λ_{max}^{EtOH} 276 mμ, ε 343; λ_{max}^{EtOH} 283 mμ, ε 295. The n.m.r. spectrum in carbon tetrachloride with internal tetramethylsilane showed peaks at −1.70 τ (COOH) + 2.95 τ (ArH) and a poorly defined series of four peaks with areas approximately: 7.15 τ (3), 7.62 τ (2), 8.50 τ (8), 9.35 τ (4).

The *p*-bromoanilide of IV was prepared by conventional procedures[30]; m.p. 199–200°.

(30) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 200.

Anal. Calcd. for $C_{21}H_{24}ONBr$: Br, 20.68. Found: Br, 20.85.

Acknowledgment.—The authors are indebted to Professor D. J. Cram, University of California at Los Angeles, for the samples of the [8]- and [9]paracyclophane which were used for the ultraviolet spectra, and to Drs. P. DeMayo and J. P. Stothers, University of Western Ontario, for the proton magnetic resonance spectra and helpful discussion regarding same.

[CONTRIBUTION FROM THE MCPHERSON CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY, COLUMBUS 10, OHIO]

Synthesis and Properties of Highly Hindered Aliphatic Acids[1]

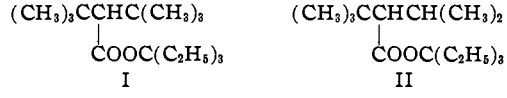
BY MELVIN S. NEWMAN AND TADAMICHI FUKUNAGA[2]

RECEIVED NOVEMBER 24, 1962

The synthesis of several highly hindered aliphatic acids is described as well as certain reactions of these acids. The failure of triethylcarbinyl di-*tert*-butylacetate to react with amide ion provides an example of steric hindrance to proton removal. Ionization constants in 40% methanol at 40° for a number of hindered aliphatic acids have been determined and are listed in Table I.

In previous studies from this Laboratory, the syntheses of highly sterically hindered acids by alkylation of nitriles followed by hydrolysis of these nitriles have been described.[3] When the degree of hindrance became too great, hydrolysis of nitriles to amides proceeded in such poor yield that this route to acids was poor.[3] Accordingly, we were interested in finding out if the Hauser method[4] of alkylation of triethylcarbinyl esters could be used in highly hindered cases.

Using this method we were able to prepare diisopropylmethylacetic, diisopropylethylacetic and triisopropylacetic acids from diisopropylacetic acid and *tert*-butylisopropylacetic acid from *tert*-butylacetic acid, but attempts to alkylate triethylcarbinyl di-*tert*-butylacetate (I) and triethylcarbinyl *tert*-butylisopropylacetate (II) failed, because of different reasons, as described below.



I II

The failure to alkylate I using potassium amide and alkyl iodides in mixtures of ether and liquid ammonia is explained by the failure of amide ion to abstract the α-proton, as judged by the lack of any green color in the reaction mixture. This provides an example of steric inhibition of proton abstraction by an amide ion. In all cases (except one; see below) we have studied, a green color[5] (undoubtedly due to enolate formation) was formed when successful alkylations resulted. The one exception was ester II, which under the usual conditions gave a yellow color. On the addition of isopropyl iodide this yellow color was discharged. However, the original ester II was recovered in 83% yield. Here the failure to alkylate may be explained by the competition of an elimination reaction involving isopropyl iodide. Thus, when the bulk of the anion becomes too great, elimination is favored over displacement.

Attempts to prepare anhydrides from highly hindered acids are of interest: for example, the behavior of diisopropylacetic acid and triisopropylacetic acid with ethoxyacetylene. The former acid, on refluxing with excess ethoxyacetylene in ether for one hour, yielded the anhydride in 39% yield, whereas the latter under similar conditions afforded a 61% yield of anhydride after five days. Thus, highly sterically hindered acids can be converted into their anhydrides by means of ethoxyacetylene but require much more drastic conditions than unhindered acids.[6] The present examples provide other cases in which reactions involving cyclic mechanisms proceed in spite of a large amount of steric hindrance.[7]

In one attempt to prepare triisopropylacetic anhydride from the acid using trifluoroacetic anhydride[8] the reaction failed because of evolution of carbon monoxide, even at 0°. The evolution of carbon monoxide is an indication that this reaction involves an oxocarbonium ion,[9] formed by dissociation of the mixed anhydride into trifluoroacetate anion and triisopropylmethyl oxocarbonium ion.

In this connection the facile reaction of triisopropylacetyl chloride with methanol to afford methyl triisopropylacetate in 90% yield is of interest. Because of the ease of reaction one would surely rule out a carbonyl-addition mechanism on the basis of steric hindrance. Undoubtedly, then, the reaction involves ionization of the acid chloride to an oxocarbonium ion which reacts with methanol more rapidly than it decarbonylates. Gas evolution during the reaction period (in which the temperature rapidly rose from 0° to 40–50°) was not observed. When one recalls that a solution of triisopropylacetic acid in trifluoroacetic anhydride at 0° evolves carbon monoxide, the failure of the triisopropylmethyl oxocarbonium ion to lose carbon monoxide in methanol at 40–50° is noteworthy. Either the carbonium ion is stabilized by methanol as solvent before reaction to yield ester or the reaction of the carbonium ion with methanol is much faster than its cleavage to carbon monoxide and other products

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(2) The material herein presented was taken from the Ph.D. Thesis, O.S.U., 1959, of T. F., who held a fellowship in 1956–1957 donated by the Research Corporation.

(3) L. Tsai, T. Miwa and M. S. Newman, *J. Am. Chem. Soc.*, **79**, 2530 (1957).

(4) C. R. Hauser and W. J. Chambers, *ibid.*, **78**, 3837 (1956).

(5) In ref. 4 above, the formation of a green color is also mentioned.

(6) For the mechanism of anhydride formation see G. Eglinton, E. R. H. Jones, B. L. Shaw and M. C. Whiting, *J. Chem. Soc.*, 1860 (1954), and H. H. Wasserman and P. S. Wharton, *J. Am. Chem. Soc.*, **82**, 1411 (1960).

(7) R. H. Dewolfe and W. G. Young, *Chem. Rev.*, **56**, 875 (1956), show that allylmagnesium bromide adds to the highly hindered carbonyl group in certain mesityl ketones.

(8) E. J. Bourne, M. Stacey, J. C. Tatlow and R. Worrall, *J. Chem. Soc.*, 2006 (1954).

(9) (a) C. Schuerch, Jr., and E. H. Huntress, *J. Am. Chem. Soc.*, **71**, 2233 (1949), footnotes 13 and 14; (b) H. A. Smith and R. J. Smith, *ibid.*, **70**, 2400 (1948); (c) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 283.

(in trifluoroacetic anhydride a second olefinic layer is formed).

Ionization Constants of Hindered Acids.—In a previous publication the effect of steric hindrance on ionization of hindered aliphatic[10] and aromatic[11] acids has been discussed. We have measured the ionization constants of a few additional highly hindered aliphatic acids and recorded the results in Table I. The acids in this table are grouped so that monosubstituted, disubstituted and trisubstituted acetic acids can be considered as groups in which the six-number[12] increases by increments of three. When grouped in this way a regular progression (with one exception, acid 10) to weaker acidity is noted as the six-number increases. This effect undoubtedly is due to increasing steric hindrance to solvation as previously suggested.[10,13] Triisopropylacetic acid is the weakest unsubstituted aliphatic acid yet encountered, having an ionization constant one-fortyseventh of that of acetic acid in the same medium. An interesting series may be noted when one progresses from *tert*-butylacetic acid (six no. 9) to *tert*-butylethylacetic acid (six no. 12) to *tert*-butylisopropylacetic acid (six no. 15) to di-*tert*-butylacetic acid (six no. 18). Each acid is weaker than the preceding one by about 0.26 pK_a unit.

It is not immediately apparent why there should be such a large difference between the ionization constants for acids 7 and 8. If one uses acid-catalyzed esterification with methanol as a model for steric hindrance, acid 8 has a rate constant (0.0170) somewhat smaller than acid 7 (0.0214).[14] There are other points of some interest in Table I, but further discussion will not be made at this time.

TABLE I

IONIZATION CONSTANTS OF ALIPHATIC ACIDS, $R_1R_2R_3CCOOH$, IN 50% BY VOLUME METHANOL–WATER AT 40°

	R_1	R_2	R_3	Six no.	pK_a[a]	$K_{ion}\,CH_3COOH / K_{ion}\,RCOOH$
1	H	H	H	0	5.69	1
		Monosubstituted acetic acids				
2	$(CH_3)_3C-$	H	H	9	6.24	3.5
		Disubstituted acetic acids				
3	$(CH_3)_2CH-$	$(CH_3)_2CH-$	H	12	6.48	6.2
4	$(CH_3)_3C-$	CH_3CH_2-	H	12	6.50	6.5
5	$(CH_3)_3C-$	$(CH_3)_2CH-$	H	15	6.76	12
6	$(CH_3)_3C-$	$(CH_3)_3C-$	H	18	7.04	22
		Trisubstituted acetic acids				
7	CH_3CH_2-	CH_3CH_2-	CH_3CH_2-	9	6.65	9.1
8	$(CH_3)_3C-$	CH_3-	CH_3-	9	6.95	18
9	$(CH_3)_2CH-$	$(CH_3)_2CH-$	CH_3-	12	6.97	19
10	$(CH_3)_2CH-$	$(CH_3)_2CH-$	CH_3CH_2-	15	7.23	35
11	$(CH_3)_3CCH_2-$	$(CH_3)_3C-$	CH_3-	12	7.31	42
12	$(CH_3)_2CH-$	$(CH_3)_2CH-$	$(CH_3)_2CH-$	18	7.36	47

[a] Values given in ref. 10 are: 1, 5.55; 5, 6.40; 7, 6.44; 8, 6.72; 11, 6.97.

Experimental[15]

Triisopropylacetic Acid.—To a stirred suspension of 0.52 mole of sodium amide in 500 ml. of liquid ammonia was added 64 g. (0.55 mole) of triethylcarbinol in 50 ml. of dry ether. The ammonia was then removed by warming with concomitant addition of 400 ml. of dry ether. The ether solution was then refluxed for 3 hr. to remove the remaining ammonia, about 100 ml. of ether being distilled during the process. To the stirred suspension of sodium alcoholate was added at room temperature during 30 min. 81.4 g. (0.50 mole) of diisopropylacetyl chloride, b.p. 87–88° at 48 mm.,[16] in 50 ml. of ether. After refluxing for 1 hr. the mixture was cooled and treated with 200 ml. of water. After treatment in the usual manner,[14] fractionation afforded 106.6 g. (88%) of triethylcarbinyl diisopropylacetate, b.p. 99–102° at 3 mm. An analytical sample, b.p. 101° at 3 mm., $n^{20}D$ 1.4442, infrared absorption at 5.75 μ, was obtained on further rectification.

Anal.[15] Calcd. for $C_{15}H_{30}O_2$: C, 74.3; H, 12.5. Found: C, 74.2, 74.3; H, 12.4, 12.2.

To a stirred solution of potassium amide prepared from 16.5 g. of potassium and 900 ml. of liquid ammonia was added a solution of 97.0 g. of triethylcarbinyl diisopropylacetate in 200 ml. of ether. The resulting mixture became green after 0.5 hr. and stirring was continued for 1 hr. before addition of a solution of 70 g. of isopropyl iodide in 100 ml. of ether. The resulting mixture became bright yellow and then light gray within 5 min. After stirring for 2 hr., 200 ml. of wet ether was added slowly and the ammonia was slowly evaporated by gentle warming. After the usual work-up, distillation afforded 52.7 g. (46%) of triethylcarbinyl triisopropylacetate, b.p. 141–146° at 4 mm., $n^{20}D$ 1.467–1.469, and 41.0 g. of a mixture of triethylcarbinyl di- and triisopropylacetates, b.p. 107–141° at 4 mm., $n^{20}D$ 1.446–1.459.

After refluxing a mixture of 21.0 g. of the higher boiling fraction with 15 ml. of concentrated hydrochloric acid and 25 ml. of dioxane for 4 hr., the mixture was distilled until the temperature rose to 100°. On cooling, colorless crystals of triisopropylacetic acid (13.3 g., 97%), m.p. 148–149°, separated. The analytical sample, m.p. 148.5–149.3°, was obtained by vacuum sublimation.

Anal. Calcd. for $C_{11}H_{22}O_2$: C, 70.9; H, 11.9. Found: C, 70.8, 70.9; H, 11.8, 11.9.

On similar hydrolysis of the above 107–141° ester fraction the same acid was obtained in 70–90% yields after one crystallization of the crude acid from dioxane–water.

Isopropyl-*tert*-butylacetic Acid.—Triethylcarbinyl *tert*-butylacetate, b.p. 94.5–96.5° at 9.5 mm., $n^{20}D$ 1.4292, was prepared in 86% yield by treating *tert*-butylacetyl chloride,[17] b.p. 125–128°, $n^{20}D$ 1.4213, with sodium triethylmethoxide essentially as described above in the preparation of triethylcarbinyl diisopropylacetate.

Anal. Calcd. for $C_{13}H_{26}O_2$: C, 72.8; H, 12.2. Found: C, 72.9, 72.7; H, 12.2, 12.4.

Alkylation of the potassium derivative with isopropyl iodide in liquid ammonia was effected essentially as described above for the diisopropylacetate ester. A 70% yield of redistilled triethylcarbinyl isopropyl-*tert*-butylacetate, b.p. 94–96° at 1.5 mm., $n^{20}D$ 1.4482, was obtained.

Anal. Calcd. for $C_{16}H_{32}O_2$: C, 74.9; H, 12.6. Found: C, 75.1, 75.0; H, 12.7, 12.4.

In addition, 27% of the starting ester was recovered by fractional distillation.

Hydrolysis of the ester by refluxing 12.3 g. with 8 ml. of concd. hydrochloric acid and 5 ml. of dioxane for 2 hr. yielded 6.8 g. (90%) of isopropyl-*tert*-butylacetic acid, b.p. 92–95° at 3 mm. Redistillation afforded a pure sample, b.p. 100.0–100.2° at 4 mm., $n^{20}D$ 1.4350.[18]

Triethylcarbinyl Di-*tert*-butylacetate.—When esterification of di-*tert*-butylacetyl chloride[19] with sodium triethylmethoxide as described above was attempted, there were isolated 63% of di-*tert*-butylacetic acid[19] and 30% of triethylcarbinyl di-*tert*-butylacetate, b.p. 105–111° at 2 mm. The analytical sample, b.p. 110° at 2 mm., $n^{20}D$ 1.4570, was taken from the center cut.

Anal. Calcd. for $C_{17}H_{34}O_2$: C, 75.5; H, 12.7. Found: C, 75.8, 75.6; H, 12.5, 12.4.

Attempts to alkylate this ester as described above with methyl iodide and ethyl iodide were in vain, recovered ester being obtained in high yield. The solution of this ester in liquid ammonia–ether remained colorless on standing in the presence of potassium amide for 3 hr. If color is used as the criterion, no anion formation occurred. The starting ester was recovered pure in 91% yield after distillation.

(10) G. S. Hammond and D. H. Hogle, *J. Am. Chem. Soc.*, **77**, 338 (1955).

(11) M. S. Newman and H. Boden, *ibid.*, **83**, 115 (1961).

(12) M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 206 ff. The six-number is the number of atoms in the sixth position starting from the carbonyl oxygen of the carboxyl group.

(13) See H. L. Goering, T. Rubin and M. S. Newman, *J. Am. Chem. Soc.*, **76**, 787 (1954), for a discussion of steric effect on ionization constants of hindered aromatic acids.

(14) Reference 12, p. 205; see acids 17 and 13, respectively.

(15) All melting points of pure compounds are corrected. Analyses by Galbraith Microanalytical Laboratories, Knoxville, Tenn. The term "treated in the usual manner" means that ether–benzene extracts of the aqueous layer were washed with dilute acid or dilute alkali as indicated by proper judgment, washed with saturated sodium chloride solution and then filtered by gravity through a layer of anhydrous magnesium sulfate. The solvents were then removed by distillation and the residue processed as indicated.

(16) A. A. Sacks and J. G. Aston, *J. Am. Chem. Soc.*, **73**, 3902 (1951). The diisopropylacetic acid used was prepared as described by L. Tsai, T. Miwa and M. S. Newman, *ibid.*, **79**, 2530 (1957).

(17) J. G. Traynham and M. A. Battiste, *J. Org. Chem.*, **22**, 1551 (1957), reported b.p. 68–71° at 100 mm., $n^{20}D$ 1.4229.

(18) A. A. Sacks and J. G. Aston, *J. Am. Chem. Soc.*, **73**, 3902 (1951), reported b.p. 122.5–123.8° at 22 mm., $n^{20}D$ 1.4343.

(19) M. S. Newman, A. Arkell and T. Fukunaga, *ibid.*, **82**, 2498 (1960).

Diisopropylacetic Anhydride.—A solution of 1.4 g. (0.01 mole) of diisopropylacetic acid[16] and 0.5 g. (0.007 mole) of ethoxyacetylene in 3 ml. of dry ether was held at room temperature for 2 hr. and was then refluxed for 1 hr. Distillation yielded 0.52 g. (39%) of the anhydride, b.p. 105° at 2 mm., $n^{20}D$ 1.4420, and 0.59 g. (42%) of acid.

Anal. Calcd. for $C_{16}H_{30}O_3$: C, 71.1; H, 11.2. Found: C, 70.8, 71.0; H, 10.9, 11.1.

Triisopropylacetic Anhydride.—A solution of 1.9 g. (0.01 mole) of triisopropylacetic acid and 0.5 g. of ethoxyacetylene in 25 ml. of dry ether was refluxed for 5 days. After removal of solvents the residue was recrystallized from petroleum ether, b.p. 90–100°, to yield 1.1 g. (61%) of crude anhydride, m.p. 88–90°, and 0.74 g. (39%) of crude starting acid. Recrystallization of the anhydride from this solvent afforded large hexagonal crystals of triisopropylacetic anhydride, m.p. 92–93°.

Anal. Calcd. for $C_{22}H_{42}O_3$: C, 74.5; H, 11.9. Found: C, 74.8, 74.8; H, 11.7, 11.8.

When a similar reaction was run for 18 hr. only a very small amount of anhydride was formed.

Reaction of Triisopropylacetic Acid.—To 2.2 g. of trifluoroacetic anhydride was added 1.9 g. of triisopropylacetic acid. Within 5 min. the acid dissolved completely and slow evolution of gas occurred. The rate of gas evolution slowed when the reaction mixture was cooled in an ice-bath, but did not stop entirely. On standing at room temperature the color deepened to brown and two layers were visible, the top being colorless. After 1.5 hr. the top layer was separated and washed with water. It readily decolorized permanganate solution and bromine in carbon tetrachloride. The gas evolved did not give a precipitate on passing through barium hydroxide solution and hence was assumed to be carbon monoxide.

When diisopropylacetic acid was treated in a similar way no gas was evolved and no deepening of color was noted. However, no attempt to isolate diisopropylacetic anhydride was made.

When a mixture of triisopropylacetic acid and a large excess of pure thionyl chloride was heated at reflux the acid slowly went into solution. After refluxing for 2 hr. the excess thionyl chloride was evaporated and the residue distilled to yield triisopropylacetyl chloride, b.p. 100–101° at 6 mm., in 95% yield. The distillate solidified to a waxy solid, m.p. 49–52°. This material was used in further work. Recrystallization from petroleum ether, b.p. 65–70°, at −78°, yielded pure acid chloride, m.p. 54.2–55.2° in a sealed tube (infrared absorption at 5.60 μ) but no sample was sent for analysis as it was so unstable in the presence of the slightest trace of moisture.

The addition of 20 ml. of pure absolute methanol to 8.1 g. of triisopropylacetyl chloride at 0° resulted in instantaneous reaction. The reaction mixture separated into two phases. After 1 hr. at room temperature (no gas evolution noticed) distillation afforded 7.2 g. (90%) of methyl triisopropylacetate as a colorless oil, b.p. 91.5–92.5° at 6.5 mm., $n^{20}D$ 1.4518 (infrared absorption, 5.75 μ).

Anal. Calcd. for $C_{12}H_{24}O_2$: C, 72.0; H, 12.1. Found: C, 72.0, 71.7; H, 12.0, 12.1.

A solution of 9.9 g. of triisopropylacetyl chloride in 30 ml. of dry ether was added to a suspension of freshly prepared sodium amide in dry liquid ammonia. After stirring for 30 hr., excess ammonium chloride was added and the ammonia evaporated by gentle warming. Crystallization from benzene–petroleum ether, b.p. 65–70°, yielded 8.3 g. (93%) of triisopropylacetamide, m.p. 141.8–142.8° (infrared absorption, 6.1 μ).

Anal. Calcd. for $C_{11}H_{23}NO$: C, 71.3; H, 12.5; N, 7.6. Found: C, 71.4, 71.6; H, 12.6, 12.4; N, 7.5, 7.6.

In a similar experiment except that only a 3.5-hr. reaction period was used, the yield of amide was 47%. In a similar reaction except that the sodium amide was omitted (reaction time 30 hr.) the yield was 68%.

Ionization Constants of Acids.—The ionization constants listed in Table I were determined by potentiometric titration using a glass electrode, calomel reference electrode and Beckman *p*H meter, model G, in 50 volume per cent methanol–water at 40°. The ionization constants were calculated by the Henderson equation[20] using 1/4, 1/2 and 3/4 neutralization points. The values thus calculated were accurate to ±0.03 pK unit.

$$pH = pK + \log([A^-]/[HA])$$

The values we obtained (Table I) do not agree too well with the values cited.[10] The system was standardized before and after each titration with 0.05 *M* phthalate buffer for *p*H 4.03, 0.05 *M* phosphate buffer for *p*H 6.84, and 0.01 *M* borax buffer for *p*H 9.07.[21] Sample solutions were prepared by weighing the acid sample directly in the 180-ml. titrating beaker and adding 50.0 ml. of absolute methanol kept in a reservoir in the thermostated bath at 40°. After the acid had dissolved completely, 50.0 ml. of water held at 40° in the same thermostat was added and the titrations were carried out with 0.0967 *N* carbonate-free methanolic sodium hydroxide solution in a 25-ml. needle valve buret at room temperature.

(20) See S. Glasstone, "Textbook of Physical Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1940, p. 982.

(21) H. H. Willard, L. L. Merrit and J. A. Dean, "Instrumental Methods of Analysis," D. Van Nostrand Co., Inc., Princeton, N. J., 1958, pp. 447–469.

[CONTRIBUTION FROM THE MERCK SHARP & DOHME RESEARCH LABORATORIES, DIVISION OF MERCK & CO., INC., RAHWAY, N. J.]

Synthesis of the New 3,4-Dihydro-2-H-naphtho[1,2-b]pyran-6-yl Phosphate from Vitamin $K_{1(20)}$[1]

BY ARTHUR F. WAGNER, PAUL E. WITTREICH, BYRON ARISON, NELSON R. TRENNER AND KARL FOLKERS

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A role for the 6-chromanyl derivatives of vitamin K in microbial oxidative phosphorylation was suggested on the basis of enzyme studies with a light-inactivated, cell-free extract of *Mycobacterium phlei*. As a part of a program to study such intermediates, 3,4-dihydro-2,5-dimethyl-2-(4,8,12-trimethyltridecyl)-2-H-naphtho[1,2-b]-pyran-6-yl phosphate (VIII) and the corresponding acetate V were synthesized from vitamin $K_{1(20)}$. The new reaction of the synthetic sequence is the sodium hydride-catalyzed cyclization of the naphthoquinone derivative to a corresponding 6-chromenyl intermediate.

The effect of certain naphthoquinones on the electron transport and oxidative phosphorylation processes of cellular respiration has been studied in light-inactivated (360 mμ), cell-free extracts of *Mycobacterium phlei*.[2-6] The light-inactivated system is dependent upon the addition of vitamin $K_{1(20)}$ or certain closely related derivatives for the restoration of oxidative phosphorylation. Evidence suggestive of participation by a 6-chromanol and a 6-chromanyl phosphate in this process was obtained by adding vitamin $K_{1(20)}$ in substrate quantity to the light-inactivated *M. phlei* extract; the biosynthetic intermediates were stabilized by acetylation, and diacetyldihydrovitamin $K_{1(20)}$ and the 6-chromanyl acetate (V) derived from vitamin $K_{1(20)}$ were identified in the reaction mixture on the basis of certain spectral and chromatographic properties.[5,6] In later studies,[7] the 6-chromanyl acetate V was isolated in pure form from the enzymic and acetylated mixture, but it was shown that this acetate may be derived, at least in part, from a non-enzymic cyclization of dihydrovitamin $K_{1(20)}$; whether the chromanol is

(1) Coenzyme Q. XLI.

(2) A. F. Brodie, M. W. Weber and C. T. Gray, *Biochim. et Biophys. Acta*, **25**, 448 (1957); (b) A. F. Brodie and B. R. Davis, *Federation Proc.*, **18**, 198 (1959).

(3) A. F. Brodie and J. Ballantine, *J. Biol. Chem.*, **235**, 226 (1960).

(4) A. F. Brodie and J. Ballantine, *ibid.*, **235**, 232 (1960).

(5) P. J. Russell and A. F. Brodie, *Federation Proc.*, **19**, 38 (1960).

(6) A. F. Brodie, P. J. Russell and E. Kashet, Abstracts, 137th National Meeting of the American Chemical Society, 1960, p. 25C.

(7) A. F. Wagner, P. E. Wittreich, C. H. Hoffman, K. Folkers and A. F. Brodie, *Biochem. Biophys. Research Commun.*, **8**, 38 (1962).