6-*cis*: 8.73, 9.74, 11.36 μ; 2,6-di-*cis*: 14.02 μ; neoretinene-*b*: 8.93, 9.26 μ.

(b) **With Iodine.**—The aldehyde (*e.g.*, 1.0 g.) in benzene (500 ml.) containing iodine (2 mg.) was allowed to stand at room temperature under the specified conditions of time and amount of light. The work-up procedure has already been described.[23] Isomerizations run "in darkness" were done in red glassware, covered with a black cloth, and worked up in red glassware.

Reaction of Neovitamin Ab (2,4-Di-*cis*-vitamin A with Maleic Anhydride.—The procedure was the same as that used in the analytical method for neovitamin A.[23] For one sample of neovitamin Ab concentrate ($E(1\%,$ 1 cm.)(322 mμ) 921; the 5-cc. aliquot contained 0.35 mg. of concentrate) the percentage recovery of vitamin A, as measured by the antimony trichloride method, was 60% after reaction with maleic anhydride for 15 hours. The reaction thus proceeded slowly (apparent "neovitamin A" content = 71%), indicating the presence of a *cis* bond in the 2- or 4-position. For another sample of neovitamin Ab concentrate ($E(1\%,$ 1 cm.)(320 mμ) 1080) the percentage recovery of vitamin A after 15 hours was 65% (apparent "neovitamin A" content = 77.5%).

Acknowledgment.—It is a pleasure to acknowledge our indebtedness to Mr. A. J. Chechak and Dr. L. Weisler for making available the α-vitamin A alcohol used in the work, to Dr. W. J. Humphlett for assistance in preparing the vitamin A aldehyde derivatives and to Mr. R. H. Delaney and Dr. M. H. Stern for assisting in the isomerization experiments. Many helpful suggestions were received from Dr. N. D. Embree on the general conduct of the work.

ROCHESTER, N. Y.

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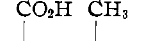
[23] C. D. Robeson and J. G. Baxter, THIS JOURNAL, **69**, 136 (1947).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF DISTILLATION PRODUCTS INDUSTRIES]

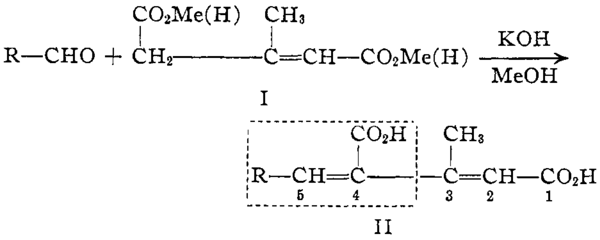
Chemistry of Vitamin A. XXVI. The Condensation of Aldehydes with Methyl β-Methylglutaconate[1]

BY JOHN D. CAWLEY

RECEIVED AUGUST 24, 1954

The condensation of a variety of aldehydes with methyl β-methylglutaconate to yield γ-alkylidene-β-methylglutaconic acids,  $R-CH=\overset{\overset{CO_2H}{|}}{C}-\overset{\overset{CH_3}{|}}{C}=CH-CO_2H$, is described. The ultraviolet absorption spectra of these are consistent only with their having a *cis* relationship of the R and $C(CH_3)=CH-CO_2H$ groups about the newly created double bond. This is also true for the 4-carboxyvitamin A acids previously prepared in this Laboratory from *trans*- and *cis*-β-ionylideneacetaldehyde and methyl β-methylglutaconate. Certain of the compounds differ in chemical and physical properties from those previously reported by Petrow and Stephenson.

In 1941 Hurd and Abernethy[2] demonstrated again[3] the ability of an ester of β-methylglutaconic acid (I) to condense with benzaldehyde to yield γ-benzylidene-β-methylglutaconic acid (II, R = C_6H_5), and suggested that this reaction with appropriate aldehydes might be used in a synthesis of vitamin A and other isoprenoid compounds.



$$R-CHO + \overset{\overset{CO_2Me(H)}{|}}{CH_2}-\overset{\overset{CH_3}{|}}{C}=CH-CO_2Me(H) \xrightarrow[MeOH]{KOH}$$

I

$$\underset{5}{R-CH}=\underset{4}{\overset{\overset{CO_2H}{|}}{C}}-\underset{3}{\overset{\overset{CH_3}{|}}{C}}=\underset{2}{CH}-\underset{1}{CO_2H}$$

II

The realization of this suggestion requires the removal of the 4-carboxyl group from II, and although Petrow and Stephenson[4] later successfully applied the reaction to other aldehydes, the diacids II obtained by them resisted all attempts at decarboxylation.

The synthesis in this Laboratory of vitamin A by the application of this reaction to β-ionylideneacetaldehyde has been described.[5] The present paper deals with the synthesis and properties of diacids II from aldehydes other than β-ionylideneacetaldehyde, but considers the geometry of the diacids obtained from this latter together with that of the other compounds.

The methylene group of β-methylglutaconic acid is less reactive than the methylene group of malonic acid, of which it is a (substituted) vinylog. In agreement with Petrow and Stephenson, it was found that the condensation of the acid or its ester with aldehydes is not mediated by amines, even under forcing conditions; a strong base is required, and nothing superior to alcoholic potassium hydroxide, as originally used by Feist and Beyer,[3] has been found. The acid itself fails to react even with this—the ester must be used.[6]

Petrow and Stephenson have reported that the reaction is applicable to alkyl, aryl and heterocyclic aldehydes, and our results also demonstrate the broad scope of the reaction. However, alkyl- (but not acyl-)aminobenzaldehydes give diacids which spontaneously decarboxylate to monoacids,[7]

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[1] Communication No. 198 from this Laboratory. Presented in part before the Division of Biological Chemistry of the 126th Meeting of the American Chemical Society, New York, New York, September, 1954.

[2] C. D. Hurd and J. L. Abernethy, THIS JOURNAL, **63**, 976 (1941).

[3] F. Feist and O. Beyer, *Ann.*, **345**, 117 (1906).

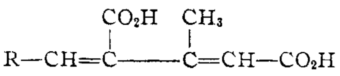
[4] V. Petrow and O. Stephenson, *J. Chem. Soc.*, 1310 (1950).

[5] C. D. Robeson, J. D. Cawley, L. Weisler, M. H. Stern, C. C. Eddinger and A. J. Chechak, THIS JOURNAL, **77**, 4111 (1955).

[6] This is reminiscent of the Stobbe condensation of carbonyl compounds with a succinic ester, but not with the acid, to yield alkylidenesuccinic half-esters (*cf.* W. S. Johnson and G. H. Daub in "Organic Reactions," Vol. VI, Ch. 1). Some evidence, based largely on equivalent weight by titration, has been found that half-esters of II may also be formed if minimal amounts of potassium hydroxide at room temperature are used. No pure compounds were isolated and the position of the ester group was not determined.

[7] J. D. Cawley and D. R. Nelan, THIS JOURNAL, **77**, 4130 (1955).

TABLE I



$R{-}CH{=}C(CO_2H){-}C(CH_3){=}CH{-}CO_2H$

II, R =	M.p., °C., dec.[a]	λ_{max},[b,c] mμ	ϵ_{max}	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
n-Hexyl	125.5–6.5	<220	...	68	65.0	65.2	8.4	8.6
n-Pentyl	127.5–8.5	<220	...	64	63.7	63.7	8.0	8.1
Nonadienyl[d]	172.5–3.5	280	22,200	56	69.0	69.2	8.0	7.8
2-Furyl	201–3	305	20,700	82	59.5	59.5	4.5	4.8
C_6H_5	189–90	276	17,600	93	67.2	67.5	5.2	5.3
m-$NO_2C_6H_4$	156–8	263	19,400	95	56.3	56.4	4.0	4.2
p-$MeOC_6H_4$	192.5–3.5	300	21,100	84	64.1	64.3	5.4	5.5
p-ClC_6H_4	197.5–8.5	282	20,800	95	58.5	58.4	4.2	4.3
m-HOC_6H_4	177–8	277	15,900	92	62.9	63.7	4.9	5.2
p-$AcNHC_6H_4$	197.5	312	26,100	83	62.3	62.6	5.2	5.3
3,4-$CH_2O_2C_6H_3$	209.5–10.5	323	15,350	93	60.9	61.2	4.4	4.6
		293	11,050					
3,4-$(MeO)_2C_6H_3$	173–4	317	16,800	75	61.6	61.3	5.5	5.6
		~300	...					
2,6-$Cl_2C_6H_3$	174.5–6.5	<220	...	61	51.2	52.1	3.4	3.5
$C_6H_5CH{=}CH$	187–7.5	316	35,600	52	69.8	70.2	5.5	5.4

[a] All of the compounds melted with gas evolution. [b] All spectra in this paper were determined in absolute ethanol. [c] With the exceptions noted, the compounds showed only the one maximum in the region 220–400 mμ. [d] From citral.

TABLE II

II, R =	M.p., °C. P. & S.	M.p., °C. J.D.C.	λ_{max}, mμ P. & S.	λ_{max}, mμ J.D.C.[b]	ϵ_{max} P. & S.	ϵ_{max} J.D.C.
C_6H_5	180	189–90	271[c]	276	14,150	17,600
$C_6H_5CH{=}CH$	199–200	187–7.5	313[c]	316	31,500	35,600
2-Furyl	213	201–3	300[c]	305	29,300	20,700
Nonadienyl[a]	148	172.5–3.5	279[d]	280	20,800	22,200

[a] From citral. [b] *Cf.* Table I, footnote *b*. [c] The solvent was cyclohexane. Since the compounds are α,β-unsaturated acids, both λ_{max} and ϵ_{max} would be expected to be lower had the solvent been ethanol, *i.e.*, the discrepancies would be still greater. *Cf.* K. Dimroth, *Angew. Chem.*, **52**, 545 (1939). [d] The solvent was isopropyl alcohol.

and *o*- and *p*-phenolic aldehydes or their acetates will not condense.[8] The reaction is not subject to steric hindrance, since 2,6-dichlorobenzaldehyde was successfully used. Only resinous products were obtained with crotonaldehyde. Table I lists the properties of the diacids II which have been prepared.

The properties of some of these compounds differ from those reported by Petrow and Stephenson. Although the most striking difference is the resistance of Petrow and Stephenson's diacids to decarboxylation,[9] as compared to the smooth, selective elimination of the 4-carboxyl group from ours,[7,5] Table II shows that there are also differences in the melting points and in the light absorption properties of comparable compounds.

Since *cis–trans* isomerism is possible in β-methylglutaconic acid[10] and its esters, the possibility that these differences arose from a difference in the configuration of the I used was investigated. However, both pure *cis*-I (for which an improved method of preparation is given in the Experimental section) and pure *trans*-I gave, with cinnamaldehyde, identical products in comparable yields.

Petrow and Stephenson prepared their compound II (R = $C_6H_5CH{=}CH$) of m.p. 199–200°, given in Table II, by the condensation of cinnamaldehyde with (*cis*- + *trans*-) I. It formed a bis-(*n*-butylamine) salt of m.p. 141–142°. They also described a *cis* isomer of this compound which they obtained by the hydrolysis of the corresponding anhydride, III.

This *cis* isomer had $\epsilon_{313\ m\mu}$ 28,600 (cyclohexane) and on heating it gradually reformed III and finally melted at the same temperature (180°) as does III. Its bis-(*n*-butylamine) salt melted at 119°. In contrast to this, hydrolysis of III in our

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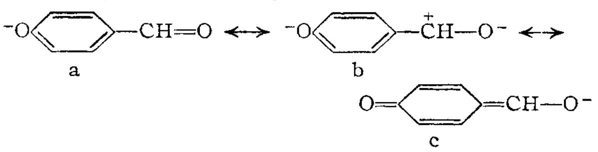
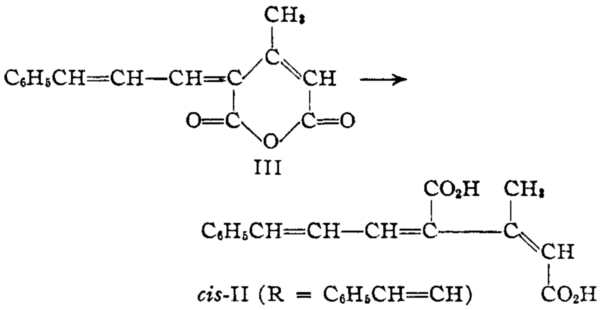
[8] Since the phenolate anion, a, will exist in the presence of the potassium hydroxide, this failure is probably the result of the dissipation of the positive charge in resonance form b (which is necessary for attack by the ester anion) by resonance with c.



With the acetates, saponification evidently proceeds faster than condensation, since the phenolic aldehydes are recovered.

[9] Although Petrow and Stephenson did not attempt decarboxylation of their diacids in the presence of copper in any form, they did try, unsuccessfully, heating them with quinoline alone, a procedure which works with our diacids (*cf.* footnote 6 of ref. 7).

[10] There is disagreement in the literature about the assignment of configurations to the acid. For example, in "Beilstein," Vol. II, p. 777, the acid of m.p. 147° is designated *cis* and the acid of m.p. 115° is designated *trans*, but in the first Supplementary series, Vol. II, p. 311, no assignments are made, while in the second Supplementary series, Vol. II, p. 658, the assignments are tentatively reversed. Since the acid of m.p. 147° is formed by the opening of the rings of either ethyl isodehydroacetate or of β-methylglutaconic anhydride under mild conditions, and it has been shown that this acid is isomerized by hot alkali to the isomer of m.p. 115° (F. Feist, *Ann.*, **345**, 78 (1906)), it is evident that Feist's assignments of a *cis* CO_2H/CH_2CO_2H configuration to the 147° acid and a *trans* CO_2H/CH_2CO_2H configuration to the 115° acid are correct. *Cf.* also R. Adams and B. L. Van Duuren, THIS JOURNAL, **75**, 2377 (1953).



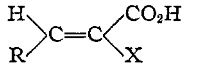
cis-II (R = $C_6H_5CH{=}CH$)

hands yielded the same II (R = $C_6H_5CH{=}CH$) as that obtained by the condensation of cinnamaldehyde with *cis*- or *trans*-I. On heating, it did not melt at the same temperature as III, and, indeed, no III was formed, since the absorption spectrum of the melt revealed no absorption whatsoever at the wave length (388 mμ) characteristic of III. The bis-(*n*-butylamine) salt of our compound melted at 119–123°; in this respect alone did it resemble Petrow and Stephenson's *cis* isomer.

Similar differences were found between the diacid prepared from β-ionylideneacetaldehyde and I (*i.e.*, 4-carboxyvitamin A acid) in this Laboratory[5] and by Petrow and Stephenson.

The configuration of our diacids appears to be deducible, in part, from the following considerations.

The condensation of an aryl aldehyde with an active methylene compound, XCH_2CO_2R (IV), leads, in many cases, to a compound V in which the R and X groups are *cis*. This is true for the Knoevenagel condensation with cyanoacetic acid (IV, X = CN),[11] and is especially true for the Perkin reaction with arylacetic acids (IV, X = aryl),[12] even



$$(H)(R)C{=}C(CO_2H)(X)$$

V

though the resulting *cis* compounds are unstable with respect to their *trans* isomers, to which they may be isomerized.[12a,c,d] *A priori*, then, the condensation of an aryl aldehyde with I (*i.e.*, IV, X = $C(CH_3){=}CHCO_2Me$) might be expected to give diacids having the configuration, analogous to V, shown in Fig. 1A (in which the configuration about the 2-double bond is arbitrarily chosen as *trans*).

Figure 1A shows that there is very severe hindrance between the 3-methyl group and an *o*-hydrogen atom of the benzene ring. This hindrance should affect the light absorption properties of the compounds. Table III compares the spectra of representative II's with the corresponding monoacids lacking the 4-carboxyl group (A), and with acids in which the $C(CH_3){=}CH{-}CO_2H$ group of II has been replaced by hydrogen (B); these latter acids correspond to that portion of the II molecule which is enclosed in dotted lines in its formula and scale drawing.

It is seen that $\lambda_{max.}$ of the diacids II is shifted far toward the violet with respect to the corresponding monoacids A, but, especially for those diacids derived from benzaldehydes, there is excellent agreement in both $\lambda_{max.}$ and $\epsilon_{max.}$ with the acids B. These aryl-II molecules are thus behaving, in their light absorption properties, as though the $C(CH_3){=}CH{-}CO_2H$ group were non-existent; the observed spectra are due solely to that portion of the molecule enclosed in the dotted lines.[13] This is understandable from Fig. 1A; the severe hindrance has been relieved by virtual 90° rotation about the 3-single bond.[14]

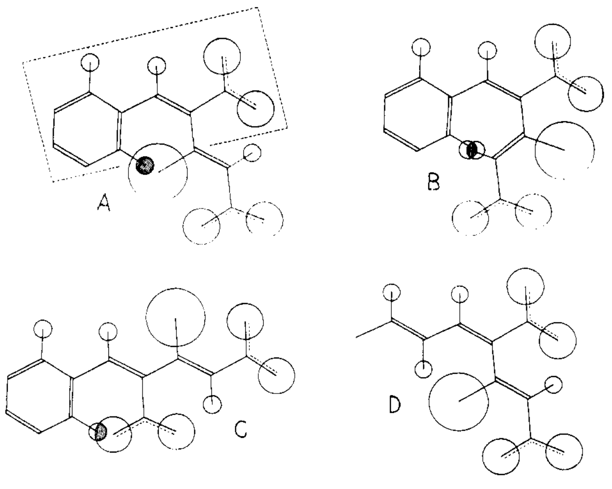


Fig. 1.—Scale drawings of: A, 4-*cis*-II (R = C_6H_5); B, 3-s-*cis*[16] isomer of A; C, 4-*trans* isomer of A; D, chain of, *e.g.*, 4-*cis*-II (R = $C_6H_5CH{=}CH$ or β-ionylidene[6]). In accordance with the suggestion of Braude, *et al.*,[19] the circles denote *covalent* radii. The carboxylate ion is shown.

Those diacids II derived from aldehydes other than benzaldehydes absorb at somewhat longer wave lengths than the corresponding acids B. This is understandable from Fig. 1D; the hindrance between the 3-methyl group and the chain hydrogen atom, while still severe, is less than that in the aryl-II's of Fig. 1A. The $C(CH_3){=}CH{-}CO_2H$ group can therefore make a small approach to coplanarity with the result of the molecule, and partake to a small extent in resonance with it.[15]

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(11) E. J. Corey and G. Fraenkel, This Journal, **75**, 1168 (1953).

(12) (a) P. Ruggli and A. Staub, *Helv. chim. Acta*, **20**, 37 (1937). (b) F. Bergmann and Z. Weinberg, *J. Org. Chem.*, **6**, 134 (1941); (c) G. B. Bachman and R. I. Hoaglin, *ibid.*, **8**, 300 (1943); (d) J. Codington and E. Mosettig, *ibid.*, **17**, 1027, 1035 (1952).

(13) The λ_{max} of the $C(CH_3){=}CHCO_2H$ (*cis*-crotonic acid) portion lies near 204 mμ, well below the range of our spectrophotometer. *Cf.* ref. *c* of Table III.

(14) The molecule is thus divided into *trans*-cinnamic and *cis*-crotonic acid systems. The 4-carboxyl group can now fully participate in resonance in the former system, whereas its cross-conjugated relation to the entire chromophoric system would preclude such complete participation in the non-hindered 4-*trans* form of Fig. 1C. This circumstance makes the 4-*cis* form relatively more stable with respect to the 4-*trans* form than would otherwise be anticipated.

The hindrance could also be relieved by rotation about the ring —C_1 single bond, giving the systems C_6H_6 and $CH_2{=}C(CO_2H){-}C(CH_3){=}CHCO_2H$. But here not only would the latter fragment still contain a cross-conjugated carboxyl group, but also the considerable resonance energy of conjugation of a benzene ring with an unsaturated chain would be lost. Accordingly, rotation about the 3–4 single bond is energetically favored.

(15) A scale drawing of the compound II (R = 2-furyl) (furan parameters of V. Schomaker and L. Pauling, This Journal, **61**, 1769 (1939)) reveals that the distance between centers of its methyl carbon and furan oxygen atoms is virtually the same as the distance between centers of the methyl carbon and interfering chain hydrogen atoms of Fig. 1D. Since the covalent radius of an oxygen atom is considerably larger than the covalent radius of a hydrogen atom, the furyl compound is more hindered than the chain compound of Fig. 1D. This is accurately reflected in the spectral data of Table III.

TABLE III[a]

	$\mathrm{R{-}CH{=}CH{-}\overset{CH_3}{C}{=}CH{-}CO_2H}$ (A)		II		$\mathrm{R{-}CH{=}CH{-}CO_2H}$ (B)		
R	λ_{max}, mμ	Ref.	λ_{max}, mμ	ϵ_{max}	λ_{max}, mμ	ϵ_{max}	Ref.
Alkyl	259	*c*	<220	...	<220	...	*c*
Nonadienyl[b]	311	*d*	280	22,200	259	20,000	*c*
2-Furyl	330	7	305	20,700	300	...	*e*
C_6H_5	308	7	276	17,600	273	21,000	*f*
m-$NO_2C_6H_4$	300	7	263	19,400	256	...	*g*
p-$MeOC_6H_4$	331	7	300	21,100	300	28,100	*h*
m-HOC_6H_4	308	7	277	15,900	278	...	*i*
3,4-$CH_2O_2C_6H_3$	341	7	323	15,350	320	15,500	
	308	7	293	11,050	290	11,500	*j*
3,4-$(MeO)_2C_6H_3$	339	7	317	16,800	318	17,500	
			~300	...	292	14,600	*j*
$C_6H_5CH{=}CH$	336	7	316	35,600	307	36,700	*k*
trans-β-ionylidene[5]	354	5	332	31,800	324	33,500	*l*
cis-β-ionylidene[5]	346	5	328	24,500	323	23,750	*l*

[a] Only those literature values which were determined in ethanol solution are considered. [b] From citral. [c] K. Dimroth, *Angew. Chem.*, **52**, 545 (1939). [d] R. S. Cahn, A. R. Penfold and J. L. Simonsen, *J. Chem. Soc.* 3134 (1931). [e] K. Hausser, *et al.*, *Z. physik. Chem.*, **B29**, 378 (1935). [f] The published values for the light absorption properties of cinnamic acid are widely divergent. The values given were determined in this Laboratory. [g] J. E. Purvis, *J. Chem. Soc.*, **107**, 966 (1915). [h] R. Mendes da Costa, *Compt. rend.*, **196**, 1815 (1933). [i] H. Ley, *Z. physik. Chem.*, **94**, 405 (1920). [j] I. A. Pearl and D. L. Beyer, *J. Org. Chem.*, **16**, 216 (1951). [k] These values were found for 5-phenyl-2,4-pentadienoic acid, m.p. 167–167.5°, prepared in this Laboratory by the Doebner condensation of cinnamaldehyde and malonic acid at 115°. [l] H. H. Inhoffen, F. Bohlmann and K. Bartram, *Ann.*, **561**, 13 (1948).

Alternative configurations do not explain the observed spectra. Figure 1B depicts the 3-s-*cis*[16] isomer of Fig. 1A. The actual overlap here, between the 2-hydrogen and *o*-hydrogen atoms, is very nearly that found between the *o*- and *o'*-hydrogen atoms of *cis*-stilbene, and while $\lambda_{max.}$ of *cis*-stilbene is depressed to 278 mμ from the value of 294 mμ for *trans*-stilbene,[17a] it still lies well above the $\lambda_{max.}$ of styrene (244 mμ).[17b] This amount of hindrance still allows partial coplanarity. The diacid molecules thus appear to adopt the more hindered but energetically favored[18] s-*trans* configuration. This accords with previous suggestions[19] and findings[20] about the configuration of other hindered molecules.

Figure 1C shows the *trans* arrangement about the 4-double bond, the alternative to that in Fig. 1A. The steric situation here is the same as that in *cis*-cinnamic acid. Although $\lambda_{max.}$ of this (264 mμ) is lower than $\lambda_{max.}$ of the *trans* acid (273 mμ),[21] considerable resonance interaction throughout the entire molecule is still possible, since the $\lambda_{max.}$ is far above that of benzene or styrene. Further, the strain in this configuration of the diacids would be relieved by rotation about the ring-chain single bond, so that the observed agreement between the spectra of the aryl-diacids II and the aryl acids B in Table III would not be expected.

Finally, the mere presence of the 4-carboxyl group, *per se*, would be expected to have a bathochromic effect[22] on the spectra of II, not an extreme hypsochromic effect; the diacids II would, in the absence of any other effect, be expected to have their $\lambda_{max.}$ at longer wave lengths than the monoacids A.

The last two entries in Table III are for compounds of the vitamin A class. The preparation in this Laboratory of the diacids II from *trans*- and *cis*-β-ionylideneacetaldehyde (C-diacid and D-diacid of ref. 5) and from these of the corresponding monoacids A of the table (vitamin A acids) has been given.[5] It is seen that the spectral properties of the two diacids are similar to the others in the table, and especially to the diacid II (R = $C_6H_5CH{=}CH$); this is expected, since the steric situations in the chain are similar (*cf.* Fig. 1D). The C- and D-diacids of ref. 5, therefore, have also the 4-*cis* configuration.

The configuration about the 2-double bond is not certain. While the non-formation of anhydride III on heating II (R = $C_6H_5CH{=}CH$) could be interpreted as indicating a *trans* arrangement, this seems insufficient evidence on which to base a generalization. Alterations in the configuration about this bond should affect the spectra of the compounds but little, as no hindrance is involved; this is an "allowed"[23] position for *cis* bonds.

Acknowledgment.—Ultraviolet absorption spectra were determined by members of the Products Control Laboratory of this Company, under the direction of Mr. Albert Besançon. Infrared spec-

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(16) "s-*cis*" is the term coined by R. S. Mulliken, *Rev. Mod. Phys.*, **14**, 265 (1942), to describe the *cis* arrangement of two double bonds about a single bond which possesses some double bond character.

(17) (a) L. Zechmeister, *Chem. Revs.*, **34**, 267 (1944); (b) L. F. Fieser and M. M. Pechet, THIS JOURNAL, **68**, 2578 (1946).

(18) J. G. Aston and G. Szasz, *J. Chem. Phys.*, **14**, 67 (1946).

(19) E. A. Braude, E. R. H. Jones, *et al.*, *J. Chem. Soc.*, 1890 (1949); E. A. Braude, T. Bruun, *et al.*, *ibid.*, 1419 (1952).

(20) C. H. MacGillavry, A. Kreuger and E. L. Eichorn, *Proc. K. Ned. Akad. Wet.*, **54B**, 449 (1951).

(21) A. Smakula and A. Wassermann, *Z. physik. Chem.*, **A155**, 353 (1931).

(22) Since the 4-carboxyl group of II is vinylogous to the second carboxyl group of alkylidenemalonic acids, its spectral effect might be expected to be comparable to this. α-Carboxy-5-phenyl-2,4-pentadienoic acid, m.p. 201° dec., prepared by the Doebner condensation at 90° of cinnamaldehyde and malonic acid, was found in this Laboratory to have λ_{max} 331 mμ, compared to λ_{max} 307 mμ for the 5-phenyl-2,4-pentadienoic acid listed in Table III. Further, muconic acid and furan-2,5-dicarboxylic acid absorb at slightly longer wave lengths than the corresponding monoacids. *Cf.* ref. *b* of Table III.

(23) L. Pauling, *Fortschr. Chem. org. Naturstoffe*, **3**, 203 (1939).

tra were determined and interpreted by Mr. William P. Blum of these Laboratories. Analyses were by the Microanalytical Laboratory of the Eastman Kodak Company, under the direction of Mr. Donald Ketchum.

Experimental[24]

Materials.—The methyl β-methylglutaconate (I) used in the majority of the work was prepared by the base-catalyzed methanolysis[25] of ethyl isodehydroacetate,[26] b.p. 112–115° (12 mm.). Comparison of its infrared spectrum with the spectra of the pure *cis*- and *trans*-I described below showed that it was 85% pure *cis* + *trans*-I, and that the ratio of the *trans* to the *cis* isomer was 9:1. The nature of the 15% of impurity is unknown except that, by infrared, it appeared to be a saturated ester. Allowance was made for the 15% of impurity in the stoichiometric calculations.

Aldehydes were used as received from the Eastman Kodak Company.

Preparation of *cis*-Methyl β-Methylglutaconate.—Ethyl isodehydroacetate was hydrolyzed with warm aqueous sodium hydroxide according to Feist[10] to give predominantly *trans*-β-methylglutaconic acid (m.p. 110–122°). The content of *cis* isomer was increased by heating this material for 4 hours on the steam-bath with 2 vol. of 20% hydrochloric acid. Crystallization at 5° gave 70–75% recoveries of material of m.p. 110–133°. Fractional crystallization or extraction of this material with hot benzene, in which the *cis* acid is difficultly soluble did not give a satisfactory separation of the isomers, so the following procedure was used. To the material dissolved in 2 vol. of ether was added 10 vol. of hot benzene, and the ether was removed from the solution through a fractionating column while the distilland was maintained at constant volume with fresh benzene. The desired *cis* acid separated from the boiling solution in nearly pure form (m.p. 143–146°) in 28–30% yield. Material (m.p. 112–122°) recovered from the filtrate from this was recycled to give an additional 30% yield of *cis* acid. Crystallization of the combined products from acetone–benzene gave the pure *cis* acid, m.p. 146.5–147.5°.

Esterification through the silver salt with methyl iodide in ether gave *cis*-I, b.p. 107.5–108° (12 mm.), in 97.5% yield.

Pure *trans*-I was similarly prepared from the *trans* acid (m.p. 115–116°), b.p. 111–112° (12 mm.).[27]

Condensation of Aldehydes with Methyl β-Methylglutaconate. General Procedure.—One mole of the aldehyde, 1.2 moles of I and 50 ml. of methanol were mixed, and a solution of 4.8 moles of potassium hydroxide in 1300 ml. of methanol was added, with cooling if necessary. The dipotassium salt of the product II usually started to separate from the warm solution in 2–10 min. The mixture was allowed to cool to room temperature over 5–6 hours, then cooled to 5°, and the salt filtered, washed with cold methanol, and vacuum dried. It was dissolved in 4 vol. of water and concd. hydrochloric acid added to congo red acidity. The product was filtered, washed well with water, dried and crystallized from 50% methanol.

If little or no potassium salt separated (*m*-hydroxybenzaldehyde and 2,6-dichlorobenzaldehyde), about half of the methanol was removed by evaporation, water added, and, after ether extraction, the aqueous solution was acidified.

Cinnamaldehyde under these conditions gave only a 16% yield of II (R = $C_6H_5CH{=}CH$) (m.p. 185–186° dec., $\epsilon_{316 m\mu}$ 35,600), the remainder being a red-brown gum.

Condensation of Cinnamaldehyde with *cis*-I.—The directions of Petrow and Stephenson[4] were followed. To a mixture of 22.5 g. (0.131 mole) of *cis*-I, 13.2 g. (0.10 mole) of cinnamaldehyde (freshly distilled, b.p. 116–117° (8 mm.)), and 25 ml. of methanol, cooled to −20° in an ice–salt bath, was added a solution of 43 g. of 85% potassium hydroxide (0.652 mole) in 300 ml. of methanol, precooled to −20°. After 1 hr. at −20° the mixture was let stand 3 days at 5°. The yield of dipotassium salt was 19.3 g. (57.8%). Acidification of its water solution gave 13.3 g. (51.6%) of crude II (R = $C_6H_5CH{=}CH$), m.p. 158–160° dec. The mixed m.p. with the crude product from *trans*-I (below) was not depressed. Crystallization of the crude product from aqueous methanol gave 9.7 g. of pure material, m.p. 187–187.5° dec., $\epsilon_{315 m\mu}$ 35,000. The melting point taken in a capillary was 185.5–186.5° dec. There was no depression on admixture with the pure product from *trans*-I.

From the filtrate from the crystallization of the crude product there was isolated an additional 0.6 g. of material of m.p. 180–181° dec., $\epsilon_{315 m\mu}$ 35,000; the remainder was oil. Concentration of the filtrate from the potassium salt yielded an additional 3.8 g. of this, which afforded 2.1 g. of diacid after one recrystallization. This melted at 180–181° dec., and had $\epsilon_{316 m\mu}$ 34,500. The m.p. of neither of these products was depressed by admixture with the product of m.p. 187–187.5°. There was thus no evidence for the formation of more than one crystalline product.

Condensation of Cinnamaldehyde with *trans*-I.—In a manner identical to the foregoing, *trans*-I gave 21.5 g. (64.4%) of potassium salt and 13.1 g. (50.8%) of crude II (R = $C_6H_5CH{=}CH$), m.p. 166–168° dec. (m.p. 158–160° in admixture with the above crude product). Recrystallization gave 8.9 g. of pure compound, m.p. 187–187.5° dec., $\epsilon_{315 m\mu}$ 34,600. As before, work-up of the filtrate from this gave, aside from oil, 0.6 g. of material of m.p. 179.5–180.5° dec., $\epsilon_{316 m\mu}$ 35,000, while the filtrate from the potassium salt yielded 0.9 g. of product of m.p. 179–180° dec., $\epsilon_{316 m\mu}$ 34,300. Again, only one crystalline product was isolated.

Hydrolysis of Cinnamylidene-β-methylglutaconic Anhydride (III).—III, m.p. 176–178°, $\epsilon_{388 m\mu}$ 40,000, was prepared from cinnamaldehyde, β-methylglutaconic acid and acetic anhydride according to Petrow and Stephenson.[4] A solution of 33.2 g. of 85% potassium hydroxide (0.5 mole) in 565 ml. of water and 13.0 g. (0.054 mole) of III was stirred and heated on the steam-bath for 2 hr. The solution was cooled and acidified, the solid taken into ether, methanol added, and crystallization conducted at −15° to give 6.7 g. (48%) of crude product, m.p. 183–185° dec. after one recrystallization. The mixed m.p. with one of the above pure products was 187–187.5° dec. From the filtrate from the 6.7 g. was obtained an additional 2.5 g. (18%) of material of m.p. 180–182° dec., showing no m.p. depression with the pure product. Only one diacid appeared to have been formed.

The bis-(*n*-butylamine) salt of II (R = $C_6H_5CH{=}CH$) was prepared by mixing equivalent amounts of the components in methanol and crystallizing by the addition of ethyl acetate. The material melted at 119–123° dec. after repeated crystallizations from methanol–ethyl acetate, $\epsilon_{308 m\mu}$ 32,450.

Anal. Calcd. for $C_{23}H_{36}N_2O_4$: N, 6.9. Found: N, 7.2.

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[24] Melting points were determined on a 3-in. immersion thermometer in the apparatus described by A. May, *Anal. Chem.*, **21**, 1427 (1949), and may be considered to be corrected. Ultraviolet spectra were determined on a Model 11M Cary Recording Spectrophotometer, and infrared spectra were taken on a Model 21 Perkin-Elmer Infrared Spectrophotometer.

[25] N. Bland and J. F. Thorpe, *J. Chem. Soc.*, **101**, 1557 (1912).

[26] F. R. Goss, C. K. Ingold and J. F. Thorpe, *ibid.*, **123**, 327 (1923).

[27] This preparation was done by Mr. Donald R. Nelan.