A Modified Wittig Synthesis of 6,10-Dimethyl-3,9-undecadien-2-one, Ethyl 5,9-Dimethyl-2,8-decadienonate, and Their α-Alkyl Homologs: Stereochemistry of the Reaction and Conformation of the Products

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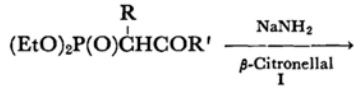
In previous papers,[1-3] the modified Wittig reaction of citrals with diethyl 2-oxophosphonates was described. When the substituent on the α-carbon atom of the phosphonate was methyl group or hydrogen, the resultant C=C double bond of the condensation product had only *trans* configuration.

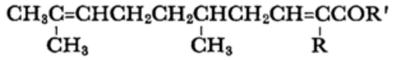
On the other hand, when the substituent was ethyl group, the formation of small amounts of *cis* isomers was observed together with the major formation of *trans* isomers.

It was of interest to investigate whether the saturation of the α,β-unsaturated linkage to the aldehydic group in citrals affects the stereochemistry of the reaction. In the present report, β-citronellal (I) was condensed with various diethyl 1-alkyl-2-oxoalkylphosphonates (II) or diethyl 1-ethoxycarbonylalkylphosphonates (III) under usual reaction conditions.



$$(EtO)_2P(O)\overset{R}{C}HCOR' \xrightarrow[\beta\text{-Citronellal}\ \mathrm{I}]{NaNH_2}$$

II: R'=Alkyl
III: R'=OEt



$$CH_3\underset{CH_3}{C}=CHCH_2CH_2\underset{CH_3}{C}HCH_2CH=\underset{R}{C}COR'$$

IV: $R=H$, $R'=CH_3$
V: $R=CH_3$
VI: $R=C_2H_5$
VII: $R=H$, $R'=C_2H_5$
VIII: $R=H$, $R'=OEt$
IX: $R=CH_3$
X: $R=C_2H_5$

The results are summarized in Table 1. From these data the following points were notable: i) The relative amounts of the *cis* isomers in the products augmented with increasing size of the alkyl substituent on the α-carbon atom of the phosphonates. ii) The ethoxycarbonyl group on the α-carbon atom of a phosphonate was advantageous over the alkyl group in increasing the *cis*-*trans* ratio of the resulted olefins. iii) Saturation of the α,β-unsaturated linkage in citrals increased the proportion of a *cis* isomer in the product, although the dominance of a *trans* isomer over a *cis* isomer was unchanged.

The infrared and ultraviolet absorption data of the products are given in Table 2. It is well known that the α,β-unsaturated carbonyl compounds may exist in two possible conformations, *i.e.*, *s-trans*- and *s-cis*-forms. In the case of 3-*trans*-V and 3-*trans*-VI, the difference of wave numbers between the C=O and the C=C stretching vibration is less than 30 cm^{-1} and the intensity of the K-band at 232—233 mμ is very strong. These spectral properties are probably ascribed to the *s-trans* conformation. On the other hand, 3-*cis*-V and 3-*cis*-VI appear to have the *s-cis* conformation, since the difference of the wave numbers between the C=O and the C=C stretching vibration is more than 60 cm^{-1} and the K-band is rather shifted bathochromically and is remarkably weakened in intensity.*1 The splitting of the C=O stretching infrared absorption bands of 3-*trans*-IV and 4-*trans*-VII may be ascribed to an equilibrium between the *s-trans*- and *s-cis*-conformations as demonstrated in the case of *trans*-3-penten-2-one and its analogs.[1,5] The ascription seems to be supported by the fact that each of the splitting carbonyl bands of 3-*trans*-IV and 4-*trans*-VII apparently corresponds in its position to the carbonyl bands of 3-*trans*-V and 3-*trans*-VI, and 3-*cis*-V and 3-*cis*-VI, respectively.

Examination of scale models reveals that 3-*trans*-IV and 4-*trans*-VII can exist as two hindrance-free conformers. In the case of 3-*trans*-V and 3-*trans*-VI, the *s-trans* conformation is less-hindered, while the steric hindrance of 3-*cis*-V and 3-*cis*-VI is apparently stronger in the *s-trans*-conformation than in the *s-cis*-. These considerations also substantiate the above conclusions.

Analogous considerations with scale models of the α,β-unsaturated carboxylates disclosed that either of the two possible conformations is substantially hindrance-free and therefore energetically more favored *s-trans* form is the preferred conformation.

In summary, apparent difference in a steric hindrance between an α,β-unsaturated ketone and the relevant carboxylate is probably one of the cause for the different *cis-trans* ratio in these compounds obtained by means of the modified Wittig reaction.

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[1] K. Sasaki, This Bulletin, **39**, 2703 (1966).
[2] K. Sasaki *ibid.*, **40**, 2967 (1967).
[3] K. Sasaki, *ibid.*, **40**, 2968 (1967).
[4] W. L. Walton and R. B. Hughes, *J. Am. Chem. Soc.*, **79**, 3985 (1957).

*1 Analogous spectroscopic ascription has been reported for the conformations of 3-methyl-, 3-ethyl-*trans*-3-penten-2-one, and 3-methyl-*cis*-3-penten-2-one by Mecke and Noack.[5]

[5] R. Mecke and K. Noack, *Chem. Ber.*, **93**, 210 (1960); *cf.* E. A. Braude and C. J. Timmons, *J. Chem. Soc.*, **1955**, 3766.

TABLE 1. YIELDS AND COMPOSITIONS OF PRODUCTS

Attempted compound	Method[a]	Bp °C/mmHg	Yield %	Composition of the product[b] cis	Composition of the product[b] trans	Formula	Analysis C, % Found	Analysis C, % Calcd	Analysis H, % Found	Analysis H, % Calcd
IV[c]	A	74—76/0.15	84	0	100	$C_{13}H_{22}O$	77.71	80.35	11.37	11.41
VII	A	83—85/0.18	83	0	100	$C_{14}H_{24}O$	80.14	80.71	11.49	11.61
V	A	74.5—78/0.15	82	5.5	94.5	$C_{14}H_{24}O$	80.62	80.71	11.49	11.61
VI	B	82—88/0.3	47	19.3	80.7					
VIII	A	88—94/0.35	75	6.5	93.5	$C_{14}H_{24}O_2$	74.93	74.95	11.04	10.78
IX	A	90—95/0.3	58	20.1	79.9	$C_{15}H_{26}O_2$	75.87	75.58	10.94	10.99
IX	B	87—94/0.3	18	17.9	82.1					
X	A	93—100/0.3	67	43.9	56.1	$C_{16}H_{28}O_2$	75.93	76.14	11.08	11.18

a) See Experimental.

b) Yields and compositions of the products were determined by gas chromatography.

c) The discrepancy between the found and the calculated values may be attributable partly to the decomposition during the distillation and partly to the contamination with a small amount of phosphorus compounds: 2,4-Dinitrophenylhydrazone of IV (mp 78.5—79.0°C) gave satisfactory results for the expected empirical formula. Found: C, 61.29; H, 6.97; N, 15.24%. Calcd for $C_{19}H_{26}N_4O_4$: C, 60.95; H, 7.00; N, 14.96%.

TABLE 2. INFRARED AND ULTRAVIOLET ABSORPTION DATA

Compound	Infrared absorption (liquid film) cm^{-1} [a] $\nu_{C=O}$	$\nu_{C=O}$	$\nu_{C=C}$	δ_{C-H}	Family band[d]	$\nu_{C=O}-\nu_{C=C}$	Ultraviolet absorption λ_{max}^{EtOH}	ε_{max}
3-*trans*-IV	1678 (vs),	1689 (s)[c]	1630 (s)	979 (s)			223.5	14900
4-*trans*-VII	1676 (vs),	1696 (s)[c]	1632 (vs)	979 (s)			225	14700
3-*trans*-V[b]	1670 (vs)		1641 (m)			29	232	13800
3-*cis*-V[b]		1689 (s)	1626 (m)			63	237	3500
3-*trans*-VI[b]	1666 (vs)		1638 (m)			28	233	15300
3-*cis*-VI[b]		1691 (s)	1629 (m)			63	238.5	4100
2-*trans*-VIII	1724 (vs)		1655 (m)	982 (m)	739 (w)		210	16100
2-*cis*-VIII[b]	1719 (vs)		1640 (m)					
2-*trans*-IX[b]	1715 (vs)		1654 (m)		741 (m)		219	13600
2-*cis*-IX[b]	1721 (vs)		1649 (m)				217.5	11600
2-*trans*-X[b]	1718 (vs)		1650 (m)		753 (m)		219	14300
2-*cis*-X[b]	1717 (vs)		1646 (w)				217.5	9400

a) Infrared spectra were measured through the kindness of Dr. Yoshitaka Matsuoka and Mr. Kenya Sakaguchi of Eisai Research Laboratories and Dr. Hisatake Ono and Dr. Asashi Kondo of Fuji Photo Film Co., Ltd.

b) These compounds were isolated by gas chromatography, the facilities of which were given by Mr. Kozo Takashima and Mr. Hiroo Miyazaki of Ohkura Rikagaku Kenkyusho Co., Ltd.

c) Splitting carbonyl bands.

d) A band characteristic of a *trans*-α,β-unsaturated carboxylate.[3,4]

Experimental

β-Citronellal (I). Commercial citronellal[*2] was purified by conversion to its sodium hydrogen sulfite-adduct followed by decomposing the adduct with sodium carbonate to yield the free aldehyde, which was gas chromatographically pure. Bp 78—79°C/8 mmHg.

2,4-Dinitrophenylhydrazone: Mp 78.5—79°C (lit.[6] mp 78°C).

Diethyl 2-Oxoalkyl- and 1-Ethoxycarbonylalkylphosphonates. These phosphonates were prepared from triethylphosphite and appropriate α-bromocarbonyl compounds by means of Michaelis-Arbuzov reaction.[1,3]

3,6,10-Trimethyl-3,9-undecadien-2-ones (V). (*A typical Example of the General Procedure*). *Method A.* To a suspension of 1.56 g (0.04 mol) of sodium amide in 30 ml of dry dimethylformamide (DMF), there was added a solution of 8.33 g (0.04 mol) of diethyl 1-methyl-2-oxopropylphosphonate in 20 ml of dry DMF with stirring and cooling in an ice-salt bath. Stirring and cooling were continued and dry nitrogen gas was passed into the mixture until the evolution of ammonia had ceased. The resultant solution was cooled below −10°C and

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[*2] This is of natural origin and the natural aldehyde is now known to be the β-form. P. Z. Bedoukian, " Perfumery and Flavoring Synthetics," 2nd ed., Elsvier Publ. Co., Amsterdam (1967), pp. 113, 168.

6) C. F. H. Allen, *J. Am. Chem. Soc.*, **52**, 2955 (1930).

treated dropwise with 6.17 g (0.04 mol) of β-citronellal in 20 m*l* of dry DMF. After the solution had stood overnight, the solvent was removed under vacuum and the residue was poured into water and extracted with ether. The ethereal extract was washed with water and dried over sodium sulfate. The solvent being evaporated, the residue was distilled under reduced pressure to yield V as a colorless oil.

Method B. To the carbanion of diethyl 2-oxopropylphosphonate, prepared from 7.77 g (0.04 mol) of the phosphonate in a manner similar to the Method A, there was added dropwise 5.96 g (0.042 mol) of methyl iodide with stirring and cooling in an ice-water bath and the mixture was allowed to stand overnight. After the mixture was cooled below −10°C, 1.56 g (0.04 mol) of sodium amide was added all at once and the mixture was stirred under a slow stream of dry nitrogen gas. The resultant carbanion of diethyl 1-methyl-2-oxopropylphosphonate was treated with β-citronellal in an analogous manner to the Method A to give V as a colorless oil.

Procedures similar to those described above gave the ketones IV, VI, and VII. A minor modification of the condensation conditions was required for the preparation of the carboxylates VIII, IX, and X; at 75°C for 3 hr (for the preparation of X, Method A) to 24 hr (for the preparation of IX, Method A).

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