 ml) was added under N_2. After having added 1 equiv. of the acyl chloride in CH_2Cl_2 (5 ml) at r.t. and further stirring (see the *Table*), the allenic esters were isolated and purified by standard conditions [4].

3.1. *Ethyl 2,5-Dimethyl-2,3,5-hexatrienoate* (**5a**) was purified by distillation (92–93°/20 Torr); yield 60%. UV (EtOH): λ_{max} 222 (4.37). IR (film): 3090 (C=CH_2); 1945 (C=C=C); 1715 (C=O); 1630 (C=C). ^{1}H-NMR (90 MHz, CCl_4): 6.05 (*q*, J = 3, H–C(4)); 4.93 (*m*, H–C(6) *cis* to CH_3); 4.85 (*m*, H–C(6) *trans* to CH_3); 4.10 (*q*, J = 7.2, CH_3CH_2O); 1.87 (*d*, J = 3, CH_3–C(2)); 1.76 (*m*, CH_3–C(5)); 1.26 (*t*, J = 7.2 CH_3CH_2O).

3.2. *Ethyl 2-Methyl-2,3,5-hexatrienoate* (**5b**). After TLC and distillation (90°/20 Torr): yield 30%. UV (EtOH): λ_{max} 220 (4.39). IR(film): 3090 (CH=CH_2); 1945 (C=C=C); 1715 (C=O); 1615 (C=C). ^{1}H-NMR (90 MHz, CCl_4): 6.35–5.90 (*m*, H–C(4), H–C(5)); 5.40–4.90 (*m*, 2 H–C(6)); 4.13 (*q*, J = 7.2, CH_3CH_2O); 1.85 (*d*, J = 3, CH_3–C(2)); 1.25 (*t*, J = 7.2, CH_3CH_2O).

---

[7]) Methyl crotonate was brominated with *N*-bromosuccinimide according to [13] in 56% yield, after distillation at 83–85°/12 Torr. ^{1}H-NMR (90 MHz, CCl_4): 7.15–6.68 (*m*, H–C(3)); 5.98 (*dt*, J = 16.5, 1.0, H–C(2)); 4.02 (*dd*, J = 7.5, 1.0, 2 H–C(4)); 3.73 (*s*, CH_3O).

3.3. *Ethyl 2,4-Dimethyl-2,3,5-hexatrienoate* (**5c**). After TLC, the yield was 50%. UV (EtOH): λ_{max} 222 (4.21). IR (film): 3090 (C=CH_2); 1945 (C=C=C); 1715 (C=O); 1618 (C=C). ^{1}H-NMR (90 MHz, CCl_4): 6.72 (*dd*, J_{trans} = 17.4, J_{cis} = 10.8, H–C(5)); 5.13 (*d*, J_{trans} = 17.4, H–C(6) *trans* to H); 5.03 (*d*, J_{cis} = 10.8, H–C(6) *cis* to H); 4.10 (*q*, *J* = 7.2, CH_3CH_2O); 1.85 (*s*, CH_3–C(2)); 1.81 (*s*, CH_3–C(4)); 1.23 (*t*, *J* = 7.2, CH_3CH_2O).

3.4. *Ethyl (Z)-2-Methyl-2,3,5-heptatrienoate* (**5d**). After TLC, the yield was 40%. UV (EtOH): λ_{max} 225 (4.42). IR (film): 3040 (C=CH); 1942 (C=C=C); 1718 (C=O); 1620 (C=C). ^{1}H-NMR (90 MHz, CCl_4): 6.20 (*qd*, *J* = 3, J_d = 10.2, H–C(4)); 6.00–5.67 (*m*, H–C(5)); 5.67–5.33 (*qd*, J_q = 6.6, J_d = 10.8, H–C(6))[8]; 4.10 (*q*, *J* = 7.2, CH_3CH_2O); 1.83 (*d*, ^5J = 3, CH_3–C(2)); 1.74 (*dd*, J_{vic} = 6.6, J_{all} = 1.5, 3H–C(7)); 1.25 (*t*, *J* = 7.2, CH_3CH_2O).

3.5. *Ethyl 4-Methyl-2,3,5-hexatrienoate* (**5e**). After TLC, the yield was 45%. UV (EtOH): λ_{max} 218 (4.43). IR (film): 3050 (C=CH_2); 1945 (C=C=C); 1718 (C=O); 1617, 1585 (C=C). ^{1}H-NMR (90 MHz, CCl_4): 6.27 (*ddd*, J_{trans} = 17.4, J_{cis} = 10.5, ^5J(2,5) = 1.2, H–C(5)); 5.65–5.45 (*m*, H–C(2)); 5.20 (*dd*, J_{trans} = 17.4, J_{gem} = 1.2, H–C(6) *trans* to H); 5.10 (*dd*, J_{cis} = 10.5, J_{gem} = 1.2, H–C(6) *cis* to H); 4.13 (*q*, *J* = 7.2, CH_3CH_2O); 2.89 (*d*, *J* = 3, CH_3–C(4)); 1.25 (*t*, *J* = 7.2, CH_3CH_2O).

3.6. *Ethyl 2,3,5-Hexatrienoate* (**5f**). After flash chromatography (hexane/Et_2O 4:1), **5f** could be isolated in only 16%[9]) yield. UV (EtOH): λ_{max} 215.5 (4.5). IR (film): 3100 (C=CH_2); 1945 (C=C=C); 1720 (C=O); 1615 (C=C). ^{1}H-NMR (90 MHz, CCl_4): 6.40–5.95 (*m*, H–C(4), H–C(5)); 5.75–5.55 (*m*, H–C(2)); 5.50–5.03 (*m*, 2H–C(6)); 4.13 (*q*, *J* = 7.2, CH_3CH_2O); 1.28 (*t*, *J* = 7.2, CH_3CH_2O).

3.7. *Ethyl (E)-or (Z)-2-Methyl-2,3,5,7-octatetraenoate* (**5g**). After TLC, the yield was 16%. UV (EtOH): λ_{max} 251.5 (4.35); 260 (4.45); 270 (4.35). IR (film): 3080 (C=CH_2); 1940 (C=C=C); 1715 (C=O); 1630, 1595 (C=C); 960 (CH=CH-*trans*). ^{1}H-NMR (90 MHz, CCl_4): 6.50–5.85 (*m*, H–C(7), H–C(6), H–C(5), H–C(4)); 5.15 (*dd*, *J* = 17, J_{gem} = 1.8, H–C(8) *trans* to H); 5.03 (*dd*, *J* = 10.2, J_{gem} = 1.8, H–C(8) *cis* to H); 4.12 (*q*, *J* = 7.2, CH_3CH_2O); 1.83 (*d*, *J* = 2.7, CH_3–C(2)); 1.33 (*t*, *J* = 7.2, CH_3CH_2O). ^{13}C-NMR ($CDCl_3$): 214.32 (*s*, C(3)); 166.81 (*s*, C(1)); 136.06 (*d*, C(7)); 133.37 (*d*, C(5)); 125.61 (*d*, C(6)); 118.10 (*d*, C(8)); 96.96 (*s*, C(2)); 96.54 (*d*, C(4)); 61.16 (*t*, CH_3CH_2O); 15.44 (*q*, CH_3–C(2)); 14.2 (*q*, CH_3CH_2O).

4. *2-(1,3-Butadienylidene)-4-butanolide* (**7**). According to the general procedure (*cf. Chap. 3*), **6** was reacted with crotonoyl chloride in the presence of Et_3N at r.t. for 60 min[10]). Usual workup followed by flash chromatography (hexane/Et_2O 4:1) yielded **7** in 31%. UV (EtOH): λ_{max} 222 (4.01). IR (CH_2Cl_2): 3060 (C=CH_2); 1955 (C=C=C); 1755 (C=O); 1615 (C=C). ^{1}H-NMR (90 MHz, $CDCl_3$): 6.25–5.85 (*m*, H–C(3'), H–C(2')); 5.35–4.85 (*m*, 2 H–C(4')); 3.80 (*t*, *J* = 7.5, 2 H–C(4)); 2.50–2.15 (*m*, 2 H–C(3)).

5. *Attempted Synthesis of Ethyl [3]Cumulenecarboxylates by Using the* Wittig *Olefination*. The reaction of an equimolar amount of **3**, of the 4-substituted cinnamoyl chloride[11]), and of Et_3N in MeCN at r.t. for several hours gave after usual workup and product purification the corresponding [3]cumulene carboxylates in low yield (< 10%). In the case of cinnamoyl chloride, *ethyl 2-methyl-5-phenyl-2,3,4-pentatrienoate* (**8**, R=H) was distilled at 80°/0.1 Torr. IR (film): 1710 (br., C=O); 1640 (C=C=C=C). ^{1}H-NMR (90 MHz, CCl_4): 7.56 (*q*, *J* = 1.5, *ca.* 2.07→*s*, H–C(5)); 7.30 (br. *s*, 5 arom. H); 4.22 (*q*, *J* = 7.2, CH_3CH_2O); 2.07 (*d*, *J* = 1.5, CH_3–C(2)); 1.34 (*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*); 129.5, 128.5, 128.1 (all *d*, 5 arom. C); 60.8 (*t*, CH_3CH_2O); 14.3 (*q*); 14.0 (*q*).

---

[8]) J_d = 10.8 for H–C(6) which corresponds to a *cis* coupling between H–C(5) and H–C(6) indicates the (*Z*)-isomer to be the only detectable product.

[9]) The exceptional low yield may be due to a 1,3-H shift in **5f**, which led to the corresponding triple-bond isomer (IR band at 2260 cm^{-1}; see also [4]) which was difficult to remove by chromatography.

[10]) The 2-(triphenylphosphoranylidene)-4-butanolide (**6**) was prepared according to [15] (m.p. 231°).

[11]) The 4-substituted cinnamoyl chlorides (R = H, Cl, CH_3O, NO_2) were prepared according to literature procedures [16].

REFERENCES

[1] 'The Chemistry of the Allenes', Ed. S. R. Landor, Academic Press, London, 1982, Vol. 1–3.
[2] H. F. Schuster, G. M. Coppola, 'Allenes in Organic Synthesis', J. Wiley & Sons, New York, 1984.
[3] E. Kohl-Mines, H.-J. Hansen, *Helv. Chim. Acta* **1985,** *68,* 2244.
[4] a) R. W. Lang, H.-J. Hansen, *Helv. Chim. Acta* **1980,** *63,* 438; b) *Org. Synth.* **1984,** *62,* 202.
[5] R. W. Lang, H.-J. Hansen, *Helv. Chim. Acta* **1980,** *63,* 1204.
[6] D. F. Horler, *J. Chem. Soc. (C)* **1970,** 859.
[7] E. Buchta, F. Andree, *Chem. Ber.* **1959,** *92,* 3111.
[8] H.-J. Bestmann, H. Hartung, *Chem. Ber.* **1966,** *99,* 1198.
[9] R. Huston, M. Rey, A. S. Dreiding, *Helv. Chim. Acta* **1982,** *65,* 1563.
[10] I. Marko, B. Ronsmans, A.-M. Hesbain-Frisque, S. Dumas, L. Ghosez, B. Ernst, H. Greuter, *J. Am. Chem. Soc.* **1985,** *107,* 2192.
[11] R. W. Lang, H.-J. Hansen, *Helv. Chim. Acta* **1979,** *62,* 1025.
[12] O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, P. Zeller, *Helv. Chim. Acta* **1957,** *40,* 1242.
[13] H. Schmid, P. Karrer, *Helv. Chim. Acta* **1946,** *29,* 573.
[14] P. D. Landor, S. R. Landor, S. Mukasa, *Chem. Commun.* **1971,** 1638.
[15] S. Flizár, R. F. Hudson, G. Salvadori, *Helv. Chim. Acta* **1963,** *46,* 1580.
[16] 'Organikum', VEB Deutscher Verlag der Wissenschaften, Berlin, 1969, 9th edn., p. 469.