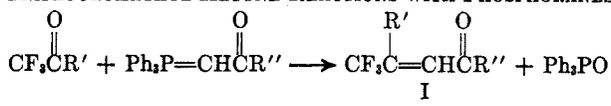
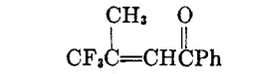
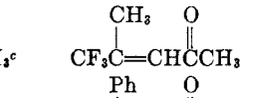
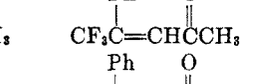
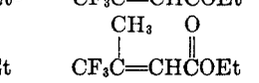
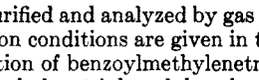
TABLE I
TRIFLUOROMETHYL KETONE REACTIONS WITH PHOSPHORANES



R′	R″	Product[a]	Yield, %	Bp (mm), °C	n_D (°C)	Calcd, % C	Calcd, % H	Found, % C	Found, % H
CH_3	Ph[b]		70	76–77 (2.5)	1.4883 (21)	61.68	4.23	61.38	4.10
CH_3	CH_3[c]		58	109–112 (760)	1.3726 (21)	47.47	4.63	47.17	4.56
Ph	CH_3		77	71–73 (1.0)	1.4760 (22)	61.78	4.23	61.61	4.13
Ph	OEt[d]		78	75–82 (1.5)	1.4660 (22)	59.01	4.54	59.42	4.53
CH_3	OEt		70	131–133 (760)	1.3750 (22)	*e*	*e*	*e*	*e*

[a] Products purified and analyzed by gas chromatography, Carbowax 20 M, 20 ft × 0.25 in., 60-ml/min helium flow, 135–195°. Representative reaction conditions are given in the Experimental Section. [b] See D. B. Denney and S. T. Ross [*J. Org. Chem.*, **27**, 998 (1962)] for the preparation of benzoylmethylenetriphenylphosphorane. [c] See F. Raminez and S. Dershowitz [*ibid.*, **22**, 41 (1957)] for preparation of acetylmethylenetriphenylphosphorane. [d] See O. Isler, H. Gutmann, M. Montavon, R. Ruegg, G. Ryser, and P. Zeller [*Helv. Chim. Acta*, **40**, 1242 (1957)] for the preparation of carbomethoxymethylenetriphenylphosphorane. [e] Reference 2.

phenylphosphorane.[7] Very recently there has been a communication[8] of the reaction of trifluoromethyl ketones with trialkylphosphines to give olefins, which has in part prompted the report of our work at this time.

Although acetone and acetophenone react only under forcing conditions with resonance-stabilized ylides,[9] we find that 1,1,1-trifluoroacetone and 2,2,2-trifluoroacetophenone react rapidly with such reagents, the former reacting even at room temperature in ether solvent. The results of these reactions are summarized in Table I.

Gas chromatographic analysis of these products indicates in each case that one geometrical isomer has been formed to the virtual exclusion of the other. This is in accord with the general observation already noted for reactions of resonance-stabilized ylides.[9]

This ease of reaction is to be expected based on the greatly enhanced electrophilicity of the carbonyl group in trifluoromethyl aldehydes and ketones. This procedure promises to be a useful method for the synthesis of many compounds of this general type. The following experimental results are representative of those reported in Table I.

Experimental Section

1,1,1-Trifluoro-2-phenyl-2-penten-4-one.—In a dry, 250-ml, three-necked flask fitted with a reflux condenser was placed 12.8 g (0.04 mole) of acetylmethylenetriphenylphosphorane,[10] 7.0 g (0.04 mole) of 2,2,2-trifluoroacetophenone (Columbia Organic Chemicals), and 60 ml of dry benzene. Upon heating to reflux, solution occurred; refluxing was then continued for 3 hr. After cooling, the benzene was removed under reduced pressure, the residue was mixed with hexane, and the mixture was filtered. Distillation of the filtrate gave 6.6 g (77% yield) of a yellow liquid, bp 71–73° (1.0 mm), (C=O) 1700 cm^{-1}. See Table I for analysis and properties.

Ethyl β-Trifluoromethylcrotonate.[2,4]—In a dry, 250-ml, three-necked flask fitted with a Dry Ice condenser were placed 34.8 g (0.10 mole) of carboethoxymethylenetriphenylphosphorane,[11] 75-ml of dry ether, and 12.8 g (0.11 mole) of 1,1,1-trifluoroacetone (Columbia Organic Chemicals). Reaction occurred immediately with formation of a thick paste. An additional 50-ml of ether was added and the mixture was stirred at room temperature for 16 hr. The reaction mixture was filtered, the ether was removed by distillation, and the residue was mixed with pentane. Distillation of the filtrate gave 12.7 g (70% yield) of ethyl β-trifluoromethylcrotonate. See Table I for properties.

Registry No.—I (R′ = Ph; R″ = CH_3), 10075-04-4; (R′ = CH_3; R″ = OEt), 691-77-0; (R′ = CH_3; R″ = Ph), 10102-92-8; (R′ = CH_3; R″ = CH_3), 10075-05-5; (R′ = Ph; R″ = OEt), 10075-06-6.

(7) V. F. Plakhova and N. P. Gamburgan, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, **681** (1962); *Chem. Abstr.*, **57**, 13596e (1962).
(8) D. J. Burton, F. E. Herhes, and K. J. Klabunde, *J. Am. Chem. Soc.*, **88**, 5042 (1966).
(9) A. Maercher, *Org. Reactions*, **14**, 277 (1965).
(10) See Table I, footnote *c*.
(11) See Table I, footnote *d*.

Synthesis of Acetal Choline Phosphatide[1]

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Plasmalogens are a group of aldehydogenic lipids, widely distributed in both animal and plant kingdoms.[3] Natural plasmalogen isolated from beef muscle[4] was at first believed to have the structure 1,2-O-alkylidine-glycerol-3-phosphorylethanolamine, the synthesis of which has been reported.[5,6] However, recent work has shown that the cyclic acetal structure may have been produced as an artifact during the isolation procedure after the alkaline hydrolysis of the natural plasmalogen.

(1) Abstracted from a part of the dissertation submitted by G. K. Chacko to the University of Illinois Graduate College, March 1966, in partial fulfillment of the requirements of the Ph.D. degree.
(2) Author to whom inquiries should be addressed.
(3) E. Klenk and H. Debuch, *Progr. Chem. Fats Lipids*, **6**, 1 (1963).
(4) R. Fuelgen and Th. Bersin, *Z. Physiol. Chem.*, **260**, 217 (1939).
(5) Th. Bersin, H. G. Moldtman, H. Nafziger, B. Marchand, and W. Leopold, *ibid.*, **269**, 241 (1941).
(6) M. J. Egerton and T. Malkin, *J. Chem. Soc.*, 2800 (1953).

Further studies have proven that they are of *cis*-1-alk-1′-enyl-2-acyl derivatives of glycerol.[3,7-9]

Although the acetal-type plasmalogen or more correctly acetal phosphatide was shown not to exist as a major component of natural plasmalogen in mammalian tissues, Bergmann and Landowne[10] have isolated by neutral solvents at room temperature an acetal phosphatide from the total lipids of sea anemone, *Anthropleura elegantassima*. The infrared spectrum of the compound was notably devoid of a carbonyl peak and the chemical analysis showed the compound to be 1,2-alkylidineglycerol-3-phosphorylcholine. However, Rouser, *et al.*,[11] could not confirm the lipid composition of sea anemone as reported by Bergmann and Landowne. Further studies on the nature of plasmalogens in other marine species were made by Rapport and Alonso.[12] The total lipids were analyzed for their content of aldehydogenic lipids and for the α,β-unsaturated ether content. The results showed that in eight species the amount of vinyl ether group accounted for almost all the aldehydogenic lipids, while in three species it accounted for only 75–80% indicating that a minor percentage of total plasmalogen in these species may have been present in the form of the acetal type although these results by no means signify that an acetal type of lipid always be present in nature. Therefore, in the present communication, the synthesis of the acetal choline phosphatide, 1,2-O-hexadecylidineglycerol-3-phosphorylcholine, is reported.

The known 1,2-O-hexadecylidineglycerol[6] was phosphorylated followed by reaction with choline iodide[13] and the acetal choline phosphatide purified by column chromatography.[14] The preparation of higher aliphatic aldehyde is known to be difficult owing to the fact that they are easily oxidized to acids and have a tendency to polymerize to trimers. In the present study, hexadecanal was prepared from its sodium bisulfite addition compound by hydrolysis with dilute hydrochloric acid at an elevated temperature in the presence of nitrogen and extraction of the regenerated aldehyde with benzene from the warm solution. This was used without further purification for the preparation of the 1,2- and 1,3-acetals of glycerol. The preparation of hexadecanal in 96% yield from its sodium bisulfite compound was recently reported[15] using aqueous sodium carbonate solution.

Attempted synthesis of the α-chloro ether of glycerol using hexadecanal and isopropylidineglycerol in chloroform by passing hydrogen chloride gas[16] through the ice-cold reaction mixture for a short period of time resulted in the formation of a compound which was identified to be 1,3-O-hexadecylidineglycerol with traces of the 1,2-acetal. Gas–liquid partition chromatographic analysis of the methylated product indicated that it contained hexadecanal as the sole component. However, the infrared spectrum of the product had no carbonyl frequency but a strong hydroxyl group absorption was present. Upon thin layer chromatography using a solvent system of Skellysolve F (petroleum ether, bp 30–60°)–ether (60:40, v/v), it had a major spot with an R_f value of 0.26 and a very small spot with an R_f value of 0.33. The small spot with the R_f value of 0.33 was shown to correspond to that of 1,2-acetal prepared by alkaline hydrolysis of 1,2-O-hexadecylidine-3-lauroylglycerol.[17] The molecular weight found by the mass spectroscopy was 314, corresponding to that of the acetal, $C_{19}H_{38}O_3$. To account for the formation of predominantly 1,3-acetal from hexadecanal and isopropylidineglycerol, it is probable that under the experimental conditions used, the free hydroxyl group of isopropylidineglycerol reacted first with hexadecanal to form a hemiacetal, followed by chlorination of the secondary hydroxyl group of the hemiacetal with subsequent displacement of the chlorine by attack of the primary hydroxyl group of the liberated glycerol.

Unlike diacylglycerolphosphorylcholine, the acetal phosphatide was found to be insoluble in ether or in 95% ethanol. Such solubility behavior is in agreement with the findings of Feulgen and Bersin.[4] The 1,2-acetal choline phosphatide was obtained in about 25% yield after silicic acid column chromatographic fractionation and using a mixture of chloroform and methanol (3:2, v/v) as the eluting solvent. The infrared spectrum of the acetal choline phosphatide was completely void of any carbonyl absorption peak. Apart from the absence of this band, it was similar to that of diacylglycerolphosphorylcholine.[18,19] Thus, it had a strong absorption peak near 1250 cm^{-1} attributable to the P=O stretch. The strong absorption at 1090 cm^{-1} indicated an ionized phosphate (PP^-). The 1050-cm^{-1} peak is typical of POC group. There was a broad bonded H_2O peak at 3460 cm^{-1}.

Experimental Section

Melting points are not corrected. Infrared spectra were determined on a Beckman Model 7 spectrophotometer. Thin layer chromatography was carried out using silica gel G as the adsorbent. Microanalyses were carried out by the Clark Microanalytical Laboratories, Urbana, Ill.

Materials.—Anhydrous pyridine, anhydrous quinoline, and anhydrous ethanol-free chloroform were prepared as described by Baer and Buchnea.[20] Choline iodide was prepared according to Baer and Kindler.[13] Silicic acid was from Mallinkrodt, 100 mesh (powder) analytical reagent.

1,3-O-Hexadecylidineglycerol.—Hydrogen chloride gas was passed slowly through an ice-cold solution of hexadecanal (6.7 g, 28 mmoles), 6.9 g of isopropylidineglycerol (100% excess of the theoretical amount), and 100 ml of chloroform for 10 min. To this solution was added 100 ml of cold water and the aqueous layer was removed. The chloroform layer was washed with water till the washings were free of mineral acid, and dried and the solvent was removed under vacuum. The residue so obtained was recrystallized from Skellysolve F at 0° to yield 2.4 g of prod-

(7) M. M. Rapport and W. T. Norton, *Ann. Rev. Biochem.*, **31**, 103 (1962).
(8) W. T. Norton, E. L. Gottfried, and M. M. Rapport, *J. Lipid Res.*, **3**, 456 (1962).
(9) H. R. Warner and W. E. M. Lands, *J. Am. Chem. Soc.*, **85**, 60 (1963).
(10) W. Bergmann and R. A. Landowne, *J. Org. Chem.*, **23**, 1241 (1958).
(11) G. Rouser, G. Kritchevsky, D. Heller, and E. Lieber, *J. Am. Oil Chemists' Soc.*, **40**, 425 (1963).
(12) M. M. Rapport and N. Alonso, *J. Biol. Chem.*, **235**, 1953 (1960).
(13) E. Baer and A. Kindler, *Biochemistry*, **1**, 518 (1962).
(14) D. J. Hanahan, J. C. Dittmer, and E. Warashima, *J. Biol. Chem.*, **228**, 685 (1957).
(15) J. C. Craig and D. P. G. Hamon, *J. Org. Chem.*, **30**, 4168 (1965).
(16) B. H. Shoemaker and C. E. Boord, *J. Am. Chem. Soc.*, **53**, 1505 (1931).
(17) 1,2-O-Hexadecylidene-3-lauroylglycerol was prepared according to the procedure of Egerton and Malkin,[6] yield 45%, mp 51–52° (lit.[6] 51.5–52.5°). *Anal.* Calcd for $C_{31}H_{60}O_4$: C, 74.99; H, 12.10. Found: C, 74.89; H, 12.05. Hydrolysis of the above compound with sodium hydroxide in ethanol produced 1,2-O-hexadecylidineglycerol: yield 100%, mp 45–47° (lit.[6] 45.5–46.5°). *Anal.* Calcd for $C_{19}H_{38}O_3$: C, 72.61; H, 12.10. Found: C, 72.41; H, 12.23.
(18) M. B. Abramson, W. T. Norton, and R. Katzman, *J. Biol. Chem.*, **240**, 2389 (1965).
(19) E. Baer, *J. Am. Chem. Soc.*, **75**, 621 (1953).
(20) E. Baer and D. Buchnea, *ibid.*, **81**, 1758 (1959).

uct (32%), mp 70–71°. Thin layer chromatography of the product in the solvent system Skellysolve F–ether (60:40, v/v) showed that only traces of the 1,2 isomer were present.

Anal. Calcd for $C_{10}H_{38}O_3$: C, 72.61; H, 12.10. Found: C, 73.10; H, 12.00.

1,2-O-Hexadecylidineglycerol-3-phosphorylcholine.—To 0.37 ml (4.0 mmoles) of freshly distilled phosphorus oxychloride, cooled by an ice bath and vigorously stirred by a magnetic stirrer, was added drop by drop under anhydrous conditions a solution containing 1.18 g (4.0 mmoles) of 1,2-O-hexadecylidineglycerol,[17] 0.52 ml (4.4 mmoles) of anhydrous quinoline, and 20 ml of anhydrous chloroform. The cold bath was then replaced by a water bath at 35° and the reaction mixture was kept at this temperature for 1 hr. To the solution was then added quickly 5 ml of anhydrous pyridine, 0.871 g (4.5 mmoles) of finely powdered choline iodide, and 15 ml of glass beads (4-mm diameter). The stirring was continued for 20 additional hr at room temperature and then 0.1 ml of distilled water was added. The solution was stirred for an additional 30 min. The reaction mixture was then filtered and the residue was washed twice with 15-ml portions of cloroform. The chloroform solution was first evaporated under vacuum using a rotary evaporator from a water bath at 37°, followed by a final drying at a vacuum of 0.1 mm until a semisolid, yellow residue was obtained. The residue was triturated at 0° with 1 *N* hydrochloric acid and immediately filtered. This was washed with cold water until the washings were free of mineral acid and dried under vacuum. The residue was dissolved in a mixture of chloroform and 95% ethanol and to the solution was then added 1.5 g of finely powdered silver carbonate and the mixture was stirred for 1 hr. The solution was filtered and the solvent was evaporated under vacuum from a water bath at 35°. The resultant residue was dissolved in a minimum amount of chloroform and acetone was added and kept at 0° to precipitate the 1,2-acetal choline phosphatide. The product was obtained by filtration on a Büchner funnel to give 1.2 g of 1,2-acetal choline plasmalogen.

The crude 1,2-acetal choline phosphatide was fractionated by silicic acid column chromatography according to the method of Hanahan, *et al.*[14] Thus, using 20 g of silicic acid and 10 g of Celite, 0.096 g (25% over-all yield) of product was obtained from 0.265 g of crude acetal phosphatide by elution with 1000 ml of a mixture of chloroform and methanol (3:2, v/v).

Anal. Calcd for $C_{24}H_{52}NO_7P$: N, 2.81; P, 6.22. Found: N, 2.33; P, 5.88.

Registry No.—1,2-O-Hexadecylidineglycerol-3-phosphorylcholine, 7731-07-9; 1,3-O-hexadecylidineglycerol, 7731-06-8.

The Thermal Decomposition of Crotyldi-*t*-butylcarbinol

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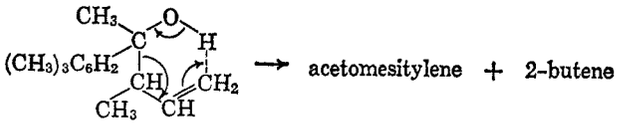
In 1950, Wilson, Roberts, and Young[1] reported that butenylmagnesium bromide reacts with hexamethylacetone to form crotyldi-*t*-butylcarbinol in 69% yield. This reaction remains of considerable interest since it is the only example of the formation of a product derived exclusively from the primary form of this Grignard reagent.[2] It was also disclosed[1] that pyrolysis of crotyldi-*t*-butylcarbinol at 215° produced 1-butene. Previously, similar thermal decompositions for compounds like α-methylallylmesitylmethylcarbinol to acetomesitylene and 2-butene had been demonstrated.[3] A cyclic process had been invoked to explain the products of such decompositions.



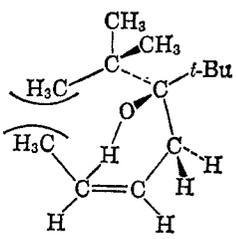
Recently we found that crotyldi-*t*-butylcarbinol is formed from butenyl Grignard reagents and hexamethylacetone predominantly in the *cis* form.[4]

We now wish to report that the thermal decomposition of a mixture of *cis*- and *trans*-crotyldi-*t*-butylcarbinol is selective, in that the *trans* alcohol decomposes to hexamethylacetone at a faster rate than the *cis* isomer. This trend is clearly delineated in Table I.

TABLE I
THERMAL DECOMPOSITION OF CROTYLDI-*t*-BUTYLCARBINOL
COMPOSITION OF CARBINOL

Time, hr	Temp, °C	*cis*	*trans*	Hexamethylacetone, %
0	246	71	29	0
1.17	248	71	28	1
2.00	248	71	24	5
3.00	245	72	20	8
4.17	244	71	15	14
5.17	245	70	13	17
6.08	245	70	12	18
7.08	245	71	10	19
10.00	244	74	7	19

If the intramolecular cyclic transition state which has been proposed[3] for these decompositions is correct, a cursory examination of molecular models provides a possible explanation for the differences in decomposition rates which are observed. The *cis* isomer (**1**)



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would suffer severe steric interactions between one of the methyls of the *t*-butyl group and the terminal methyl of the crotyl group as shown. A considerable amount of this strain would be relieved in the *trans* isomer wherein the methyl of the *t*-butyl group would be opposed only by one of the vinylic hydrogens.

Further work is obviously necessary to decide whether these interesting decompositions are truly intramolecular and whether the steric proposals invoked here are valid.

Experimental Section

General.—All samples were analyzed by vpc using a 20-ft, 20% stainless steel DEGS column on 60–80 AW-DMCS treated

(1) K. W. Wilson, J. D. Roberts, and W. G. Young, *J. Am. Chem. Soc.*, **72**, 218 (1950).

(2) See J. E. Nordlander, W. G. Young, and J. D. Roberts [*ibid.*, **83**, 494 (1961)] who discuss the structural problems associated with this Grignard reagent.

(3) W. G. Young and J. D. Roberts, *ibid.*, **68**, 1472 (1946).

(4) The butenyl Grignard prepared from either *trans*-1-chloro-2-butene or 3-chloro-1-butene forms crotyldi-*t*-butylcarbinol in about the same *cis*/*trans* ratio, namely 2.2:1. Details of these and similar results will be published shortly.