hydride) in a nitrogen atmosphere was stirred in an ice bath. To this, a solution of 1.4 ml of a 22% *n*-butyllithium–hexane mixture (0.0031 mol of *n*-butyllithium) in 15 ml of tetrahydrofuran was added dropwise. The colorless slurry turned yellow and, after 0.15 hr, the reaction was warmed and heated at reflux for 0.15 hr. The reaction was cooled, a solution of 0.547 g (0.003 mol) of benzophenone in 15 ml of tetrahydrofuran was added dropwise, and, after the mixture stirred for 1 hr at room temperature, 700 ml of water was added, which precipitated a solid. Extraction with two portions of ether yielded 0.96 g of a mixture of a liquid and an oily solid. The nmr spectrum in chloroform indicated that the mixture consisted of benzophenone and morpholine or derivative thereof.

A short-path vacuum distillation of 0.70 g of the mixture gave 0.48 g of distillate (the distillation was not continued to dryness), collected at 0.50 mm (pot temperature 100–140°). Tlc of the distillate showed only one spot—a streak, R_f 0.55–0.75. A sample of reactant benzophenone showed a similar R_f value and the ir spectrum of the distillate (liquid film) showed a strong band at 1660 cm^{-1}, which is characteristic of benzophenone.[8] The nmr spectrum of the distillate showed a triplet at 1.22, a quartet at 2.73 and overlapping into the NCH_2 absorption of morpholine centered at 2.95, the OCH_2 absorption at 3.65, and aromatic protons from 7.24 to 7.92. The integration was 19 (triplet): 36 (total of quartet and NCH_2):24:158. These data suggested that the distillate was a mixture of benzophenone and either N-ethylmorpholine or the sulfenamide **5** [N-(ethylthio)morpholine].

Vpc of the distillate (10 ft × 1/4 in. 10% SE-30 on 80–100S, column temperature 180°, flow rate 24 ml of He/min) showed seven peaks, with those at 4.3 and 27 min accounting for 95% of the material. The 4.3-min peak corresponded with the retention time of an authentic sample of the sulfenamide **5** (prepared as below), and coinjection enhanced this peak without showing additional peaks. Furthermore, the chemical shifts observed for the ethyl and morpholine protons in the mixture were identical with those for the sulfenamide **5**. The broad peak at 27 min was identical in shape and retention time with that obtained from injection of an acetone solution of benzophenone. An injection of the benzophenone solution and the mixture increased the 27-min peak with the only additional peak observed due to acetone at 1 min.

Based on the nmr integrations, the minimum yields were 36% sulfenamide and 90% recovery of benzophenone.

N-(Ethylthio)morpholine. The Sulfenamide 5.—Chlorine (0.5 ml, 0.11 mol, trapped in a Dry Ice–acetone bath) was allowed to evaporate and the vapors were passed over a stirred solution of 12.3 ml (0.1 mol) of ethyl disulfide (Aldrich) in 50 ml of petroleum ether at −20°. The reaction was stirred for an additional 0.25 hr after complete evaporation of the chlorine. The yellow solution was added in portions to a stirred solution of 53 ml (0.6 mol) of morpholine in 200 ml of petroleum ether in an ice bath. The white slurry that resulted was extracted with three portions of water to remove morpholine hydrochloride. The petroleum ether solution was dried and concentrated. Distillation of the residue gave 20.75 g (72%) of colorless sulfenamide, bp 76–77° (14 mm). Its nmr spectrum showed a triplet at 1.22 (3 H) and a quartet centered at 2.72 (SCH_2) which overlapped into a complex triplet at 2.93 for the NCH_2 (total of 6 H) and with the OCH_2 at 3.62 integrating for 4 H.

Anal. Calcd for $C_6H_{13}NOS$: C, 48.94; H, 8.90. Found: C, 48.69; H, 8.63.

N,N-Dimethylmorpholinium Triiodide (7) from Sulfide and Methyl Iodide.—A solution of 2.50 g (0.012 mol) of morpholine sulfide and excess methyl iodide (7.5 ml, 0.12 mol) in 15 ml of methylene chloride was stirred for 16 hr at room temperature. The resulting solid was collected and washed with 15 ml of cold methylene chloride; the product was 2.00 g of dark violet solid, mp 118–122° dec. The nmr spectrum of the crude product (in acetonitrile) showed only the absorptions expected for N,N-dimethylmorpholinium iodide. Recrystallization of the product from 25 ml of methanol gave 0.841 g of violet solid, mp 118–119°. Repeated recrystallizations from methanol gave a violet solid, mp 125–126° (apparently with decomposition). Although the solid had the same melting point as morpholine sulfide, its color, the depression of a mixture melting point, and its nmr spectrum showed it to be a different compound. The nmr spectrum (in acetonitrile, TMS as reference) showed the characteristic complex triplets of the morpholine ring from 3.70 to 4.10 (OCH_2) and 3.22 to 3.57 (NCH_2) with a singlet at 3.18. The integration was 4:4:6 respectively. The elemental analysis was correct for N,N-dimethylmorpholinium triiodide.

Anal. Calcd for $C_6H_{14}I_3NO$: C, 14.50; H, 2.84; I, 76.62; N, 2.82. Found: C, 14.52; H, 2.86; I, 76.60; N, 2.83.

Evaporation of the red filtrate from the first recrystallization gave 0.65 g of pale violet solid, mp 188–205°, which, after crystallization from 2 ml of hot methanol, yielded a small amount of the violet triiodide. Further concentration of the filtrate gave a small amount of white crystals, mp 245.5–247° dec; the melting point and nmr spectrum of the crude solid indicated that it was N,N-dimethylmorpholinium iodide, reported[9] to melt at 246°.

Registry No.—**2**, 24407-43-0; **5**, 24378-12-9; **7**, 24378-13-0.

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(9) L. Knorr, *Ann.*, **301**, 1 (1898).

Triphasiaxanthin, a New Carotenone[1]

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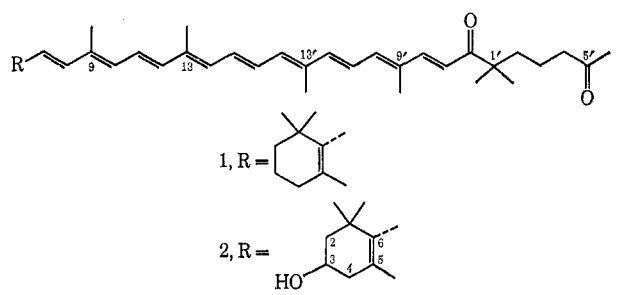
Semi-β-carotenone (1) occurs as the principal carotenoid constituent in the fruit of the *Citrus* relative



Triphasia trifolia.[3] A new, more polar carotenone, triphasiaxanthin, was isolated.

The visible absorption spectrum of triphasiaxanthin was very similar to that of the semi-β-carotenone. Its infrared spectrum indicated the presence of two carbonyl groups: saturated, 1715 cm^{-1}; and conjugated, 1660 cm^{-1}. Reduction with $LiAlH_4$ caused a hypsochromic shift (*ca.* 25 nm) in the visible absorption maxima. Taken together these evidences indicated a decaenone chromophore in the isolated pigment.

The infrared spectrum also indicated the presence of a secondary hydroxyl group (3450 and 1025 cm^{-1}). Tlc[4] tests indicated the facile quantitative formation of the trimethylsilyl derivative on silylation of the new carotenone. On allylic oxidation with nickel peroxide[5] or on treatment with acid chloroform, no bathochromic shift in the visible absorption maxima

(1) Part X in the series Citrus Carotenoids.

(2) A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

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TABLE I
CHARACTERISTIC FRAGMENTS FROM HIGH RESOLUTION MASS SPECTRUM OF TRIPHASIAXANTHIN

Intensity	m/e Measured	m/e Calcd	Formula	Remarks
15.78	584.4221	584.4215	$C_{40}H_{56}O_3$	Mol-ion (molecular ion)
4.48	582.4066	582.4059	$C_{40}H_{54}O_3$	Mol-ion − H_2
5.10	566.4150	566.4110	$C_{40}H_{54}O_2$	Mol-ion − H_2O
5.47	564.4017	564.3967	$C_{40}H_{52}O_2$	$(M^+ - H_2) - H_2O$
1.42	492.3586	492.3591	$C_{33}H_{48}O_3$	Mol-ion − C_7H_8 (toluene)
16.53	478.3396	478.3435	$C_{32}H_{46}O_3$	Mol-ion − C_8H_{10} (xylene)
1.05	474.3481	474.3486	$C_{33}H_{46}O_2$	Mol-ion − $C_7H_{10}O$ (toluene + water)
4.04	470.3210	470.3174	$C_{33}H_{42}O_2$	Mol-ion − $C_7H_{14}O$ (loss of terminal carbonyl and rearrangement)
1.45	460.3337	460.3330	$C_{32}H_{44}O_2$	Mol-ion − $C_8H_{12}O$ (xylene + water)
0.55	445.3084	445.3096	$C_{31}H_{42}O_2$	Mol-ion − cleavage at C-6 with loss of OH
1.32	428.3045	428.3069	$C_{31}H_{40}O_1$	Mol-ion − cleavage at C-6 with loss of two carbonyl groups

of triphasiaxanthin was observed, indicating that the hydroxy group is not in the allylic position.

The nmr spectrum of triphasiaxanthin contained ten C-methyl resonances. In addition to a methyl ketone methyl at τ 7.89 (C-5′, 3 H), the nmr spectrum revealed four in-chain olefinic methyls at τ 8.00 (C-9, C-13, C-9′, and C-13′, 12 H) and two geminal methyls at τ 8.82 (C-1′, 6 H). These values are to be compared with similar values (τ 7.89, 8.00, and 8.82) recorded for semi-β-carotenone.[3] The nmr properties of triphasiaxanthin indicated the presence of the β-cyclogeranylidene ring end group. As in the β-ring end group of reticulataxanthin,[6] two geminal methyl groups are equivalent at τ 8.92 (C-1, 6 H), and a single methyl is at τ 8.26 (C-5, 3 H). The hydroxy group appears to be located at C-3 in the β-ring end group. This is indicated by the close agreement in values of the C-methyl resonances of the three methyl groups in the β rings of triphasiaxanthin and reticulaxanthin. The two geminal methyl groups at C-1 are equivalent at τ 8.92, as is common for 3-hydroxy β rings, but might not be equivalent with the hydroxy group in the 2 or 4 (allylic) position. Moreover, with the hydroxy group in the 4 position, the signal of the C-5 methyl group would be expected to be downfield from the observed value.[7]

On the basis of evidence cited above, triphasiaxanthin has been assigned structure **2**.

The mass spectrum (Table I) of triphasiaxanthin ($C_{40}H_{56}O_3$ = 584.4215) is in good accord with structure **2**. The presence of a single hydroxyl group in the ring is indicated by the loss of only one molecule of water and the loss of the ring ($C_9H_{15}O$). The loss of $C_9H_{16}O_2$ is in good agreement with the proposed structure at the acyclic end of the molecule. As expected,[8] the characteristic ions representing the loss of C_7H_8 and C_8H_{10} from both the parent and the parent minus water are found.

In addition to the ions belonging to triphasiaxanthin, ions from at least two impurities were discovered in one of the samples. The first of these has a peak of *m/e* 600.4338 corresponding to $C_{44}H_{56}O$ (600.4331). The second impurity has an apparent molecular ion at 568.4334 corresponding to $C_{40}H_{56}O_2$ (568.4280) and a parent less water at 550.4129 ($C_{40}H_{54}O$ = 550.4161). The identity of these two substances is under investigation and will be reported later.

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(8) U. Schwieter, H. R. Bolliger, L. H. Chopard-Dit-Jean, G. Englert, M. Kofler, A. Planta, R. Ruegg, W. Vetter, and O. Isler, *Chimia*, **19**, 294 (1965).

Experimental Section

Nmr data were obtained at 100 MHz and refer to deuteriochloroform solutions; the chemical shifts are in τ values relative to internal tetramethylsilane. The high resolution mass spectra were obtained on an AEI Type MS 902 mass spectrometer. All peaks were measured with an average error of less than 5 ppm at a resolving power of 1/10,000. No data with an error >10 ppm were accepted. Samples were introduced by means of a heatable probe[9] at temperatures ranging from 159 to 200°. PFK was used as a reference compound for mass measurement. The fruit collection was made in Feb 1968, by Mr. N. Almeyda at the Federal Experiment Station of the U. S. Department of Agriculture, Mayaguez, Puerto Rico.

Isolation of Triphasiaxanthin.—The carotenoid pigments were extracted from the fruits (400 g) in the manner described previously.[3] The carotenoid mixture was phase-partitioned between petroleum ether–98% methanol. The hypophase was submitted to column chromatography on Microcel C, using 15% acetone in a petroleum ether solvent system. The isolated pigment was crystallized from peroxide-free ether–petroleum ether, yielding 8 mg: mp 95–97° (evacuated capillary, uncorrected); λ_{max} ($CHCl_3$) 480 nm ($\epsilon \times 10^{-3}$ 96.6), 510 (84.9); λ_{max} (*n*-hexane) 440, 467, 495 nm; ir ν (KBr pellet) 3450, 1715, 1660, 1025 cm^{-1}; nmr signals[10] at 7.89 (s, 3 H), 8.00 (s, 12 H), 8.26 (s, 3 H), 8.82 (s, 6 H), and 8.92 (s, 6 H).

Reduction of Triphasiaxanthin.—Reduction of triphasiaxanthin (0.5 mg) with $LiAlH_4$ in dry ether afforded the reduced product: λ_{max} (*n*-hexane), 420, 442, 471 nm.

TMS Derivative of Triphasiaxanthin.—Treatment of the isolated pigment (0.5 mg) in dry pyridine (1 ml) with hexamethyldisilazane (0.5 ml) and trimethylchlorosilane (0.3 ml) for 30 min resulted in the quantitative formation of triphasiaxanthin trimethyl silylether as judged by tlc.

Attempted Oxidation of Triphasiaxanthin.—Triphasiaxanthin (2 mg) in 5 ml benzene was treated with NiO_2 (30 mg, available oxygen 4.1 $\times 10^{-3}$ g-atom/g of NiO_2 determined by titration) for 60 min.[4] No bathochromic shift in its visible absorption maxima was observed.

Attempted Dehydration of Triphasiaxanthin.—Triphasiaxanthin (1 mg) in 5 ml of $CHCl_3$ was treated with 4 drops of chloroform–HCl reagent and allowed to stand at room temperature for 10 min. The mixture was then washed with sodium bicarbonate solution and water and dried over anhydrous Na_2SO_4. The visible spectrum remained unchanged.

Registry No.—2, 23939-69-7.

(9) H. G. Boettger and A. M. Kelly, 17th Annual Conference on Mass Spectrometry and Allied Topics, Dallas, Texas, May 1969.
(10) C-Methyls only.

Acknowledgments.—The authors are indebted to Dr. Robert Lundin for the nmr spectra and to Dr. H. M. Gaskins, Officer-in-Charge, and Mr. N. Almeyda of the Federal Experiment Station for the fruit collections.

An Efficient Synthesis of Symmetrical 1,3-Diglycerides[1]

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The symmetrical 1,3-diglycerides have been obtained by a variety of procedures, most of which involve protecting groups requiring chemical or catalytic cleavage.[3] Syntheses of the unsymmetrical 1,2-diglycerides also require the use of protective groupings which must be removed under very mild conditions in order to prevent acyl migration from the C-2 to the terminal positions. Hydrogenolysis overcomes this problem but limits the route to the synthesis of saturated diglycerides.

Recently, Windholz and coworkers[4] described the use of β,β,β-trichloroethoxycarbonyl chloride as a generally applicable protecting group for hydroxyl and amino functions. The carbonates and urethans formed are stable under a variety of oxidation and reduction conditions but are easily removed by treatment with zinc dust in acetic acid or methanol.

This reagent has been utilized by Pfeiffer[5] in the synthesis of 1,2-diglycerides thus avoiding many of the drawbacks of the earlier methods. There is as yet, however, no satisfactory synthetic approach to the synthesis of the symmetrical 1,3-diglycerides, particularly those with unsaturated side chains.

Rearrangement of the 1-iodo-2,3-diglyceride by refluxing with silver nitrite in 80% aqueous alcohol,[6] a convenient procedure for the synthesis of saturated 1,3-diglycerides, proved unsatisfactory in our hands for the corresponding unsaturated compounds owing to silver catalyzed isomerization of the olefinic center. The catalytic part played by the silver in this rearrangement was established by treating pure oleic acid with silver nitrite under the prescribed experimental conditions, *viz.*, reflux in 80% aqueous alcohol for 2–3 hr—this produced a mixture containing 32% elaidic acid.

Use of dihydroxyacetone as a starting material has been examined by Barry and Craig,[7] but the synthetic sequence used was elaborate, requiring the protection of the carbonyl group as a mercaptal, and no further work has appeared in the literature since that time. We have found that dihydroxyacetone is an ideal starting material for the synthesis of long-chain 1,3-diglycerides, *i.e.*, glycerol 1,3-dipalmitate and -dioleate since it is readily acylated with a fatty acid chloride in the presence of pyridine in high yield and the central keto group rapidly reduced by borohydride in tetrahydrofuran solution at 5° to give the 1,3-diglyceride without detectable amounts, by thin layer chromatography, of the 1,2-diglycerides. Synthesis of short-chain diglycerides is also possible by this method, but results are less satisfactory. In a typical experiment glycerol 1,3-diacetate was obtained in over 80% yield but when examined by nmr was shown to contain approximately 10% 1,2 isomer.

Experimental Section[8]

1,3-Dihydroxypropan-2-one 1,3-Diacetate.—Dihydroxy acetone (15.0 g) was dissolved in pyridine (50 ml) and acetic anhydride (50 ml). After 1 hr at 20°, the solvents were removed as completely as possible by vacuum distillation. The residue, dissolved in ethyl acetate, was washed with water, 3% aqueous hydrochloric acid, and water and dried. Evaporation and crystallization from benzene–hexane gave the diacetate (22.9 g, 81%) as long colorless needles, mp 46–47° (lit.[9] mp 46–47°).

1,2,3-Trihydroxypropane 1,3-Diacetate.—The above diacetate (10.0 g) was dissolved in tetrahydrofuran (150 ml), and water (10 ml) and treated portionwise at 5° with neutral sodium borohydride (2 g).[10] After 30 min excess borohydride was destroyed by dropwise additon of glacial acetic acid (1 ml), and the solution was diluted with chloroform, washed with water, aqueous sodium bicarbonate, and water, and dried over magnesium sulfate. Evaporation gave the diacetate as a colorless oil (9.10 g), bp 150° (12 mm) [lit.[11] bp 149° (12 mm)]. The nmr, however, showed a peak at δ 3.75 ($CDCl_3$ solution, unesterified $-CH_2OH$) indicating the presence of up to 10% 1,2 isomer.

1,3-Dihydroxypropan-2-one 1,3-Dioleate.—Dihydroxyacetone (3.0 g) was stirred under nitrogen in chloroform (150 ml). To this heterogeneous mixture was added oleoyl chloride (20 ml) in chloroform (150 ml) followed by anhydrous pyridine (10 ml). After 30-min stirring at room temperature the reaction mixture became homogeneous and 1 hr later no trace of acid chloride could be detected. The bulk of the solvent was removed under vacuum. The residue was shaken with water and ethyl acetate and the organic layer separated. The aqueous layer was again shaken with ethyl acetate and the combined extracts were washed with water, dried over sodium sulfate, and evaporated. The resulting final oil was recrystallized from methanol to give 1,3-dihydroxypropan-2-one 1,3-dioleate (15.8 g, 76%) as small plates, mp 43–44°.

Anal. Calcd for $C_{39}H_{70}O_5$: C, 75.80; H, 11.4. Found: C, 75.85; H, 11.04.

1,2,3-Trihydroxypropane 1,3-Dioleate.—The dioleate (10 g) was dissolved in tetrahydrofuran (150 ml) and water (10 ml). The heterogeneous solution was chilled to 5° and sodium borohydride[10] (1.0 g) added in small portions. After reaction and work-up as described above, an oil (9.0 g, 89%) was obtained which partially crystallized to give 1,2,3-trihydroxypropane 1,3-dioleate as needles, mp 20–22° (lit.[3] mp 25°). No trace of the 1,2 isomer was detected by thin layer chromatography [tlc system hexane–ethyl acetate (6:1)].

1,3-Dihydroxypropan-2-one 1,3-Dipalmitate.—Dihydroxyacetone (7.0 g) was stirred in chloroform (300 ml) under nitrogen at room temperature. To this was added palymitoyl chloride (44 g) followed by anhydrous pyridine (15 ml). The heterogeneous mixture was stirred for 3 hr and diluted with water and the chloroform layer separated. The aqueous layer was extracted

(1) Contribution No. 371 from the Institute of Organic Chemistry, Syntex Research. For No. 370, see H. Carpio, P. Crabbé, and W. Rooks, *J. Med. Chem.*, in press.

(2) Syntex Postdoctoral Fellow, 1967–1968.

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(6) F. L. Jackson, Ph.D. Thesis, Pittsburgh University, Pittsburgh, Pa., 1943.

(7) P. J. Barry and B. M. Craig, *Can. J. Chem.*, **33**, 716 (1955).

(8) Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Boiling points are uncorrected. Microanalyses were performed in the Microanalytical Laboratory of Dr. A. Bernhardt, Max Planck Institute, West Germany.

(9) "Heilbron's Dictionary of Organic Compounds," Vol. 2, Oxford University Press, Oxford, England, 1965, p 1046.

(10) The sodium borohydride used was first stirred in ethyl acetate overnight, washed with ether, and dried. Thanks are due to Dr. Ian Harrison for suggesting this procedure.

(11) See ref 9, p 845.