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PREPARATION OF STERICALLY HINDERED GEOMETRIC ISOMERS OF 7-*CIS*-β-IONYL AND β-IONYLIDENE DERIVATIVES IN THE VITAMIN A SERIES[a]

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Abstract—The preparation of the relatively unknown 7-*cis* isomers of β-ionyl and β-ionylidene derivatives via one way sensitized geometric isomerization is described. These highly sterically crowded isomers, once prepared do not readily thermally revert back to the *trans*. But the trienes, at temperatures ≥100° undergo irreversible cyclization to cyclohexadienes. 7-*cis* Isomers of β-ionylideneacetone and acetaldehyde as well as higher tetraenes and pentaenes in this series could not be prepared by sensitized isomerization. Partial reduction of 7-*cis*-β-ionylideneacetonitrile isomers led to the preparation of 7-*cis*- and 7,9-di*cis*-β-ionylideneacetaldehyde; and methyl Grignard reaction with the same nitrile gave the triene-methyl ketones.

Of the 16 possible geometric isomers of retinal and Vitamin A only 6 are known.[1] Of these two contain the relatively hindered 11-*cis* geometry due to 1,6-hydrogen-methyl interaction, and none with the more hindered 7-*cis* geometry (1,6-methyl-methyl interaction).[b] In the literature we found only one report of a serious attempt to synthesize any of the missing 7-*cis* isomers involving selective hydrogenation of 7,8-dehydro-retinal.[3] This approach, reportedly under a variety of conditions, failed to produce the desired isomers. The failure was thought to be consistent with the expected severe steric interaction in such isomers. A similar situation exists in studies of β-carotene and related compounds; only isomers of the 7-*trans* geometry are known.[1,4] On the other hand, limited examples of smaller compounds with similar steric crowding have been mentioned in the literature. For example, selective hydrogenation of a 7,8-dehydro-β-ionyl derivative has been reported giving a product assumed to be the 7-*cis*-β-ionyl compound.[5] Mousseron *et al.* in their studies of direct irradiation of β-ionyl and ionylidene derivatives detected spectroscopically the presence of 7-*cis* isomers during irradiation, but the only products isolated were those involving 1,5-hydrogen migration.[6] Büchi and Yang reported the formation of two products upon direct irradiation of β-ionone.[7] The major product was identified as an α-pyran which has since been shown by Marvell *et al.* to be in rapid thermal equilibrium with *cis*-β-ionone.[8]

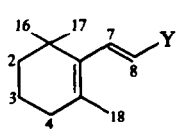
Recently in a preliminary report we described a photochemical method to effect one way geometric isomerization from *trans* to the hindered *cis* isomer in selected systems.[9] Compounds such as hindered β-ionyl, β-ionylidene derivatives, styrenes and stilbenes are now available in reasonable quantities. In this paper we report in detail the scope and limitation in the preparation of 7-*cis* isomers of dienes, trienes and higher polyenes in the vitamin A series. In the accompanying paper the synthesis of 4 new isomers of retinal with the same geometry is described.

RESULTS AND DISCUSSION

The method of one way sensitized geometric isomerization is a simple one based on the expected difference in excitation energies of the isomers in this series. Because of the severe steric interaction the 7-*cis* isomer is expected to exist in a skewed geometry (since verified in a NMR study)[10] with the consequence of raising its excitation energy considerably above that of the *trans*. Sensitizers with intermediate excitation energy should be able to transfer energy selectively to the *trans*, eventually reaching photostationary states containing only the high energy isomer. For conjugated dienes, the $S_0 \rightarrow T_1$ excitation energy is usually between 55–60 kcal/mole.[11] In this range is probably also the value for *trans*-β-ionyl derivatives. The corresponding excitation energy for the *cis* isomer, extrapolated from a Saltiel plot of sensitized isomerization of β-ionol,[9] is at least 10 kcal/mole higher. We have therefore found that all sensitizers with energy between 55–65 kcal/mole such as α- and β-acetonaphthone, phenylnaphthylketones, Michler's ketone, are acceptable for one way sensitized isomerization. In the triene series (β-ionylidene derivatives) obviously sensitizers with lower E_T's will have to be used. The satisfactory ones are those with energy between 45–52 kcal/mole such as benzpyrene, benzanthrone and fluorenone.

[a] Photochemistry of polyenes VIII. For no. VII see ref. 13.

[b] Pauling[2] earlier made the prediction that 7-*cis* and 11-*cis* isomers of carotenoids are too sterically crowded to be stable. 11-*cis*-vitamin A and 11-*cis*-carotene have, of course, since been reported.[1]



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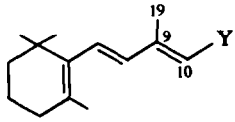

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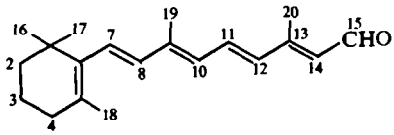

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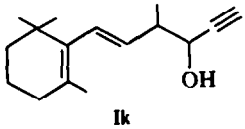
Throughout this and the accompanying papers, the IUPAC convention in numbering the carbons in carotenoids will be used for ionyl (**1**) ionylidene (**2**) derivatives as well as retinal isomers (**3**).

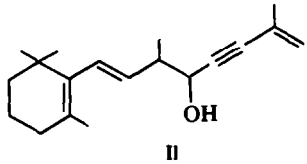
7-cis-β-Ionyl derivatives (dienes). Most of the *trans-β*-ionyl derivatives were prepared according to literature procedure starting from *β*-ionone (for **Ib-d, f, h-l**) or cyclocitral (for **Ie, g**) (Table I for structures). In the case of **Ie**, we found that Horner reaction of cyclocitral with diethyl cyanomethylphosphonate gave a mixture of geometric isomers with the *cis* isomer present in ~10%. But, with diethyl benzylphosphonate, only *trans* **Ig** was obtained.

The one way photochemical conversion of *trans* isomers to the corresponding *cis* was conducted under usual conditions for sensitized irradiation with an appropriate sensitizer mentioned above. The reactions are usually very efficient, resulting in complete conversion within 2 days of irradiation. The structure of the photoproduct, once isolated is readily recognizable from its spectroscopic properties. As an example, the PMR spectra of *β*-ionol (**Ib**) and its photoproduct are shown in Fig 1. They are clearly those of two geometric isomers. The smaller vinyl coupling constant ($J_{7,8}$ = 11·5 Hz) clearly agrees with the *cis* geometry.† This configuration change is further characterized by the IR absorption at 745 cm^{-1} replacing the 950 cm^{-1} band in the *trans*. Additional information indicative of the new geometry is the upfield shift (an average of 0·12 ppm for ionyl derivatives) of the signal for CH_3-18. This shift, even more prominent in higher polyenes in this series (see below), must be due to shielding of the methyl group by the side chain (C-8 and C-9) now assuming a conformation orthogonal to the ring.[10] In Table I are listed characteristic NMR data of these compounds.

Compounds **Ik** and **Il** in Table I are the following:



Ik



Il

Photochemically, they also cleanly isomerized to the corresponding 7-*cis* isomer. Subsequent elimination

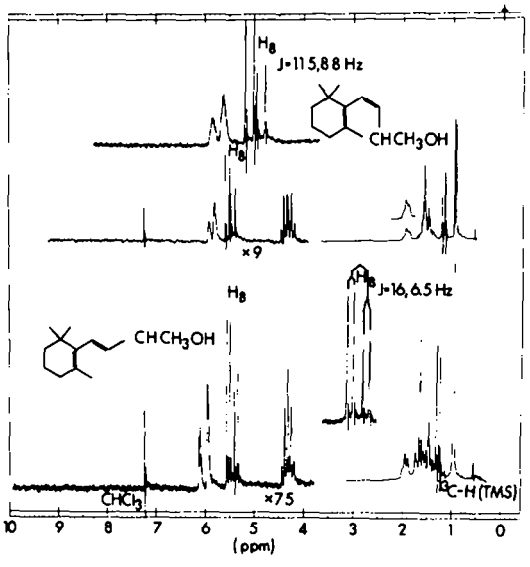


Fig 1. 100 MHz NMR spectra of *β*-ionol isomers, taken in $CDCl_3$ with TMS as internal standard: upper, *cis*, lower, *trans*.

reactions could, therefore, provide an entry to higher polyene with the 7-*cis* geometry. The possibility of using compounds of similar structure to synthesize the 8 missing 7-*cis* isomers of vitamin A is being explored in our laboratory.

Tertiary alcohol **If** is the odd member of the series in that so far we have not been able to isomerize photochemically in either direction with a variety of sensitizers. The *cis* isomer was therefore prepared by a non-photochemical route by reacting *cis*-ionone with methyl Grignard. A plausible explanation for the lack of photo-reactivity is the group being too bulky to allow a rate of "rotation" in the excited state to be competitive with triplet decay. In agreement with this rationale is the similar lack of reactivity observed in the ethylene ketal of *trans-β*-ionone.

These compounds with the 7-*cis* geometry usually show high thermal stability, therefore no special precautions are required in handling. For example *cis-β*-ionol is stable up to 130°. At higher temperatures degradation by

†E. Marvell[12] *et al.* obtained the same compound by LAH reduction of *cis-β*-ionone. They attributed the non-equivalence of geminal dimethyl groups to restricted rotation. But from variable temperature NMR studies,[10] it is clear that the remote asymmetric center must be the cause of the non-equivalence.

Table I. NMR spectral characteristics of β-ionyl (I) derivatives[a]

Compound Y =	Isomer	Chemical Shift, δ					
		H_7	H_8	CH_3-18	CH_3-19	CH_3-16, 17	$J_{7,8}$, Hz
Ia	*trans*[b]	7·17	6·02	1·77	2·20	1·08	16·0
$COCH_3$[b]	*cis*[b]	6·38	6·03	1·52	2·09	1·02	12·5
Ib	*trans*[c]	6·10	5·41	1·64	1·24	0·98	16·0
$CHCH_3OH$	*cis*	5·75	5·45	1·54	1·16	0·75	11·5
Ic	*trans*[c]	7·02	5·81	1·50	—	0·70	15·5
CO_2H	*cis*	6·53	5·76	1·48	—	0·74	12·0
Id	*trans*[c]	6·04	5·51	1·80	(4·12)[d]	1·12	15·9
CH_2OH	*cis*	5·79	5·57	1·42	(3·10)[d]	0·90	11·0
Ie	*trans*	7·10	5·30	1·82	—	1·12	17·0
CN	*cis*	6·84	5·46	1·76	—	1·08	11·0
If	*trans*	6·03	5·53	1·66	1·34	1·02	16·2
$(CH_3)_2COH$	*cis*	5·71	5·46	1·70	1·23	1·04	12·5
Ig	*trans*	6·64	6·34	1·80	—	1·12	17·0
C_6H_5	*cis*	6·00	6·34	1·54	—	1·08	12·0
Ih	*trans*	5·73	5·25	1·60	1·72	0·98	16·0
CH_3	*cis*	5·83	5·55	1·48	1·62	0·74	12·0
Ii	*trans*	5·73	5·32	1·58	(?)	0·94	16·0
C_2H_5	*cis*	5·65	5·29	1·40	(?)	0·88	12·0
Ij	*trans*	5·91	5·19	1·60	1·12	?	16·0
$CHCH_3CHO$	*cis*	6·02	5·28	1·52	1·06	?	11·0
Ik[e]	*trans*	5·97	5·39	1·68	1·15	1·02	15·5
		5·97	5·31[f]		1·16		
	cis	5·67	5·58	1·60	1·10	1·02	11·5
		5·69	5·45[f]				
Il[e]	*trans*	5·97	5·39	1·68	1·15	1·02	16·0
		5·97	5·31[f]		1·16		
	cis	5·67	5·58	1·60	1·10	1·02	11·5
		5·69	5·45[f]				

[a] HA-100 in $CDCl_3$ internally locked on TMS.
[b] Data of E. N. Marvell *et al.*, *J. Am. Chem. Soc.* **88**, 619 (1966).
[c] Data also available in M. Mousseron-Canet and J. Mani, *Bull. Soc. Chim. Fr.* 3285, 3291 (1964).
[d] CH_2-signals.
[e] See text for structures.
[f] Two diastereomers are present in each isomer.

dehydration was observed, probably catalyzed by trace acid present. At room temperature in solution, the 7-*cis* geometry of **Ie** was found unaffected upon addition of catalytic amounts of trifluoroacetic acid, or iodine. But it was converted to the *trans* isomer when the iodine sample was irradiated briefly with UV light.

7-cis-β-*Ionylidene derivatives* (*trienes*). The 7-*trans* isomers of β-ionylidene derivatives were prepared according to literature procedures giving usually a mixture of two geometric isomers (9-*trans*, 9-*cis*). The procedure for separating some of these isomers are available in the literature; however, for our purpose it is not necessary and in fact unwise to obtain isomerically pure starting material because during photosensitized irradiation isomerization around the 9,10-bond takes place concomitantly with that around the 7,8-bond. While it is possible to effect exclusive formation of the 7-*cis* geometry by selective sensitization for most of the compounds, such control is not possible around the 9,10-bond simply because of the absence of steric crowding. Therefore, selective sensitization in this triene series always resulted in the formation of a mixture of two isomers, nonetheless, both with the 7-*cis* geometry.

The types of compounds we have successfully converted to the mixture of 7-*cis* isomers include nitrile (**2a**), ester (**2b**), acid (**2c**), hydrocarbon (**2d**) and alcohol, amine and acetate. Separation of the 7-*cis* isomers could not easily be accomplished. Their thermal lability (see below) limited available separation techniques. Column chromatography usually provided the best chance but even so usually resulted in poor separation. However, for structural assignments, separation of isomers was not necessary. They were readily identified from the PMR spectra of the two isomer mixtures. Unambiguous assignments for all signals informative of structures, i.e., the vinyl hydrogens and all the methyls, were made usually after comparison with corresponding signals in the 7-*trans* isomers and occasionally further aided by the addition of paramagnetic shift reagents.

In Table II are listed the NMR characteristics of these isomers along with those of 7-*trans* for comparison. Clearly, all new isomers show the expected smaller vinyl

Table II. NMR spectral characteristics of β-ionylidene derivatives (2)[a]

Compound	Isomer	Chemical Shift, δ						
		H_7	H_8	H_{10}	CH_3-18	CH_3-19	CH_3-16, 17	$J_{7,8}$, Hz
2a	all-*trans*	6·48	6·10	5·09	1·70	2·14	1·04	16·5
CN	7-*cis*	6·14	6·01	5·24	1·48	2·05	1·00	12·5
	9-*cis*	6·55	6·63	5·02	1·72	2·06	1·04	16·0
	7,9-di*cis*	6·22	6·47	5·03	1·52	1·96	1·00	12·0
2b	all-*trans*	6·48	6·04	5·68	1·64	2·29	1·02	17·0
CO_2Et	7-*cis*	5·96	5·96	5·67	1·44	2·10	1·00	12·0
	9-*cis*	6·51	7·67	5·57	1·72	1·98	1·02	16·5
	7,9-di*cis*	6·07	7·10	5·48	1·44	1·79	1·00	12·5
2c	all-*trans*[b]	6·59	6·11	5·72	1·70	2·34	1·06	16·5
CO_2H	7-*cis*	6·15	6·05	5·84	1·52	2·23	1·06	12·0
	9-*cis*[b]	6·61	7·63	5·65	1·72	2·06	1·02	16·0
	7,9-di*cis*	6·22	7·12	5·64	1·52	1·96	1·06	12·5
2d	*trans*	6·12	6·12	4·92	1·74	1·96	1·08	—
H	*cis*	6·13	5·71	4·78, 5·08	1·60	1·82	1·08	12·0
2e	all-*trans*	6·63	6·11	5·79	1·68	2·18	1·02	16·0
CHO	7-*cis*	6·15	6·05	5·85	1·52	2·16	1·02	12·0
	9-*cis*	6·56	7·03	5·79	1·68	2·00	1·02	16·0
	7,9-di*cis*	6·19	6·86	5·68	1·52	1·93	1·02	12·0
2f	all-*trans*	6·57	6·03	6·06	1·68	2·26	1·00	15·5
$COCH_3$	7-*cis*	6·13	6·03	5·98	1·52	2·08	1·00	12·0
	9-*cis*	6·59	7·76	5·94	1·76	2·00	1·00	16·5
	7,9-di*cis*	6·16	7·06	5·90	1·52	1·92	1·00	12·0
2g[c]	*trans*	7·1	6·82	—	1·80	2·36	1·08	16·0
	cis	6·6	6·61	—	1·48	2·26	1·04	12·0

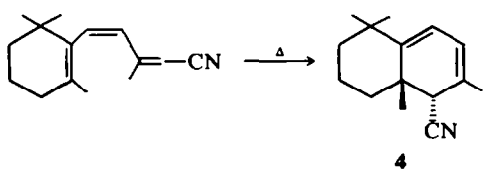
[a] HA-100 in $CDCl_3$ locked on TMS.
[b] Data also available in: M. Mousseron-Canet and J. Mani, *Bull. Soc. Chim. Fr.* 3285, 3291 (1964).
[c] β-ionylidenemalononitrile.

coupling constants and the prominent upfield shift of the CH_3-18 signals from 7-*trans* to *cis* (an average $\Delta\delta$ of 0·20). Also, expectedly IR spectra show absorption around 740 cm^{-1} for all these 7-*cis* isomers.

7-*cis* Isomers of ionylideneacetaldehyde, **2e**, as in the case of the corresponding 7-*trans* isomers,[1] could be the key intermediates to retinal of the presently unknown 7-*cis* geometry. We were therefore much disappointed to find that 7-*trans*-**2e** failed to isomerize to 7-*cis* isomers under sensitized irradiation. Subsequently we found that the corresponding methyl ketone, **2f**, and other tetraenes in this series (see below) behaved in a similar manner. The preparation of 7-*cis*-**2e**, therefore, was not accomplished by the usual photochemical route. Instead we found that the 7-*cis* isomers of ionylideneacetonitrile, **2a**, could be partially reduced by di-isobutylaluminum hydride. Subsequent hydrolysis gave the aldehyde in up to 75% yield. The two 7-*cis* isomers of **2e**, first obtained as a mixture in the reduction reaction, could be separated with some difficulties on silica gel columns with the mono-*cis* isomer having a slightly longer elution time. In Fig 2a, b are NMR spectra of these two isomers with assignments listed in Table II. Other spectral data agreed with the structures.

The 7-*cis* isomers of β-ionylideneacetone (**2f**) were obtained by reaction of methyl Grignard with a mixture of 7-*cis*- and 7,9-di*cis*-**2a** followed by acid hydrolysis. The products were characterized as an isomeric mixture similar to the starting nitrile by spectral data (NMR assignments listed in Table II).

The 7-*cis* triene isomers are thermally labile. Upon heating to temperatures above 100°, they undergo facile rearrangement, believed to be electrocyclic ring closure giving the cyclohexadiene derivatives. The case of β-ionylideneacetonitrile (**2a**) was studied in some detail. Upon heating a chloroform solution of a mixture of 7-*cis*- and 7,9-di*cis*-**2a** at 100° for ½ hr, the formation of one product was observed. Its PMR spectrum showed three non-equivalent Me groups (all singlets, δ 1·00, 1·04, 1·11) now attached to saturated carbons with the hydrogens in the remaining Me being allylic (δ 1·82). Only two coupled vinyl hydrogens remained (J = 5·5 Hz). H_{10} now appeared as a singlet at δ 2·51. These data agreed with the cyclized cyclohexadiene structure shown. That only one cyclized product was formed indicated that geometric isomerization accompanied cyclization. Since only the *s-cis*, *s-cis* conformation, (necessary for cyclization), of the mono-*cis* isomer is relatively free of steric interaction between Me-18 and CN groups, the product must have been derived from this isomer. After disrotatory cyclization it must have the stereochemistry shown. In agreement with this stereo-chemical prediction is the observation that the



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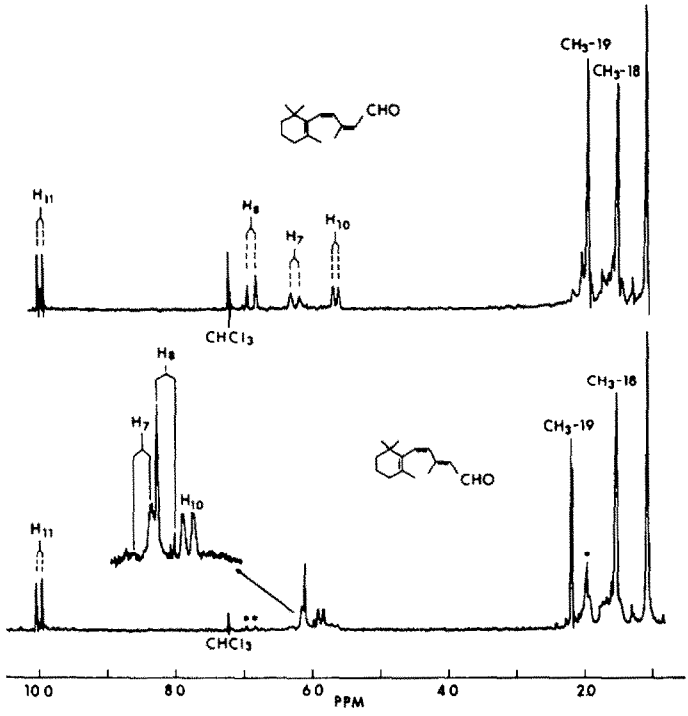
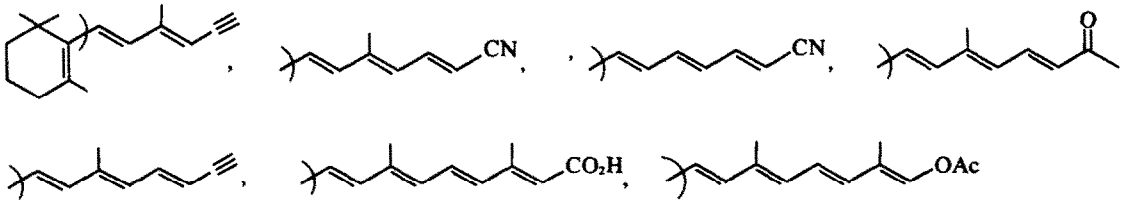


Fig 2. 100 MHz NMR spectra of 7-*cis* isomers of β-ionylideneacetaldehyde: upper, 7,9-di*cis*; lower, 7-*cis* (* = 7,9-di*cis*).



same mixture of 7-*cis* isomers of **2a** photochemically gave a different cyclized product, believed to be the epimer of **4** from conrotatory cyclization.

Higher polyenes. The following tetraenes and pentaenes in the series were studied under sensitized irradiation. Similar to the triene ketone and aldehyde, under no circumstances the formation of any amounts of the 7-*cis* isomers were observed. The triplets of these compounds apparently decay prohibitively in favor of the *trans*, probably a natural consequence of the distorted excited tortional potential curve around the 7,8-bond.[13] This result clearly says that the method of selective sensitization to prepare 7-*cis* isomers is only applicable to the dienes and trienes in this series.

EXPERIMENTAL

PMR spectra were recorded on a Varian HA-100 spectrometer with $CDCl_3$ as solvent and TMS as internal standard. UV spectra were recorded on a Beckman Acta III or a Cary-14 spectrometer, IR on a Beckman IR-10. Mass spectra were recorded on a Hitachi-Perkin Elmer RMU-6D spectrometer.

7-cis-β-*Ionol* (**Ib**). A soln of 10·0 g (0·051 mole) of 7-*trans*-β-ionol, prepared by $NaBH_4$ reduction of β-ionone,[14] and 0·4 g β-acetonaphthone in 100 ml benzene was added to a water cooled Pyrex immersion apparatus. The soln was first deoxygenated by passing through a stream of N_2 for 1–2 min. While kept under N_2, the soln was irradiated with a 200 W Hanovia medium pressure Hg lamp. After approximately 48 hr, the reaction was complete. The soln was concentrated then distilled under vacuum through an 8" Vigreaux column: 91–2°/1·2 mm, 8·6 g (86% yield) [UV (EtOH) 210 mμ (4,700 ε); IR (film) 3400 (OH), 735 (cis alkene); NMR, Fig I, and Table I]. The compound is identical to that obtained by LAH reduction of *cis*-β-ionone.[12]

The above procedure can be used for preparation of all other 7-*cis*-ionyl derivatives. For ionylidene derivatives, it is advisable to use a uranium glass filter to eliminate direct irradiation.

cis-β-*Ionone*, **Ia**. The procedure of Büchi and Yang[7] of direct irradiation of *trans*-β-ionone could be used to prepare *cis*-ionone (primarily existing in the form of the cyclized α-pyran). However, the product was often contaminated with the 1,5-hydrogen migration product with its amount increasing with prolonged irradiation period. We found similar conversion could be accomplished via sensitized irradiation with fluorenone as sensitizer and using a uranium-glass immersion well, or with

sunlight. The rate of conversion was slower due to lower quantum yield in sensitized reaction as well as loss of part of the lamp out-put to filtering system; but the hydrogen migration product was minimized.

β-Cyclocitrylideneacetic acid, **Ic**. The *trans* isomer was prepared by sodium hypochlorite oxidation of β-ionone.[15] The *cis*-isomer is a low melting solid.

β-Cyclocitrideneethanol, **Id**. The *trans*-isomer was prepared by LAH reduction of **Ic**.[15] Yield, 60% [IR (neat) 3400 (OH), 970 cm^{-1} (*trans* alkene)]. Sensitized irradiation converted the compound to its *cis* isomer: [IR (neat) 3400 (OH), 730 cm^{-1} (*cis* alkene)].

β-Cyclocitral. The reported procedure of acid catalyzed cyclization of citral was followed.[16] However, we found better yield (~65%) was obtained by extraction of product mixture with light petroleum rather than the more laborious steam distillation.

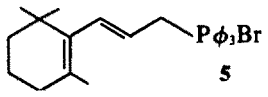
β-Cyclocitrylideneacetonitrile, **Ie**. To a DMF (150 ml) suspension of NaH (4·5 g) was added 17·7 g of diethyl cyanomethylphosphonate. After 20 min 15·2 g of β-cyclocitral was added dropwise. The mixture was kept at 50° for 3 hr. After ether extraction and vacuum distillation (b.p. 70°/0·01 mm), the nitrile was obtained in 85% yield: [UV (pentane) 265 mμ ($7·3 \times 10^3$ ε); IR (neat), 2204 (CN), 970 cm^{-1} (*trans* double bond); NMR (Table I) revealed the presence of the *cis* isomer in ~10% of the total product mixture].

The mixture was converted completely to the *cis* isomer by sensitized irradiation: b.p. 70°/0·01 mm: [UV (pentane) 265 nm ($4·8 \times 10^3$ ε); IR (neat) 2210 (CN), 730 cm^{-1} (*cis* double bond)].

9-Methyl-β-ionol, **If**. Methyl Grignard is known not to add to β-ionone. The procedure developed by Kipping and Wild was followed in preparing the *trans* isomer.[17] The compound, however, failed to isomerize to *cis* under sensitized irradiation. Instead, *cis*-**If**, was obtained by reaction of methyl magnesium iodide with *cis*-β-ionone.

Preparation of **Ig** (*Y* = *Ph*). The *trans* isomer was prepared by reaction of cyclogeranyltriphenyl phosphonium bromide with NaOMe and benzaldehyde (yield: 40%). The compound was converted to its *cis* isomer by sensitized irradiation with benzanthrone.

Preparation of **Ih** (*Y* = *Me*). *trans*-**Ih** was obtained as a major by-product from reaction of Wittig salt **5** with NaOMe and cyclocitral.[18] It was characterized by its NMR spectrum (Table I). The *cis* isomer was routinely obtained by sensitized isomerization.



5

Preparation of **Ii** (*Y* = *Et*). Wolff-Kishner reduction of β-ionone failed to give the desired product. Instead the compound was obtained by reaction of β-ionyl bromide, prepared by reaction of β-ionol with PBr_3, with LAH_4. The product was purified by column chromatography. Sensitized isomerization routinely gave the *cis* isomer.

Preparation of iso-C_{14}-aldehyde, **Ij** (*Y* = *CHCH*$_3$*CHCHO*). A procedure slightly modified from that reported[19] was used giving product consistently in high yield.

β-Ionone (96 g, 0·5 mol), ethylchloroacetate (82·7 g, 0·675 mol) pyridine (50 mol) and phenothiazine (250 mg) were added to a 1 l, 3-necked RBF equipped with a N_2 inlet, a thermometer, a through-bore stirrer and a solid addition funnel. The flask was flushed with N_2, then maintained under N_2 throughout the reaction. The mixture was cooled to −15°, then freshly prepared NaOMe (40·5 g, 0·75 mol) was added over a period of 30 min. After the addition was completed, the mixture was stirred at −5° for 30 min, then allowed to come to room temp during which time the mixture became deep red. The mixture was again cooled to −5° and stirred for 3·5 hr. The solid addition funnel was then replaced with a pressure equilibrated dropping funnel and 15% NaOH in MeOH was added (203 ml) over a period of 30 min at −5°. The mixture was then stirred at 10° for 1 hr and then cooled to −30° and poured into 3 l beaker containing glacial AcOH (300 ml) and a magnetic stirrer. The mixture usually solidified at this point, but began to melt in about 5 min. When the mixture had warmed to 10°, water (500 ml) was added and the mixture was stirred for 15 min. The mixture was extracted with ether 3-4 times. The combined organic extracts were washed with water and dried over $MgSO_4$. Filtration followed by removal of the solvent yielded the C-14 aldehyde (98 g) as an orange oil, yield: 92%,

The C_{14}-aldehyde thus prepared possessed a clean NMR spectrum and was sufficiently pure for further use. A portion of this C_{14}-aldehyde was purified by column chromatography over silica gel (Bio-Sil A) using benzene-hexane (1:1) as solvent.

The chromatographically pure sample was readily isomerized to the 7-*cis* isomer upon sensitized irradiation.

Preparation of **Ik**. Ethynyl magnesium bromide was prepared in accordance with the literature procedure[20] from Mg turning (12 g), EtBr (60 g), acetylene and THF (500 ml). At 0°C while a stream of acetylene was maintained, a solution of crude **Ij** (80 g) in THF (60 ml) was added over an hr period. The acetylene stream was then stopped and the mixture allowed to warm to room temp and stirred overnight. Sat NH_4Claq was then added slowly at 0°. After extraction with ether, drying over $MgSO_4$ and evaporation of solvent, a red viscous oil was obtained.

The mixture was purified by passing through a silica gel column with benzene–hexane (1:1) as eluant. NMR clearly indicated the presence of a mixture of diastereomers (Table I). Sensitized irradiation gave the *cis* isomers.

Preparation of **Il**. To an ether soln of EtMgBr prepared from 30 g of EtBr and 6 g of Mg was added under N_2 20 g 3-methylbuten-3-yn-1 in 50 ml of ether over a period of 30 min. After complete addition the mixture was refluxed for about 4 hr and cooled to room temp. To this was added 30 g of **Ij** in 50 ml of ether, followed by refluxing for an hr and stirring at room temp for about 10 hr. The mixture was quenched at 0° by the addition of sat NH_4Claq and the product was isolated by extraction with ether and evaporation of the solvent, yield: 85%.

The product was purified by column chromatography using silica gel (Bio-Sil A) and hexane–benzene (1:2) solvent mixture [IR (neat 3400 (OH), 970 (*trans* double bond), 895 cm^{-1} (*exo*-methylene); NMR Table I]. Similar to **Ik**, a mixture of diastereomers was obtained. *cis*-**Il** was obtained via sensitized irradiation.

β-Ionylideneacetonitrile, **2a**. The two 7-*trans* isomers were prepared according to the procedure of Stilz and Pommer[21] by reacting β-ionone with diethyl cyanomethylphosphonate. Sensitized irradiation (benzanthrone) of the *trans* isomers gave a mixture of 7-*cis*- and 7,9-di*cis*-**2a**.

The same mixture of 7-*cis*- and 7,9-di*cis*-**2a** was also obtained by reaction of diethyl cyanomethylphosphonate with *cis*-β-ionone.

Sodium hydride (19 g) as a 57% oil dispersion was stirred in 200 ml of DMF. To this diethyl cyanomethylphosphonate (62 g) was added slowly followed by equivalent amounts of *cis*-ionone and stirred at room temp for about 10 hr. The mixture was worked up by adding 300 ml water and extracting with ether. The organic layer was dried over $MgSO_4$. Evaporation of solvent gave 7-*cis* and 7,9-di*cis*-β-ionylideneacetonitrile (71 g), yield: 95%. [UV (EtOH 210, 253, 290 nm; IR (neat) 2230 (CN), 845 (trisubstituted alkene) and 745 cm^{-1} (*cis* alkene); NMR (100 MHz) Table I]. From NMR it was evident that the product mixture consisted of 65% 7-*cis* and 35% 7,9-di*cis* isomers.

Ethyl β-ionylideneacetate, **2b**. Reaction of β-ionone with diethyl carbethoxyphosphonate gave the two 7-*trans* isomers.[24]

The 7-*cis* isomers were obtained via sensitized irradiation and purified by chromatography over silica gel: [IR (film) 1710 (CO), 830 (trisubstituted alkane), 735 cm^{-1} (*cis* alkene). The 7-*cis* isomers could also be prepared by reaction of diethyl carbethoxyphosphonate with *cis*-ionone following the same procedure for **2a**.

β-Ionylideneacetic acid, **2c**. Hydrolysis of 7-*trans* mixture of **2a** gave a mixture of *trans* acid **2d**. The 7-*cis* isomer was obtained by sensitized irradiation in the form of viscous oil. Effort to crystallize the isomer(s) was unsuccessful.

Cyclocitrylidenepropyne, **2d** (Y = H). To a soln of n-BuLi (0·05 mol) in 100 ml ether was added 17·8 g (0·05 mol) methyltriphenylphosphonium bromide. The mixture was stirred under N_2 at room temp for 4 hr. β-Ionone (12 g) in 50 ml ether was added to the above suspension and the mixture was stirred for 20 hr. The reaction was quenched by slow addition of water then extracted with ether. Evaporation of ether gave the crude product along with triphenyl phosphine oxide. Triphenyl phosphine oxide was filtered off and washed with light petroleum (30–60). The light petroleum extract was dried over $MgSO_4$; evaporation of light petroleum gave triene **2f** yield: 32%. This was purified by column chromatography [IR: 3100, 2930, 1775, 1609, 963, 874 cm^{-1}]. The 7-*cis* isomer was obtained by sensitized irradiation with fluorenone as sensitizer.

β-Ionylideneacetaldehyde, **2e**. The 7-*trans* isomers were prepared by reduction of **2a** with di-isobutylaluminum hydride.[23] These isomers, however, failed to isomerize to the 7-*cis* under sensitized irradiation. The latter were, instead, prepared by the following procedure.

A mixture of 7-*cis* and 7,9-di*cis*-β-**2a** (15 g) in 50 ml of hexane was cooled to 0°. To this 10 g of di-isobutylaluminumhydride in 50 ml hexane cooled to 0° was added. After complete addition the mixture was stirred at 40° for about 3 hr. Then the mixture was carefully poured over ice. Dilute HCl was added to hydrolyse the complex and the mixture extracted with ether. The ether extract was dried over $MgSO_4$. Evaporation of solvent gave a mixture of 7-*cis*- and 7,9-di*cis*-β-ionylideneacetaldehyde, yield: 75%.

The 7-*cis* and 7,9-di*cis*-β-ionylideneacetaldehyde were separated over Bio-Sil A (200-325 mesh) using benzene–hexane (2:3) solvent mixture with the help of automatic fraction collector. The 7,9-di*cis*-isomer appeared in first few fractions and 7-*cis* isomer in last few fractions whereas the middle fractions contained both isomers. Longer columns resulted in partial isomerization of 7-*cis* isomers over Bio-Sil A. Also, we found it is advisable to wash Bio-Sil A with water several times then activate the material at 120° for 10 hr before use to minimize isomerization: [7-*cis*: IR 1655 (CO), 860 (trialkylalkene), 735 cm^{-1} (*cis*-alkene); UV (EtOH) 272 (14,800), 313 nm (9,180); 7,9-di*cis*: IR 1665, 815, 715 cm^{-1}, UV (EtOH) 258 (14,600), 304 (6,880); NMR in Fig II].

β-Ionylideneacetone, **2f**. To a soln of methyl Grignard, prepared from 1·2 g of Mg and 7·1 g of MeI in 100 ml of abs ether, was added 11 g of **2a** in ether. After complete addition the mixture was stirred at 40° for 15 hr, then quenched with sat NH_4Cl aq and extracted with ether. The ether layer was dried over $MgSO_4$ and evaporation of ether gave the above product along with unreacted β-ionylideneacetonitrile.

The product mixture was chromatographed over silica gel using hexane–benzene (1:1) solvent mixture. β-Ionylideneacetonitrile had a shorter retention time compared to β-ionylideneacetone. NMR (Table I) agreed with the trienone structure.

7-*cis* and 7,9-di*cis*-β-Ionylideneacetone were prepared by a similar procedure except that 7-*cis* isomers of **2a** was used. NMR (Table I) agreed with those of 7-*cis* isomers.

β-Ionylidenemalononitrile, **2g**. The *trans* isomer was obtained from condensation of β-ionone with malononitrile in acetic acid with ammonium acetate (yield: 85%). Sensitized irradiation with benzanthrone gave the *cis* isomer [NMR: Table II].

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