[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

Ultraviolet Absorption Spectra of Chalcones. Identification of Chromophores[1]

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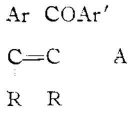
This paper deals with *cis-* and *trans*-chalcones, *cis–trans* photoequilibria, ultraviolet absorption spectra and effects of substituents on the ethylene linkage or in either or both phenyl nuclei, including the effects of *o*-methyls. The middle wave length ultraviolet absorption bands at 250–270 mμ of chalcones having the *cis* configuration, of chalcones with α- or β-substituents, of mesitalacetophenone, and of phenylbenzoylacetylene, are unequivocally identified as benzoyl or acrylophenone bands by the disappearance of these bands when two *o*-methyls are substituted into the benzoyl group to destroy its normal planarity. The cinnamoyl system appears primarily to be responsible for the intensity of the long wave length maximum above 285 mμ. *Para* substitution of nitro into the benzoyl group of *cis*-chalcone and *cis*-α-bromochalcone almost doubles absorptivity at the long wave length ultraviolet band; it is suggested that the styrene system in this and other related chalcones functions to some extent as a partially independent chromophore.

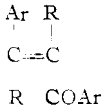
Of the two or three important regions of ultraviolet absorption which often appear simultaneously in the chalcone series (I and II) it has been suggested that the longest wave length band (usually above 285 mμ) is due to the molecule as a whole[3] and not just to the cinnamoyl portion[4] and that the shortest wave length bands (below *ca.* 240 mμ) are due to secondary absorption of the main chromaphore.[3] The bands in the intermediate area (250–270 mμ) which often appear and which may at times overlap the others, appear to be due to a partially independent chromophore (the benzoyl[3,4a,5] or acrylophenone group), and will be referred to as middle wave length bands whenever they clearly appear. The present investigation which includes further studies on *cis–trans* isomerism, photoequilibria and the effect of *para* substitution, has as its main purpose the unequivocal identification of the middle wave length bands.



$\overset{Ar}{\underset{R}{C}}=\overset{COAr'}{\underset{R}{C}}$

I *cis*

Ar = aryl



$\overset{Ar}{\underset{R}{C}}=\overset{R}{\underset{COAr'}{C}}$

II *trans*

***cis* Isomers and *cis–trans* Photoequilibria.**—Five *cis*-chalcone derivatives (three new) have been prepared by sunlight inversions of the *trans* compounds. In 0.00005 *M* ethanol solutions the photoequilibrium concentrations of *cis* isomer varied from 57–92% and were determined by proportions from the absorptivities, in four cases from both the middle and long wave length maxima and in the fifth from the long wave length maxima only (see Table I[6]). The photoequilibrium of the parent chalcones in isoöctane lies 74% on the side of the *cis* isomer[5a] whereas that of the α-bromochalcones lies almost entirely on the side of the *cis* (also in isoöctane).[5b]

The photoequilibrium spectra of chalcone derivatives which have been isolated in only one form (*trans*) have proved to be of value in assigning configurations and may be useful to some extent in estimating roughly the *cis–trans* ratio involved (see Table I).

The non-formation of other than the *cis* and *trans* compounds during irradiation was shown by the constancy of the photoequilibrium maxima under prolonged irradiation and by inspection of the slope and nature of the absorption curves. At 0.00005 *M* dilutions under exposure to sunlight or sunlamp the photoequilibria always were attained within a few seconds or minutes, whereas dimerization which is a likely competing reaction normally requires a long exposure time[7] and would be detectable by a continued rise in benzoyl group absorptivity and drop in chalcone absorptivity.

The *cis* isomers of chalcones bearing neither ethylenic nor *o*- or *o'*-substituents, which are the "labile" isomers, show lower absorptivities at the long wave length maxima than do the *trans* isomers; but only in the *cis* isomers do the spectra regularly show a directly observable middle wave length band in the 260 mμ region attributable to the benzoyl or acrylophenone group. Chalcones of this type when prepared by acid- or base-catalyzed condensation of aldehydes and acetophenones always have been *trans*. The absorption phenomena have been correlated with the configurational differences and with relative planarities of the *cis* and *trans* systems as evidenced from examination of scale models.[8] Where only the *trans* forms have been isolated the configurations are established unequivocally as *trans* by comparison of their spectra with those of photoequilibrium mixtures arrived at by irradiation of dilute solutions of these compounds; in going from the one chalcone (*trans*) to the photoequilibrium mixture the long wave length band

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[1] This project was supported in part by a contract with the Office of Ordnance Research. The work is described in a doctorate dissertation (W.B.B.), University of Virginia, May, 1954, and was reported at the September Meeting of the American Chemical Society, New York, N. Y., 1954 (Abstracts, B, 66-O).

[2] Du Pont Co. Postgraduate Fellow, 1953–1954.

[3] H. H. Szmant and A. J. Basso, THIS JOURNAL, **74**, 4397 (1952).

[4] (a) E. R. Katzenellenbogen and G. E. K. Branch, *ibid.*, **69**, 1615 (1947); (b) L. F. Ferguson and R. P. Barnes, *ibid.*, **70**, 3907 (1948).

[5] (a) R. E. Lutz and R. H. Jordan, *ibid.*, **72**, 4090 (1950); (b) R. E. Lutz, D. F. Hinkley and R. H. Jordon, *ibid.*, **73**, 4667 (1951); (c) W. B. Black and R. E. Lutz, *ibid.*, **75**, 5990 (1953).

[6] Ethanol is the least favorable solvent for a high ratio of *cis* isomer to *trans* in the photoequilibrium solutions of azobenzenes [W. R. Brode, J. H. Gould and G. M. Wyman, *ibid.*, **75**, 1856 (1953)]. In view of this it seems likely that had isoöctane been used instead of ethanol in the examples cited above then even higher proportions of *cis* isomers would have been found.

[7] *Cf.* (a) H. Stobbe and F. Wilson, *Ann.*, **374**, 237 (1910); (b) H. Stobbe and A. Hensel, *Ber.*, **59**, 2254 (1926); (c) H. Stobbe and K. Niedenzu, *ibid.*, **34**, 3897 (1901); *cf.* (d) P. L. Southwick, L. A. Pursglove and P. Numerof, THIS JOURNAL, **72**, 1600 (1950).

[8] The cinnamoyl system itself is necessarily less planar in the *cis* configuration than in the *trans* because of interference of an *o*-hydrogen of the benzal group with either the carbonyl oxygen or the carbonyl substituent, phenyl, mesityl, methyl [(a) R. E. Lutz, C. R. Bauer and R. H. Jordan, *ibid.*, **72**, 4300 (1950)], or even hydrogen; and this lowered planarity is primarily responsible for the sharply lowered absorptivities of the *cis* compounds at the long wave length maxima.

TABLE I

ULTRAVIOLET ABSORPTION DATA[a]

Compound[b]	$\lambda_{\max}$, mμ	$\epsilon_{\max}$
trans-$C_6H_5CH{=}CHCOC_6H_5$[c]	227.5	9,800
	307.5	24,300
cis-$C_6H_5CH{=}CHCOC_6H_5$[c]	250	13,700
	295	8,900
trans-$C_6H_5CH{=}CHCOC_9H_{11}$[d]	220	15,700
	295	24,900
at photoequilibrium	295	16,300
trans-$C_9H_{11}CH{=}CHCOC_6H_5$[c]	250	10,430
	321	14,670
cis-$C_9H_{11}CH{=}CHCOC_6H_5$	255	13,600
	320[h]	2,850
at photoequilib. from *trans*	255	13,170
% *cis*[f]: 86.5; 91.8	320[h]	3,830
at photoequilib. from *cis*	255	13,240
% *cis*[f]: 88.9; 91.8	320[h]	3,830
trans-$C_9H_{11}CH{=}CHCOC_9H_{11}$[30]	309	15,900
at photoequilibrium	295	5,900
trans-$C_6H_5CH{=}CBrCOC_6H_5$[g]*	257.5	10,600
	305	15,400
cis-$C_6H_5CH{=}CBrCOC_6H_5$[i,5b]	252.5	19,000
	297.5	9,300
trans-$C_6H_5CH{=}CBrCOC_9H_{11}$[11a]	302.5	20,500
at photoequilibrium	302.5	12,700
trans-$C_6H_5CBr{=}CBrCOC_6H_5$[i,j]	240	12,000
	254[k]	12,500
cis-$C_6H_5CBr{=}CBrCOC_6H_5$[i,j]	252.5[m]	16,300
trans-$C_6H_5CBr{=}CHCOC_6H_5$[i,j,g]*	257.5	13,900
	284[n]	13,200
at photoequilibrium[i,p]	254	18,200
	281[h]	15,100
$(C_6H_5)_2C{=}CHCOC_6H_5$[q,27b]	232.5	15,800
	250[h]	13,500
	298	10,100
trans-$C_6H_5CH{=}C(CH_3)COC_6H_5$[c,g]*	222.5	10,500
	260[h]	11,200
	290	17,400
at photoequilibrium	247.5	17,600
	285	8,000
trans-$C_6H_5C(CH_3){=}CHCOC_6H_5$[c]	227.5	9,600
	262.5[h]	10,500
	295	16,000
at photoequilibrium	252.5	12,300
	285	9,100
$C_6H_5C{\equiv}CCOC_6H_5$[j,g]*	222.5	14,200
	275[h]	16,100
	296	18,500
4-$CH_3OC_6H_4C{\equiv}CCOC_6H_5$	242.5	13,700
m.p. 82.5–83.5° (B[33] 81°)	262.5	12,900
	327.5	21,400
4-$CH_3OC_6H_4C{\equiv}CCOC_9H_{11}$	320	23,500
trans-4-$NO_2C_6H_4CH{=}CHCOC_6H_5$	316	28,800
cis-4-$NO_2C_6H_4CH{=}CHCOC_6H_5$	262.5	12,420
	299	16,080
at photoequilib. from *trans*	260[h]	10,650
% *cis*[f]: 80.3	305	18,590
at photoequilib. from *cis*	260[h]	10,600
% *cis*[f]: 83.3	305	18,180
trans-4-$NO_2C_6H_4CH{=}CHCOC_9H_{11}$[r]	307.5	26,500
at photoequilibrium	302.5	17,900
trans-4-$NO_2C_6H_4CH{=}CBrCOC_6H_5$[25]	265[h]	10,000
	310	18,770
cis-4-$NO_2C_6H_4CH{=}CBrCOC_6H_5$[25]	265	14,900
	302.5	15,900
at photoequilibrium from *trans*	266	12,850
% *cis*[f]: 58.2; 60.7	302.5	17,030
at photoequilibrium from *cis*	264	12,800
% *cis*[f]: 57.2; 60.0	305	17,110
trans-4-$CH_3OC_6H_4CH{=}CHCOC_6H_5$[s]	245	11,750
	341	24,000
cis-4-$CH_3OC_6H_4CH{=}CHCOC_6H_5$	252.5	17,760
	340	10,610
at photoequilib. from *trans*	251	16,240
% *cis*[f]: 74.7; 76.9	341	13,710
at photoequilib. from *cis*	251	16,250
% *cis*[f]: 75.0; 80.7	341	13,200
trans-4-$CH_3OC_6H_4CH{=}CHCOC_9H_{11}$	234[h]	10,100
	330	27,200
at photoequilibrium	234[h]	10,400
	331	22,900
trans-4-$CH_3OC_6H_4CH{=}CBrCOC_6H_5$	252.5	12,310
	336	20,110
cis-4-$CH_3OC_6H_4CH{=}CBrCOC_6H_5$	265	25,220
	335	3,490
at photoequilib. from *trans*	262.5	23,060
% *cis*[f]: 84.1; 83.3	335	6,140
at photoequilib. from *cis*	264	22,720
% *cis*[f]: 80.1; 83.6	335	6,210
trans-4-$CH_3OC_6H_4CH{=}CBrCOC_9H_{11}$	240[h]	7,500
	335	26,600
at photoequilibrium	240[h]	9,500
	337.5	15,000

[a] All spectra were obtained at 0.00005 *M* concentrations, in 95% ethanol unless otherwise indicated, using a Beckman DU quartz spectrophotometer. The known compounds in Table I were carefully purified; and all samples actually used for measurement except those indicated by asterisk were analyzed as a check on their purity and gave the correct values for carbon and hydrogen. The curves have been deposited as Document number 4551 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting in advance $2.50 for photoprints, or $1.75 for 35 mm. microfilm payable to: Chief, Photoduplication Service, Library of Congress. [b] C_9H_{11} denotes mesityl. "Photoequilibrium" in Table I and figures refer to the condition reached in 0.00005 *M* solutions of the specified compound or isomer after irradiation by sunlight or under a General Electric R. E. Sunlamp until no further change occurred. [c] Spectrum was obtained by Dr. Colin L. Browne.[10b] [d] E. P. Kohler, *Am. Chem. J.*, **38**, 553 (1907). [e] Yield 49%, m.p. 101–102.5° (F. and J. 97.5–98.5°): *Anal.* Calcd. for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.11; H, 7.24. See R. C. Fuson and H. L. Jackson, THIS JOURNAL, **72**, 1637 (1950); *cf.* also E. P. Kohler and L. W. Blanchard, *ibid.*, **57**, 367 (1935). [f] These figures denote the amount of *cis* isomer present at photoequilibrium, and were calculated by proportions from the absorptivities at the $\lambda_{\max}$ and those of the pure *cis* and *trans* isomers which had been determined separately. [g] These samples were purified carefully but were not analyzed (see *a**). [h] Shoulder or plateau. [i] These spectra were determined in isoöctane (see ref. 20). [j] The m.p. of samples used matched closely those reported in the literature. See C. Dufraisse, *Ann. chim.*, **17**, 133 (1922). [k] $\lambda_{\min}$ 243 mμ (ϵ 11,500); broad shoulder bounded by inflections at 280 mμ (ϵ 3000) and 310 mμ (ϵ 2000). [m] Inflection at 280 mμ (ϵ 5000) and linear drop in absorptivity to zero at 325 mμ. [n] $\lambda_{\min}$ 270 mμ (ϵ 12,500). [p] No real photoequilibrium could be obtained because of the fast deterioration of the sample; the values shown are the highest maxima obtained on exposure of dilute solutions of the sample to sunlight. [q] W. Dilthey and E. Last, *J. prakt. Chem.*, **94**, 49 (1916). [r] R. P. Barnes, G. E. Pinkey and W. A. DaCosta, THIS JOURNAL, **69**, 3129 (1947). [s] M.p. 77–78.5° (K. and C. 76° [E. P. Kohler and J. B. Conant, *ibid.*, **39**, 1702 (1917)]).

decreases in intensity and there appears the typical middle wave length band in the 250 mμ region.

The α,β-Bromo- and Dibromochalcones (I, II; R or/and R′ = Br).—The *cis*- and *trans*-α-bromochalcones both show a middle wave length band which is relatively higher in the *cis* than in the *trans*, and conversely the long wave length band is lower.[5b]

In the case of the *cis*- and *trans*-α,β-dibromochalcones steric interferences of groups are similar and very considerable, and the absorptivities at the long wave length maxima although similar are very small. It is believed that the isomer of m.p. 113.5–114.5° having the smaller absorptivity at the long wave length band and the larger absorptivity at the middle wave length band is the *cis* isomer. The isomer of m.p. 79–80°, believed to be *trans*, shows a double peak in the 240–260 mμ region which suggests that the benzoyl, dibromostyryl and dibromoacrylophenone systems may all be participating as partially independent chromophores. It is not known which isomer is the stable one.

The one known β-bromochalcone is believed from the absorption characteristics to be *trans*.

The *trans*-α-bromo derivatives of *p*-anisalacetophenone and *p*-anisalacetomesitylene were obtained by dehydrohalogenation of the corresponding dibromides by the action of base, and the lower-melting *cis* isomer of the former was made by sunlight inversion of the *trans* isomer.

The α-bromo-*p*-nitrochalcones (IV) are exceptional in that in this pair the *cis* isomer (m.p. 129°) is the higher melting and is the one obtained by dehydrohalogenation of the corresponding chalcone dibromide.[9] The *trans* isomer (lower melting 56°) is obtained by irradiation of ethanol solutions of the *cis* isomer; here the photoequilibrium at 0.00005 *M* dilution involves a 60:40 *cis–trans* ratio of the isomers (which is quite near the 55:45 ratio found for the α-phenylchalcone photoequilibrium). The normal type (catalytic) equilibrium on the other hand lies far over on the side of the *cis* isomer, and the *cis* isomer thereby is shown to be the stable form; this is consistent with the fact that the photoequilibrium, although also on the side of the *cis* isomer, lies relatively more toward the *trans*.

In three α-phenylchalcone types[5c] evidence of the formation of other products upon exposure of either stereoisomer to sunlight was found in two cases, namely, the *cis*- and *trans*-α-phenylchalcones themselves and *cis*- and *trans*-α-(*p*-nitrophenyl)-chalcones. For 0.00005 *M* solutions of each type photoequilibrium was attained within several minutes; then in each case the band near 260 mμ began to increase in intensity over one hour from about 15,000 to about 30,000. Here, therefore, the photoequilibrium ratios are not as certain as are those obtained for the other five chalcone pairs mentioned above; for α-phenylchalcones the ratio involves approximately 55% of *cis* isomer, for the α-phenyl-4-nitrochalcones about 30%, and for the α-(4-nitrophenyl)-chalcones about 20%.

The normal type (catalytic) equilibrium between *cis*- and *trans*-α-phenylchalcones,[7c] arrived at by heating either isomer, directly at 160° for several days or in a benzene–iodine solution, also involves a relatively even balance between the isomers and it is comparable with the somewhat evenly balanced photoequilibrium position.

In the case of α-phenyl-*p*-nitrochalcone the predominant product of the acid-catalyzed condensation is the *cis* isomer,[5c] a fact which indicates that the normal type (catalytic) equilibrium must lie on the side of the *cis* isomer and that here the *cis* isomer is the "stable" form.

The α- and β-methylchalcones are known each in only one form which is clearly *trans*,[10] and the ultraviolet absorption spectra show unmistakable evidence of middle wave length absorption areas in the form of shoulders at 260 and 262.5 mμ on the main bands of λ_{max} 290 and 295 mμ, respectively (Table I).[10b] The steric hindrance introduced by the two ethylenic substitutions of methyl into *trans*-chalcone has brought about hypsochromic shifts of the long wave length bands of 17.5 and 12.5 mμ, respectively, and has increased greatly the effectiveness of the chromophore responsible for the middle wave length band. It was predicted that the *cis* isomers (not yet isolated) would show very marked and separate middle wave length bands and considerable suppression of the long wave length bands; and this has been found to be true by conversion of ethanol solutions of the *trans* compounds into photoequilibria, and determination of the absorption spectra of the resulting mixtures which thereby were shown to contain considerable amounts of the *cis* isomers.[10b] These relationships are consistent with and support the assumption of *trans* configurations for the two known α- and β-methylchalcones.

Steric Effects in Elimination Reactions of Compounds Containing Mesityl Groups.—Attempts to obtain the α-bromochalcones (IV) from mesitalacetophenone and mesitalacetomesitylene dibromides (III), the latter by treatment with acetone–triethylamine, gave only the debrominated product V.

$$\begin{tikzcd}
\text{ArCHBrCHBrCOAr}' \arrow[r] \arrow[d, "\text{III}"'] & \text{ArCH}{=}\text{CBrCOAr}' \arrow[d, "\text{IV}"] \\
\text{ArCH}{=}\text{CHCOAr}' & \text{ArC}{\equiv}\text{CCOAr}' \\
\text{V} & \text{VI}
\end{tikzcd}$$

(Ar = aryl)

Since similar treatment of *p*-anisalacetomesitylene and *p*-anisalacetophenone dibromides gave only the corresponding α-bromochalcones (IV), the debromination effect cannot be attributed to the nature of the solvent.[11] It would seem therefore that the debrominations in the mesitalacetophenone dibromides series are favored by the steric effect of the *o*-methyl groups in the benzal group, a phenomenon which may be due in part to B-strain at the β-bromine.

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[9] Isolation of both stereoisomers from the dehydrohalogenation mixture has been reported (see Experimental, *cis*-α-Bromo-4-nitrochalcone) but no assignment of configurations was made.

[10] (a) E. P. Kohler, *Am. Chem. J.*, **31**, 642 (1904); (b) C. L. Browne, Dissertation, University of Virginia, 1953.

[11] (a) Others [R. P. Barnes, C. I. Pierce and C. C. Cochrane, This Journal, **62**, 1084 (1940)] obtained both the dehydrohalogenated and debrominated products from a treatment of mesitalacetophenone dibromide with an acetic acid–potassium acetate mixture. (b) It has been reported [C. L. Bickel, *ibid.*, **72**, 349 (1950)] that acetone solutions of potassium hydroxide cause debrominations of a number of chalcone dibromides but that both acetone–potassium acetate and ethanol–potassium acetate solutions cause only dehydrohalogenations.

Dehydrohalogenation of α-bromo-*p*-anisalacetomesitylene to the corresponding acetylene VI proceeded at approximately one-third of the speed of dehydrohalogenation of α-bromo-*p*-methoxychalcone under the same conditions, a phenomenon to be expected on the basis of both steric and electronic effects of the methyls on the β-hydrogen.

Identification of the Middle Wave Length Bands.—*trans*-Chalcones which have no substituents on the ethylene linkage or in the *o*- or *o′*-positions have a high degree of planarity and they usually show no middle wave length absorption bands in the 240–250 mμ region where acetophenone and acrylophenone show absorptivities of 13,300 and 20,900, respectively.[12] The 250 mμ absorption bands which occur in the spectra of all of the corresponding *cis*-chalcones, of *trans*-mesitalacetophenone and of *cis*- and *trans*-α-bromochalcones, are presumed to be due primarily to the benzoyl or acrylophenone systems which are brought out as partially independent chromophores by the several types of steric interference toward coplanarity of these systems with the rest of the molecule. If this is so these bands should be deleted or greatly reduced upon substitution of a mesityl for phenyl at the benzoyl end of the molecule because of disruption of the planarity of the aroyl system (acetomesitylene shows the very low absorptivity of 3,000[12d] at 240 mμ).

As seen from Table I the middle wave length bands of *trans*-α-bromochalcone (257.5 mμ) of *trans*-α-bromo-*p*-methoxychalcone (252.5 mμ) and of *trans*-mesitalacetophenone (250 mμ) actually are deleted by the substitution of a mesitoyl group for the benzoyl. This demonstrates that the middle wave length bands in these three *trans* compounds are actually benzoyl or acrylophenone bands.

Unsuccessful attempts were made to prepare and isolate pure *cis*-chalcones with the benzoyl replaced by mesitoyl, in order to make similar comparisons. Four *trans*-mesitoyl compounds in dilute ethanol solutions were converted into *cis*–*trans*-photoequilibrium mixtures which were shown from their absorptivities to involve considerable proportions of the *cis* isomers and these mixtures were used instead of the pure *cis* isomers. The absorption curves for the four pure *cis* reference isomers, namely, *cis*-chalcone, *cis*-mesitalacetophenone, *cis*-*p*-methoxychalcone and *cis*-*p*-nitrochalcone, and the curves for their *cis*–*trans* solution–photoequilibrium mixtures, all show strong molar absorptivities near 250 mμ. On the other hand, the curves for the solution–photoequilibria from the corresponding *trans*-mesitoyl analogs of these compounds which contain appreciable amounts of the respective *cis* isomers, show no evidence of significant absorption in the 250 mμ region. Thus in these *cis*-chalcones the deletion of the 250 mμ bands by the *o′*-substitution of methyls in the benzoyl group is demonstrated.

The intensity of absorption at the long wave length maximum of both *cis*- and *trans*-chalcones, it should be noted, is not affected seriously by steric interference with the planarity of the benzoyl group as a result of the introduction of *o*-methyls into this group. That the cinnamoyl system is primarily responsible for the intensity of absorption at the long wave length band is evident from the fact that cinnamaldehyde, *trans*-benzalacetone, *trans*-chalcone and *trans*-benzalacetomesitylene, where the aroyl planarity is destroyed by steric hindrance, all have comparable absorptivities of 25,000,[13] 23,500,[12b] 24,300 and 24,900, respectively.[14]

Acetylene Analogs of the Chalcones.—Phenylbenzoylacetylene (VI), which presumably has a planar molecule,[16] has a major long wave length absorption band, but this band (in contrast to that of *trans*-chalcone) has a pronounced shoulder at 271 mμ which corresponds to a middle wave length band attributable to the benzoyl group. Substitution of a *p*-methoxyl at the benzilidine end shifted the long wave length band 30 mμ bathochromically and exposed the shoulder in the form of a now-isolated maximum at approximately the same position (265 mμ). Then subsequent substitution of a mesitoyl group for the benzoyl caused deletion of this middle wave length band and thereby showed it to be due to the benzoyl group.[17] That phenylbenzoylacetylene has a pronounced benzoyl absorption in spite of the necessarily high degree of planarity comparable with that of the analogous *trans*-chalcone is consistent with the lower polarizability of the acetylene linkage.[18]

Some Effects of Substituents in the Phenyl Groups.—Substitution of mesital for the benzal group of *trans*-chalcone produced a bathochromic

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(12) (a) T. W. Campbell, S. Linden, S. Godshalk and W. G. Young, THIS JOURNAL, **69**, 880 (1947); (b) A. L. Nussbaum, O. Mancera, R. Daniels, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3263 (1951); (c) The intensity of the main band of *trans*-chalcone itself on its shorter wave length slope is greater than can be accounted for by overlapping the secondary band, and this suggests that there might be involved a masked low intensity band such as is revealed by graphical resolution[10b] (*ca.* λ_{max} 270 mμ, ε 6,700). (d) L. H. Schwartzman and B. B. Corson, THIS JOURNAL, **76**, 781 (1954).

(13) J. F. Thomas and G. E. K. Branch, *ibid.*, **75**, 4793 (1953).

(14) **Exclusion of Other Interpretations.**—It is unlikely that the middle wave length chalcone bands at *ca* 250 mμ are due to the cinnamoyl group because of the shortness of the wave length involved (benzalacetone absorbs at 289 mμ[15]); the possibility was excluded by the fact that substitution of a *p*-methoxyl in the benzal group (which in benzalacetone produces a 33 mμ bathochromic shift[15]) causes no significant shift in the middle wave length bands of *cis*-chalcone and of *cis*- and *trans*-α-bromochalcones. That the middle wave length bands cannot be due to the styrene system is demonstrated by the fact that replacement of the benzoyl group by mesitoyl in several cases caused them to disappear even though there had been introduced no appreciable interference with the planarity of the styrene system as is shown by the continued existence of the strong band at 290 mμ or higher in the spectrum of each mesitoyl compound. That the vinyl ketone system alone could be responsible for the middle wave length absorption is excluded on similar grounds. That the middle wave length bands are not due to secondary absorption of the molecule as a whole is shown by the fact that true secondary bands often do appear as third bands at the shortest wave length. These secondary bands (to be considered in a later paper by W. B. B.) are identified as such by the fact that in several cases *para* substitution of auxochromic groups in the benzal group causes a significant bathochromic shift of these bands; middle wave length bands due to the benzoyl or acrylophenone group undergo no comparable bathochromic shift as a result of such a substitution.

(15) V. Alexa, *Bull. soc. chim. Romania*, **18A**, 93 (1936).

(16) *Cf.* J. F. Music and F. A. Matsen, THIS JOURNAL, **72**, 5256 (1950).

(17) The short wave length absorption at *ca.* 230 mμ must involve some contribution by the mesityl group. In the spectrum of mesitylene [J. R. Platt and H. B. Klevens, *J. Chem. Phys.*, **16**, 832 (1948)] there is a pronounced shoulder at 220 mμ (ε 9000) (hexane) (see also Ref. 12d).

(18) *Cf.* A. D. Walsh, *Quart. Revs. (London)*, **2**, 78 (1948); *Ann. Repts. Prog. Chem. (Chem. Soc., London)*, **44**, 35 (1947).

effect of 12.5–15 mμ. On the other hand, substitution of mesitoyl for the benzoyl group produced a hypsochromic shift of 12.5 mμ in *trans*-chalcone, and of 12.5, 12.5 and 7.5–10 mμ, respectively, in *trans-p*-methoxybenzal-, *p*-nitrobenzal- and mesitalacetophenones. As might then have been expected substitutions of mesityls for both phenyls resulted in practically no shift at all.

Substitution of an electron-donating group in the *para* position of the benzal group of *trans*-chalcone produces a bathochromic shift of the primary band roughly in proportion to the donative ability of the substituent,[3,15] and the absorptivity increases roughly in proportion to the displacement.[15] Substitution of the electron-attracting nitro group likewise resulted in a bathochromic shift although a considerably smaller one,[15,19a] a result which is logical because by this substitution the ground state of the system has gained one more conjugated double bond.[19b]

Some Evidence of Partial Independence of the *p*-Nitro and *p*-Methoxystyrene Chromophores.—The absorptivities at the long wave length maxima of the *p*-nitro-*cis* and *trans*-chalcones, respectively, are greater than those of the parent chalcones. The almost twofold increase in absorptivity caused by substitution of the *p*-nitro group in the *cis* isomer (from 8,900 to 16,080) is a far greater increase than that by similar substitution in the *trans* isomer (from 24,300 to 28,800). Again, in the α-bromochalcone series, *p*-nitro substitution in the benzal group of the *cis* isomer resulted in an almost twofold increase in absorptivity at the long wave length maximum (from 9,300[20] to 15,900).[21] On the other hand, while *para* substitution of methoxyl into the benzal group of *cis*-chalcone had little effect on the absorptivity at the long wave length maximum (8,900 to 10,610) such a substitution in *cis*-α-bromochalcone resulted in a considerable diminution of absorptivity (from 9,300 to 3,490), and a significant increase in the absorptivity at the middle wave length band (from 18,800[20] to 25,200).

The abnormally high absorptivities at the primary maxima of the *cis-p*-nitrochalcone types can be explained in terms of an appreciably absorbing and partially independent chromophore, namely, the *p*-nitrostyrene system, which is not absorbing to a comparable extent in the *trans* isomers, and whose absorption at *ca.* 300 mμ[22] overlaps that of the cinnamoyl chromophore. The polarization of the *p*-nitro group in opposition to that of the carbonyl, particularly in the *cis* isomer where the styrene system is necessarily less coplanar with the carbonyl than it is in the *trans* isomer, should significantly increase the individual relative planarity and independence of the styrene chromophore and decrease those of the acrylophenone system.[23]

Possibly the opposite and lowering effect of substitution of *p*-methoxy in *cis*-α-bromochalcone on the absorptivity at the long wave length band and the raising of the middle wave length absorptivity is due also to an increase in the relative planarity and resonance of the styrene system. The different effect on absorptivity may be explained by the expectation that absorption by the anisal system would not overlap the long wave length band of the chalcone chromophore, but rather would overlap and reinforce that of the benzoyl group. However, the polarization of the anisal group is in the direction of that of the parent chalcone system, and it is logical to suppose that individual effectiveness of the styrene system might not be very great in the parent *cis-p*-methoxychalcone series and would be significant only in the less planar *cis*-α-bromo types.

Acknowledgment.—Dr. Colin L. Browne, while National Science Foundation Postgraduate Fellow in this Laboratory (1952–1953),[10b] carried out a graphical analysis of the spectrum of *trans*-chalcone and determined the spectra and photoequilibrium spectra of the methylchalcones.

Experimental[24]

***cis*-α-Bromo-4-nitrochalcone**[25] was prepared by refluxing for 1.5 hr. a solution of 4-nitrochalcone dibromide of m.p. 151–152.5° (W.[26] 151°) and an equimolar amount of fused potassium acetate in a minimum amount of ethanol; crystallized from low boiling petroleum ether as yellow needles, m.p. 127–129°. No other solid product was isolated. (Using cold methanol–acetone as solvent K. and A.[25] isolated both isomers, m.p. 130° and 62°.)

***trans*-α-Bromo-4-nitrochalcone**[25].—Sunlight exposure of a solution of 0.75 g. of the *cis* isomer of m.p. 128–129° in 400 ml. of benzene for 5.5 hr., evaporation and addition of 20 ml. of ethanol, gave 0.35 g. (46%) of starting material. The dark yellow *cis* isomer was isolated from the filtrate by fractional crystallization and manual separation; yield 20%, m.p. 54.5–56°. *Anal.* Calcd. for $C_{15}H_{10}BrNO_3$: C, 54.24; H, 3.04. Found: C, 54.24; H, 2.91.

Equilibrium between *cis*- and *trans*-α-Bromo-4-nitrochalcones.—A benzene solution of the *trans* isomer of m.p. 55–56° containing sufficient iodine to maintain color, was exposed to sunlight for 5 hr. Evaporation and crystallization from isoöctane gave chiefly *cis* isomer of m.p. 114–120° which was identified by mixture melting point. Equilibrium thus is shown to lie far on the side of the *cis* isomer.

Refluxing a similar solution of the *cis* isomer in the presence of iodine for 4 hr. was without apparent effect.

***cis*-4-Methoxychalcone** was prepared by exposing a benzene solution of the *trans* isomer of m.p. 76–78° to sunlight

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(19) (a) It has been pointed out that in *para*-disubstituted benzenes involving like groups, the resultant bathochromic shift is approximately that which one group alone would produce, and no cancellation of effects is involved [L. Doub and J. M. Vandenbelt, THIS JOURNAL, **69**, 2714 (1947)]. In *p*-nitrochalcone a similarity to *p*-disubstituted benzenes exists in that at the end of the styrene system there are similar groups which do not cancel each other in effectiveness; (b) *cf.* H. Kuhn, *J. Chem. Phys.*, **17**, 1198 (1949).

(20) The value for *cis*-α-bromochalcone, although obtained in isoöctane, is valid for comparison because it should not be appreciably different from that which would be obtained in ethanol: for example, the intensity of the long wave length band of *trans*-α-bromochalcone in isoöctane (ref. 5b) is 15,700 and in ethanol it is 15,400.

(21) It will be noted that the differences in absorptivities at the long wave length maxima of the *p*-nitro *cis–trans* pairs are smaller than in the other pairs studied (except the α-phenyl- and α,β-dibromochalcones) and in the benzalacetones[8a]; in the absence of the *p*-nitro group the *cis–trans* differences are usually about threefold and are attributed to the severe deviation in the *cis* isomers from the planarity of the cinnamoyl system.

(22) It is supposed that the *p*-nitrostyrene group would have a molar absorptivity of *ca.* 10,000 at *ca.* 300 mμ; for *p*-nitrostyrene, λ_{max} 303 mμ (ε 14,500) in methanol [M. Pestemer, T. Langer and F. Manchen, *Monatsh.*, **68**, 326 (1936)].

(23) *Cf. trans*-α-phenyl-4-nitrochalcones (ref. 5c) where both the *cis-p*-nitrostilbene and the *trans-p*-nitrochalcone systems seem to be functioning simultaneously as partially independent chromophores [*cf.* communication which appeared since this paper was submitted, Y. Urushibara, F. Iimura and K. Ikeda, *J. Chem. Phys.*, **22**, 1943 (1954)].

(24) Microanalyses by Miss Patricia L. Paynter; alkoxyl determinations by Clark Microanalytical Laboratories.

(25) E. P. Kohler and C. R. Addinall, THIS JOURNAL, **52**, 3728 (1930).

(26) H. Wieland, *Ber.*, **37**, 1148 (1904).

and sunlamp for 5 days. Crystallization from ethanol and from isoöctane gave unchanged material. Concentration of the isoöctane and cooling in the "deep freeze" gave lemon-yellow clusters; recrystallized, m.p. 33–33.5°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.76; H, 6.00.

Stobbe, *et al.*,[7a,b] were unsuccessful in obtaining the *cis* isomer of 4-methoxychalcone by the action of sunlight on iodine-containing solutions of the *trans* isomer, by heating the *trans* isomer above its melting point, or by irradiation of its solution in acetic acid, ethanol or chloroform, both in the presence of air or *in vacuo*. Illumination of the solid *trans* isomer (1000 hr.) gave a dimer of m.p. 164°.

trans-**α-Bromo-4-methoxychalcone**[27] was prepared from 25 g. of 4-methoxychalcone dibromide of m.p. 132–134° by treatment with 40 ml. of triethylamine in 200 ml. of acetone at room temperature (reagent grade acetone is used because the β-bromine is so reactive that it is replaced readily by an alkoxy group even during crystallization from alcohol[27]). After 4 hr. the amine hydrobromide (73%) was filtered off. Evaporation under reduced pressure left a residual oil which was crystallized from ethanol; 7.5 g. (38%), light yellow, m.p. 80–90°; recrystallized, m.p. 94.5–96° (P. and S.[27] 94.5°).

cis-**α-Bromo-4-methoxychalcone**.—A solution of 8.0 g. of the *trans* isomer of m.p. 94.5–96° in 2.5 l. of 95% ethanol was exposed for one week to sunlight and sunlamp. Evaporation left starting material and oil. The oil was taken up in isoöctane and on cooling at −20° more *trans* isomer came down slowly during one week; the solution was decanted and again placed in the "deep freeze." Bright yellow crystal clusters of *cis* isomer appeared and grew slowly, m.p. 52–55°; recrystallized, m.p. 54–54.5°.

Anal. Calcd. for $C_{16}H_{13}BrO_2$: C, 60.58; H, 4.13. Found: C, 60.68; H, 4.13.

trans-**4-Bromochalcone**[28] was obtained in 97% yield by condensation of 4-bromobenzaldehyde and acetophenone in 3% potassium hydroxide–85% ethanol (5 min. at room temperature and 5 hr. at 0°); m.p. 127–128° (W.[28] 123.5°).

Anal. Calcd. for $C_{15}H_{11}BrO$: C, 62.74; H, 3.86. Found: C, 62.47; H, 3.75.

trans-**3-Methylchalcone**[29] was prepared by addition of a solution of 25 g. of acetophenone in 30 ml. of ethanol dropwise with stirring to a solution at 0° of 1.8 g. of sodium and 25 g. of *m*-methylbenzaldehyde in 85 ml. of 95% ethanol. After 3 hr. at 0° the pale yellow slurry was filtered and the residue was washed with a little ethanol; lemon yellow, 27.5 g.; melting was nearly complete around 50° but a trace of solid persisted up to 120°. Subsequent recrystallizations from ethanol showed that the product was primarily 3-methylchalcone, yield about 50%, m.p. 67.5–68.5° (W. and S.[29] 66°).

A **secondary product** [$(C_6H_5COCH_2)_2CHC_6H_4CH_3$(*meta*)?] was obtained from one experiment carried out as above but allowing the solution to stand overnight; m.p. 234–236°. *Anal.* Calcd. for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48. Found: C, 84.17; H, 6.21. Another **secondary product** was obtained when the reaction mixture was heated at 100° overnight; m.p. 194–195.5°. *Anal.* C, 84.95; H, 6.17.

α-Bromo-β-ethoxy-β-mesitylpropiophenone was obtained in small yield as the only homogeneous product of an attempt to obtain *trans*-α-bromomesitalacetophenone by the dehydrobromination of mesitalacetophenone dibromide with alcoholic potassium hydroxide. To a refluxing solution of 7.5 g. of mesitalacetophenone dibromide (m.p. 141–143°) in 450 ml. of ethanol and 60 ml. of water was added dropwise a solution of 1.0 g. of potassium hydroxide in 90 ml. of water, with addition of 200 ml. of acetone to increase solubility; refluxing time one hour. Slow crystallization of the product from ethanol gave colorless plates, m.p. 80–82°.

Anal. Calcd. for $C_{20}H_{23}BrO_2$: C, 64.00; H, 6.18; OC_2H_5, 12.01. Found: C, 63.84; H, 6.10; OC_2H_5, 12.34.

Attempts to Obtain α-Bromo-2,4,6-trimethylchalcone (α-Bromomesitalacetophenone).—The above α-bromo-β-ethoxy compound remained unchanged on vacuum sublimation. Attempts to dehydrobrominate mesitalacetophenone dibromide by the action of ethanolic potassium acetate were unsuccessful; using a glacial acetic acid–potassium acetate mixture, only *trans*-mesitalacetophenone (the debrominated product) could be isolated. Mesitalacetophenone was the first product isolated by earlier authors[11a] who were successful in obtaining a small yield of α-bromomesitalacetophenone. In attempting dehydrobromination with an ethanolic solution of triethylamine only the debromination product, *trans*-mesitalacetophenone, was isolated in 63% yield.

cis-**2,4,6-Trimethylchalcone** (*cis*-mesitalacetophenone) was obtained by exposure of a benzene solution of the *trans* compound of m.p. 96–101° in sunlight for one day; light yellow crystals from ethanol, m.p. 65–66° (mixture melting point with *trans* isomer, 52–70°).

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.24; H, 7.02.

Mesitalacetomesitylene Dibromide.—Bromine was added dropwise to a solution of *trans*-mesitalacetomesitylene[30] in 100 ml. of hot glacial acetic acid; recrystallization from ethanol gave a yield of 70%, m.p. 93–97°; recrystallized, m.p. 99–101°.

Anal. Calcd. for $C_{21}H_{24}Br_2O$: C, 55.77; H, 5.35. Found: C, 55.65; H, 5.14.

An attempt to prepare α-bromomesitalacetomesitylene by dehydrobromination of mesitalacetomesitylene dibromide (acetone–triethylamine) gave instead 36% of the debrominated product, *trans*-mesitalacetomesitylene (identified by mixture m.p.).

trans-**4-Methoxy-2′,4′,6′-trimethylchalcone** (*trans*-4-methoxybenzalacetomesitylene)[31] was obtained in two polymorphic modifications. In the first condensation experiment a 50% yield of yellow lower melting polymorph (new) was obtained; recrystallized twice from ethanol and thrice from isoöctane, m.p. 78–79°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.52; H, 7.09.

After standing for one week the m.p. of this analytical sample had changed to 104–106°, and no more of the lower melting polymorph could be produced. All subsequent condensations of anisaldehyde and acetomesitylene yielded only the higher melting polymorph (known), m.p. 106.5–107.5° (B. and D.[31] 103–104°). *Anal.* Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.09; H, 7.02.

4-Methoxy-2′,4′,6′-trimethylchalcone Dibromide.—Bromination of the *trans*-chalcone was carried out in carbon tetrachloride at 0°; first crop, m.p. 125–140°, the second m.p. 125–130°, yield 99%; recrystallized from an acetone–water mixture, m.p. 136–137° dec. (each subsequent recrystallization from either an acetone–water mixture or low-boiling ligroin resulted in a further lowering of the m.p. (*cf.* below)).

Anal. Calcd. for $C_{19}H_{20}Br_2O_2$: C, 51.84; H, 4.58. Found: C, 52.14; H, 4.71.

α-Bromo-β-methoxy-β-(p-anisyl)-propiomesitylene.—The early procedure for making *p*-anisalacetomesitylene dibromide by the bromination of the chalcone in carbon disulfide[32] was followed; a melting point of the crude product (the true dibromide described above) was taken; m.p. 133° Barnes and Reed in their procedure[32] had evaporated the carbon disulfide from the bromination mixture and dissolved the residue in hot methanol; the product which they obtained from this procedure and which they believed to be the dibromide, melted at 153.5–154.5° and was undoubtedly α-bromo-β-methoxy-β-(p-anisyl)-propiomesitylene. The β-bromine of the dibromide is very reactive just as it is in the dibromide of 4-methoxychalcone,[27a] and it is very easily displaced by methoxyl. The 136–137° compound, which is actually the dibromide, was subsequently "recrystallized" from methanol and gave an 88% yield of the β-methoxy compound which melted at 154–155°.

Anal. Calcd. for $C_{20}H_{23}BrO_3$: C, 61.38; H, 5.92; OCH_3, 15.88. Found: C, 61.53; H, 5.85; OCH_3, 16.56.

trans-**α-Bromo-4-methoxy-2′,4′,6′-trimethylchalcone** (*trans*-**α-Bromo-p-anisalacetomesitylene**).—A solution of 15 g. of the chalcone dibromide in 250 ml. of pure acetone

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[27] (a) F. J. Pond and A. S. Schoffstall, THIS JOURNAL, **22**, 658 (1900); (b) E. P. Kohler and R. M. Johnstin, *Am. Chem. J.*, **33**, 35 (1905), P. and S. incorrectly formulated the compound as β-bromo; for proof see K. and J.).

[28] C. Weygand, E. Bauer, H. Gunther and H. Heynemann, *Ann.*, **459**, 99 (1927).

[29] C. Weygand and F. Schacher, *Ber.*, **68**, 227 (1935).

[30] R. C. Fuson and J. S. Meek, *J. Org. Chem.*, **10**, 551 (1945).

[31] R. P. Barnes and H. Delaney, THIS JOURNAL, **65**, 2155 (1943).

[32] R. P. Barnes and G. W. Reed, *ibid.*, **69**, 3132 (1947).

and 30 ml. of triethylamine was allowed to stand overnight at room temperature. After filtering from amine hydrobromide and evaporating under reduced pressure, the residue was taken up in ethanol. Slow evaporation over several days gave light yellow crystals of m.p. 82.5–86.5°, yield 50%; recrystallized from ethanol, m.p. 91–92° (B. and R.[32] 87.5°); it gave no mixture m.p. depression with a sample prepared by the Barnes procedure[32] from the β-methoxy compound above.

Anal. Calcd. for $C_{19}H_{19}BrO_2$: C, 63.52; H, 5.33. Found: C, 63.22; H, 5.20.

Attempts to prepare *cis* isomers in the 2′,4′,6′-trimethylchalcone (benzalacetomesitylene) series by exposure of benzene solutions of *trans* isomers to sunlight for 2.5 hr., for 4 days or for 15 days, gave only starting compound and resins.

p-Anisylmesitoylacetylene was prepared by dehydrobromination of *trans*-α-bromo-4-methoxybenzalacetomesitylene (m.p. 91–92°) by the Bickel procedure[33] except that a threefold reaction time was necessary; recrystallized from ethanol, m.p. 66.5–67° (colorless).

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.58; H, 6.54.

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[33] C. L. Bickel, THIS JOURNAL, **69**, 2134 (1947).

CHARLOTTESVILLE, VA.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, CHEMICAL DIVISION, MERCK & CO., INC.]

Synthesis of DL-Dimethyldihydro-α-lipoic Acid

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DL-Dimethyldihydro-α-lipoic acid has been synthesized. It showed no α-lipoic acid activity in the enzymatic POF assay. Attempts to convert this acid to DL-α-lipoic acid gave only low yields of α-lipoic acid as determined by enzymatic assay.

Several syntheses of DL-α-lipoic acid (XI) have been reported.[1] A preliminary account of the synthesis of (+)-, (−)- and DL-α-lipoic acid has been reported from these laboratories.[2] This paper describes a synthesis of DL-dimethyldihydro-α-lipoic acid (X). Demethylation of this acid gave only low yields of α-lipoic acid as determined by the enzymatic POF assay.[3]

γ-Butyrolactone (I) was converted to 2,4-dibromobutyric acid (II).[4] The first sulfur-containing intermediate of this sequence, 2,4-di-(methylthio)-butyric acid (III), was prepared by adding 2,4-dibromobutyric acid (II) to an excess of sodium methyl mercaptide in methanol solution. Although syntheses of the 2,4-dihalobutyric acids are described in the literature,[4,5] preparation of the pure acids was complicated by the ready elimination of the 4-halogen to give mixtures of the dihalo acid and the corresponding α-halo-γ-butyrolactone. Consequently, the crude bromination mixtures were treated immediately with the sodium mercaptide. The dithioether was purified by distillation, although the undistilled product was sufficiently pure for use in the next step.

A second synthesis of this dithioether, involving the addition of an alkyl mercaptide to a substituted γ-butyrolactone,[4] gave lower yields. α-Methylthio-γ-butyrolactone was prepared from sodium methyl mercaptide and α-bromo-γ-butyrolactone. A toluene suspension of sodium methyl mercaptide reacted with α-methylthio-γ-butyrolactone to yield an intermediate addition product. Fusion of this product at 165–170° for one hour yielded the sodium salt of 2,4-di-(methylthio)-butyric acid. The yields from this alternate method were one-half those of the direct method.

2,4-Di-(methylthio)-butyric acid was converted to 2,4-di-(methylthio)-butyryl chloride (IV) which was purified by distillation and characterized by conversion to the methyl ester.

The acylation of ethyl *t*-butyl α-ethoxymagnesiomalonate with 2,4-di-(methylthio)-butyryl chloride yielded the intermediate, ethyl *t*-butyl [2,4-di-(methylthio)-butyryl]-malonate (V). This product was not isolated but was converted to the β-keto ester VI by elimination of the *t*-butyl group and decarboxylation[6] using catalytic amounts of *p*-toluenesulfonic acid in refluxing benzene solution. Ethyl [2,4-di-(methylthio)-butyryl]-acetate (VI) was purified by distillation and showed ultraviolet absorption characteristic of α-keto thioethers.[7] Absorption maxima were observed at 246 and 294 mμ.

The β-keto ester VI was converted to methyl 4-carbethoxy-4-[2,4-di-(methylthio)-butyryl]-butyrate (VII) by either a condensation with methyl acrylate or alkylation with methyl β-chloropropionate. The product VII distilled as a viscous high-boiling oil and showed ultraviolet absorption maxima characteristic of α-keto thioethers.[7] Hydrolysis and decarboxylation of the keto diester VII with hydrochloric acid in glacial acetic acid solution was not complete. Although the acidic product gave the calculated neutralization equivalent for acid VIII, extra carbonyl absorption was noted in the infrared. The crude product was saponified with cold 1 *N* sodium hydroxide. After acidification and extraction a semi-solid mixture was obtained. Fusion of this mixture at 80–85° for one hour completed the decarboxylation to yield 4-

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[1] C. S. Hornberger, Jr., R. F. Heitmiller, I. C. Gunsalus, G. H. F. Schnakenberg and L. J. Reed, THIS JOURNAL, **75**, 1273 (1953); M. W. Bullock, J. A. Brockman, Jr., E. L. Patterson, J. V. Pierce, M. H. von Saltza, F. Sanders and E. L. R. Stokstad, *ibid.*, **76**, 1828 (1954); Q. F. Soper, W. E. Buting, J. E. Cochran, Jr., and A. Pohland, *ibid.*, **76**, 4109 (1954); L. J. Reed and Ching-I Niu, *ibid.*, **77**, 416 (1955).

[2] E. Walton, A. F. Wagner, L. H. Peterson, F. W. Holly and K. Folkers, *ibid.*, **76**, 4748 (1954).

[3] I. C. Gunsalus, M. I. Dolin and L. Struglia, *J. Biol. Chem.*, **194**, 849 (1952).

[4] H. Plieninger, *Ber.*, **83**, 265 (1950).

[5] J. E. Livak, E. C. Britton, J. C. Vander Weele and M. F. Murray, THIS JOURNAL, **67**, 2218 (1945); E. C. Britton and J. C. Vander Weele, U. S. Patent 2,530,348 (1950); E. C. Britton, J. C. Vander Weele and J. E. Livak, U. S. Patent 2,557,779 (1951).

[6] D. S. Breslow, E. Baumgarten and C. R. Hauser, THIS JOURNAL, **66**, 1286 (1944).

[7] E. A. Fehnel and M. Carmack, *ibid.*, **71**, 84 (1949).