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Effect of Flavonoid Sulfonates on the Photobleaching of Anthocyanins in Acid Solution

James G. Sweeny,* Marguerite M. Wilkinson, and Guillermo A. Iacobucci

The use of anthocyanins as food colorants has been hampered in the past due to the poor photostability of these pigments. This problem can be overcome if any of a series of polyhydroxylated flavone-, isoflavone-, or auronesulfonates are used as copigments. These materials give a 1-50-nm bathochromic shift in the λ_{max} of the pigment and more than double its resistance to sunlight fading in acidic solution.

Anthocyanins are the largest group of water-soluble colors of most fruits, flowers, and leaves. Their use as food colorants has not been widely practiced to date due to their limited commercial availability and, in certain cases, poor stability.

The degradation of anthocyanins in food systems has been studied extensively (Markakis, 1974; Hrazdina, 1974). Instability in aqueous solutions is pronounced at pH values above 4, at high temperature, or in the presence of H_2O_2 or ascorbic acid. In addition, even when anthocyanins are stable under normal laboratory lighting conditions, direct exposure to sunlight causes extensive decoloration (Van Buren et al., 1968).

Obviously, methods of stabilizing anthocyanin–containing products would be of great use, especially for products which cannot be stored at low temperatures in the dark. Unfortunately, the design of materials to stabilize anthocyanins has been hampered by a lack of understanding of the mechanism of anthocyanin degradation (Markakis, 1974; Hrazdina, 1974). Only the mechanisms involved in decoloration by increasing pH (Brouillard and Dubois, 1977; Brouillard and Delaport, 1977; Brouillard et al., 1978) and by ascorbic acid/O_2 (King et al., 1979) have been determined.

One approach which appears promising, however, is the use of copigments. It has long been known (Robinson and Robinson, 1931) that in nature the various red to blue shades of flowers are caused by the association of anthocyanins with other flavonoid phenolics. These copigments cause a bathochromic shift in the λ_{max} of the anthocyanin and also an increase in absorbance. Several widely occurring flavonoids like rutin (3) and kaempferol 3-glucoside (5) have been shown to give this effect in model systems (Asen et al., 1972, 1975; Scheffeldt and Hrazdina, 1978; Williams and Hrazdina, 1979; Hoshino et al., 1980).

The importance of this and other factors for the use of anthocyanins in foods has been reviewed recently (Timberlake and Bridle, 1980). The present paper discusses the photochemical behavior of anthocyanins resulting from

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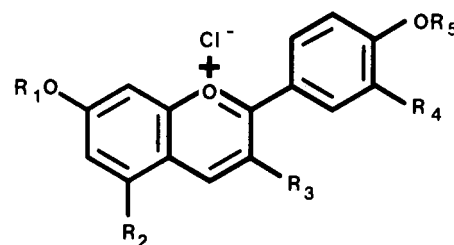
1. $R_1 = R_3 = R_4 = R_5 = H$; $R_2 = OH$.
2. $R_1 = R_5 = H$; $R_3 = O$-Rutinose; $R_2 = R_4 = OH$.
17. $R_1 = R_5 = CH_3$; $R_2 = R_3 = R_4 = OCH_3$.
18. $R_1 = R_2 = R_3 = R_4 = R_5 = H$.
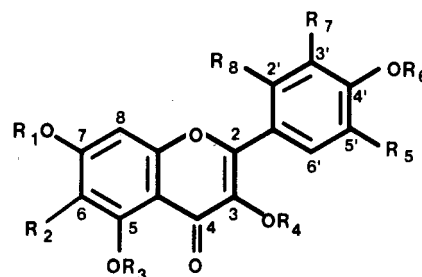
3. $R_1 = R_2 = R_3 = R_6 = R_7 = R_8 = H$; $R_4 = $ Rutinose; $R_5 = OH$.
4. $R_2 = R_3 = R_7 = R_8 = H$; $R_4 = $ Rutinose; $R_1 = R_6 = \beta$-Hydroxyethyl; $R_5 = O$-β-Hydroxyethyl.
6. $R_1 = R_2 = R_3 = R_4 = R_6 = R_8 = H$; $R_7 = SO_3H$; $R_5 = OH$.
5. $R_1 = R_2 = R_3 = R_5 = R_6 = R_7 = R_8 = H$; $R_4 = $ Glucose.
8. $R_1 = R_3 = R_4 = R_5 = R_6 = H$; $R_2 = R_7 = SO_3H$; $R_8 = OH$.

the complexation with water-soluble flavonoid sulfonates measured in acid solution and in model carbonated beverages.

EXPERIMENTAL SECTION

Cyanidin 3-rutinoside (2) was obtained from the Shiraimatsu Shinyaku Co., Japan. (β-Hydroxyethyl)rutin (4) (Zyma, 1966), apigeninidin chloride (1) (Sweeny and Iacobucci, 1977); pentamethylcyanidin chloride (17) (Jurd, 1966a), 4',7-dihydroxyflavylium chloride (18) (Jurd, 1966b), and quercetin-5'-sulfonic acid (6) (Terpilowski et al., 1970) were prepared as described in the literature. Kaempferol 3-glucoside (5) was generously provided by Professor S.

Table I. Spectral Shifts in the Visible Spectrum of Cyanidin 3-Rutinoside (10 ppm in 0.01 M Citric Acid), pH 2.8, Induced by the Addition of Copigments: Effects on λ_{max} and Absorbance as a Function of Copigment Concentration
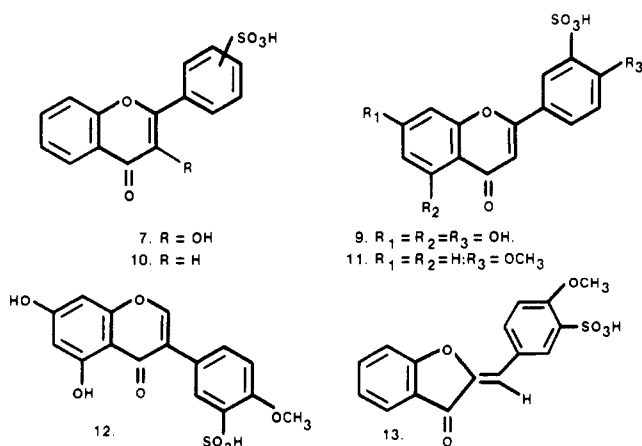
	λ_{max}, nm (absorbance)[a]						
copigment	0 ppm	20 ppm	50 ppm	100 ppm	200 ppm	500 ppm	1000 ppm
flavonols							
3	512 (1.0)	512 (1.15)	513 (1.16)	513 (1.18)	514 (1.22)	518 (1.26)	528 (1.32)
4	512 (1.0)	513 (1.01)	514 (1.02)	516 (1.04)	518 (1.05)	523 (1.08)	528 (1.10)
5	512 (1.0)	513 (1.01)	514 (1.01)	516 (1.04)	521 (1.06)	528 (1.08)	538 (1.10)
6	512 (1.0)	517 (1.05)	525 (1.07)	532 (1.08)	535 (1.08)	544 (1.08)	550 (1.08)
7	512 (1.0)	513 (1.01)	514 (1.02)	516 (1.04)	518 (1.08)	522 (1.16)	527 (1.23)
8	512 (1.0)	512 (1.04)	514 (1.08)	516 (1.14)	518 (1.23)	523 (1.35)	527 (1.43)
flavones							
9	512 (1.0)	517 (1.06)	525 (1.13)	531 (1.18)	536 (1.23)	542 (1.26)	546 (1.33)
10	512 (1.0)	514 (1.02)	517 (1.05)	519 (1.10)	522 (1.16)	528 (1.27)	535 (1.33)
11	512 (1.0)	515 (1.03)	518 (1.08)	522 (1.11)	528 (1.17)	536 (1.23)	543 (1.28)
isoflavones							
12	512 (1.0)	513 (1.02)	514 (1.04)	516 (1.07)	519 (1.10)	524 (1.14)	527 (1.11)
aurones							
13	512 (1.0)	514 (1.01)	517 (1.03)	524 (1.06)	530 (1.10)	538 (1.10)	544 (1.09)
nonflavonoids							
14	512 (1.0)	512 (1.02)	512 (1.02)	514 (1.05)	517 (1.11)	522 (1.20)	529 (1.26)
15	512 (1.0)	513 (1.04)	515 (1.09)	519 (1.15)	522 (1.21)	527 (1.28)	531 (1.28)
16	512 (1.0)	512 (1.0)	513 (1.02)	514 (1.05)	516 (1.10)	521 (1.20)	527 (1.31)

[a] Values for absorbance are in parentheses.

Sakamura of Hokkaido University, Sapporo, Japan. Enocianina was obtained from commercial sources, as a spray-dried aqueous extract of grape skins of Italian origin. Anthraquinone-1-sulfonic acid (16) was purchased from Eastman.

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16.
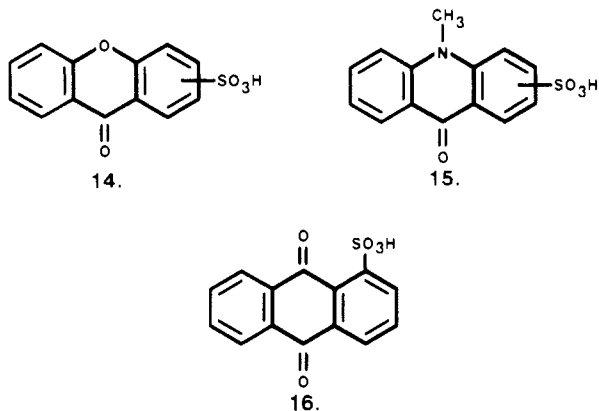
The sulfonated derivatives 7, 8, 9, 10, 11, 12, 13, 14, and

7. R = OH
10. R = H

9. $R_1 = R_2 = R_3 = $ OH.
11. $R_1 = R_2 = $ H: $R_3 = $ OCH$_3$

12.

13.

15 were prepared from the respective substrates—3-hydroxyflavone (Oyamada, 1934), apigenin (Aldrich), flavone (Aldrich), 4'-methoxyflavone (Matsuura et al., 1978), biochanin A (Aldrich), 4'-methoxyaurone (Gowan et al., 1955), xanthone (Aldrich), and N-methylacridone (Aldrich)—by reacting them with a 1:1 mixture of sulfuric acid

and fuming sulfuric acid. The derivatives were isolated as the Ca salts and converted to the Na salts by means of a strong cation-exchange resin (Na$^+$ form). Recovery yields were ~80%.

Molecular complexes between the copigment quercetin-5'-sulfonic acid (6) and the pigments apigeninidin chloride (1) and pentamethylcyanidin chloride (17) were prepared by separately dissolving the partners in 50% aqueous MeOH (20–50 mg/mL) and then mixing equimolar amounts. After the mixture was allowed to stand for 1 h at room temperature, the resulting precipitate was removed by filtration, washed with a small amount of the same solvent, and dried. The composition of the complex 1–6 was determined by high-pressure LC using AcOH (5%)–MeOH (25%)–H$_2$O (70%) as the solvent and a μBondapak C$_{18}$ column. Molar ratios were computed from the integrated areas of both partners by using $\epsilon_{360_{nm}}$(MeOH) = 18000 for 6 and $\epsilon_{470_{nm}}$(MeOH) = 32000 for 1. The composition of the complex 17–6 was obtained from its UV–vis spectrum in Me$_2$SO by using $\epsilon_{375_{nm}}$(Me$_2$SO) = 23700 for 6 and $\epsilon_{490_{nm}}$(Me$_2$SO) = 2620 for 17.

Stability Studies. The fading of color was followed either spectrophotometrically at the λ_{max} or by high-pressure LC, using a Waters chromatograph equipped with a Hewlett-Packard 3380-A peak integrator, a Schoeffel SF770 UV–vis detector and a μBondapak C$_{18}$ column. The solvent, 5% MeOH–15% AcOH–80% H$_2$O, was run at a flow of 2.0 mL/min.

Sunlight exposure is expressed in langleys (cal/cm^2) and was measured by using an Eppley black and white pyranometer, Model 8–48A, Eppley Laboratory, Inc., Newport, RI, sensitive to UV–visible and IR radiation. For the latitude of Atlanta, an exposure of 500 langleys is equivalent to a full day of summer sunlight.

Model carbonated beverages were prepared by conventional methods (Jacobs, 1959), from a syrup containing 2.0 kg of H$_2$O, 25 g of citric acid, 2.5 kg of sugar, and 40 g of grape flavor base. The syrup was diluted 4.4:1 with water, the color and copigments were added, and the resulting beverage was carbonated with 2 volumes of CO$_2$. Standard flint glass bottles were used as containers.

RESULTS AND DISCUSSION

The results summarized in Table I indicate the spectral changes observed for cyanidin 3-rutinoside (2) (10 ppm, 0.01

Table II. Spectral Shifts Induced by Quercetin-5'-sulfonic Acid (6) on the Visible Spectra of Cyanidin 3-Rutinoside (2) and Pentamethylcyanidin (17), Both at 10 ppm in 0.01 M Citric Acid, pH 2.8

antho-cyanin	λ_{max}, nm (absorbance),[a] at 6						
	0 ppm	20 ppm	50 ppm	100 ppm	200 ppm	500 ppm	1000 ppm
2	512 (1.00)	517 (1.05)	525 (1.07)	532 (1.08)	535 (1.08)	544 (1.08)	550 (1.08)
17	505 (1.00)	521 (1.26)	540 (1.93)	549 (2.10)	552 (2.34)	556 (2.40)	556 (2.44)

[a] Values for absorbance are in parentheses.

Table III. Effect of Copigments (500 ppm) on the Sunlight Fading of Cyanidin 3-Rutinoside (20 ppm) in 0.01 M Citric Acid, pH 2.8[a]

copigment added	λ_{max} complex, nm	langleys							
		0	50	100	200	300	500	1200	1600
(β-hydroxyethyl)rutin (4)	530	100	–	–	95	–	91	71	64
quercetin-5'-sulfonic acid (6)	535	100	–	–	98	–	92	86	83
morin-3',6-disulfonic acid (8)	525	100	–	–	98	–	92	86	83
apigenin-3'-sulfonic acid (9)	532	100	–	–	89	–	78	63	51
biochanin-A-sulfonic acid (12)	527	100	–	–	97	–	81	67	59
4'-methoxyaurone-3'-sulfonic acid (13)	540	100	–	–	94	–	80	65	56
none (control)	512	100	–	–	90	–	63	36	19
3-hydroxyflavonesulfonic acid (7)	525	100	–	–	1	–			
flavonesulfonic acid (10)	533	100	–	–	19	1			
4'-methoxyflavone-3'-sulfonic acid (11)	535	100	–	–	10	–			
xanthonesulfonic acid (14)	525	100	14	1	–	–			
N-methylacridonesulfonic acid (15)	530	100	13	1	–	–			
anthraquinone-1-sulfonic acid (16)	525	100	–	43	11	–			

[a] Results are expressed as the percent color remaining with respect to 0 langley.

M citric acid) in the presence of a variety of flavonoid and other heterocyclic compounds. The blue shift caused in the anthocyanin visible spectrum by copigments indicates the formation of ground-state complexes (Davidson, 1975). This molecular association among anthocyanins and copigments can occur through a variety of forces, mainly π–π interactions and H bonding. Upon irradiation of the complexes, aggregation is known to affect the energy levels of the excited states, as well as facilitate energy-transfer processes among the partners. The implications for the photochemical behavior of the anthocyanins are many, considering their well-known tendency to bleach upon sunlight exposure (Van Buren et al., 1968) through a mechanism shown to be photooxidative in nature (Sweeny and Iacobucci, 1980).

Table I also shows that the sulfonation of flavonoids improves on their ability to associate with anthocyanins. This is evident by comparing the spectral effects caused by quercetin-5'-sulfonic acid (6) with respect to the nonsulfonated quercetin glycosides 3 and 4. These observations suggest that ionic bonds between the negatively charged sulfonates and the cationic anthocyanins are playing an important additional role in the association of those species in solution. Indeed, we have observed that 6 is able to precipitate apigeninidin (1) and pentamethylcyanidin (17) from acid solutions, and the isolated complexes were shown to be 1:1 molecular adducts. Examination of molecular models indicates that 6 can juxtapose on 1 and 17 in a manner that favors π–π ring interactions, extensive H bonding, and ionic bond formation between the negatively charged sulfonate and the electron-deficient anthocyanin (Figure 1). Similar views have been advanced by Goto et al. (1979) on discussing the structure of the complex between awobanin, a delphinidin 3,5-diglucoside derivative, and flavocommelin, a flavone glycoside. These views depart considerably from the explanation currently in vogue (Williams and Hrazdina, 1979; Somers and Evans, 1979), invoking an end to end complex between the quinonemethide form of the anthocyanin and

Table IV. Sunlight Fading of Anthocyanins in Model Carbonated Beverages, in the Presence of Quercetin-5'-sulfonic Acid (6)[a]

	langleys				
	0	500	1000	2000	3000
2 (20 ppm)	100	65	48	38	12
2 (20 ppm) plus 6 (100 ppm)	100	86	74	70	63
enocianina (400 ppm)	100	80	63	52	42
enocianina (400 ppm) plus 6 (100 ppm)	100	92	83	78	73

[a] Results expressed as percent color remaining with respect to 0 langley.

the phenolic partner, stabilized by H bonding. The participation of the quinonemethide form has been postulated as a means to explain the spectral blue shifts caused by complexation in acid solution, despite the fact (Brouillard et al., 1978) that at pH below 3.0 the concentration of quinonemethide is negligible, as the phenolic hydroxyls at C7 and/or C4' are fully protonated ($pK_a' \sim 4.2$–4.5). In this regard, we have observed that pentamethylcyanidin (17), a totally blocked anthocyanin that cannot dissociate into a quinonemethide, interacts with 6 at pH 2.8 with spectral changes (Table II) identical with those recorded for cyanidin 3-rutinoside (2), also with formation of a 1:1 molar aggregate. These facts support Goto's views and make the alternative hypothesis untenable.

An unexpected observation was made when the complexes of Table I were exposed to sunlight irradiation. One group of copigments (Table III), upper half) were found to exert a pronounced photoprotective effect on the anthocyanin, while others (Table III, lower half) accelerated its photooxidative bleaching.

Only the polyhydroxylated flavonoids were found photoprotective, regardless of the type (flavonols, flavones, isoflavones, and aurones). Suppression of the phenolic

Table V. Effect of Added Alcohol on the Photostability of Cyanidin 3-Rutinoside (2) Complexes with Quercetin-5'-sulfonic Acid (6)[a]

	langleys					
	0	158	416	615	926	1345
control, 2 (20 ppm) in 0.01 M citric acid	100	83	63	51	35	18
2 (20 ppm) plus 6 (100 ppm) in 0.01 M citric acid	100	93	88	85	79	71
control, 2 (20 ppm) and 50% EtOH in 0.01 M citric acid	100	59	29	13	6	0
2 (20 ppm) plus 6 (100 ppm) and 50% EtOH in 0.01 M citric acid	100	77	58	47	34	19

[a] Results expressed as percent color remaining with respect to 0 langley.

Table VI. Photophysical Effects of Quercetin-5'-sulfonic Acid (6) on the Photooxidation of Cyanidin 3-Rutinoside (2) upon Sunlight Irradiation[a]

	langleys				
	207	376	589	910	1128
2 (20 ppm)	84	65	38	18	9
2 (20 ppm) *complexed* with 6 (100 ppm)	95	92	83	72	67
2 (20 ppm) *screened* by external 6 (100 ppm)	88	76	56	36	26

[a] Results expressed as percent color remaining with respect to 0 langley. Solvent: 0.01 M citric acid, pH 2.8. The internal container was a 30-mL test tube, placed in an external 250-mL wide-mouth flask.

Table VII. Effect of Quercetin-5'-sulfonic Acid (6) on the Photooxidation of Apigeninidin (1) in 0.01 M Citric Acid (pH 2.8)[a]

	langleys			
	0	979	2247	4005
1 (10 ppm)	100	80	47	16
1 (10 ppm) plus 6 (100 ppm)	100	99	82	35

[a] Results expressed as percent color remaining at 470 nm with respect to 0 langley.

substituents in rings A and B (for example, 6 → 7) resulted in a dramatic reversion of the photochemical behavior. All nonflavonoid copigments tested, like the sulfonated N-methylacridone 15 and anthraquinone 16, were found to belong to the second category (Table III).
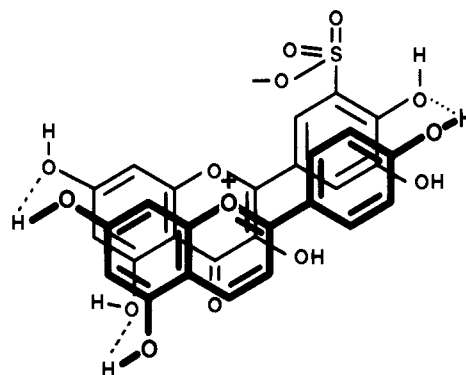
The effectiveness of quercetin-5'-sulfonic acid for the protection of anthocyanins was tested also in model carbonated beverages. The results presented in Table IV show a positive effect on pure cyanidin 3-rutinoside and on the crude anthocyanins of enocianina.

The irradiation of the complex (20 ppm of 2; 100 ppm of 6) was conducted in 0.01 M citric acid and in the same containing 50% alcohol in order to ensure that the photoprotective effect is facilitated when molecular association occurs. As shown in Table V, the photoprotective effect of 6 on 2 diminished in the presence of alcohol as the result of the dissociation of the complex that disrupted energy transfer processes between the partners. The destabilizing effect of alcohol is noticeable also in the case of 2 alone,

Figure 1. Representation of the (1:1) molecular complex between apigeninidin (1) and quercetin-5'-sulfonic acid (6).

likely due to disassociation of the self-aggregated pigment (Somers and Evans, 1979). These observations are of interest for the understanding of the color stability of wines, where the aggregation of anthocyanins between themselves and with the polyphenolic copigments of the grape is known to vary with the alcohol content of the wine (Somers and Evans, 1979).

Moreover, the photoprotection of 2 by 6 is not the result of a simple "screening effect" caused by the strong UV absorption of the flavonol (λ_{max} 360 nm). As shown in Table VI, the protective effect of 6 is largely lost if the partners are irradiated in concentrical, separated compartments, with 2 in the inside surrounded by 6 outside. These observations demonstrate conclusively that the photostabilization of 6 by 2 is the consequence of molecular association.

The photochemical behaviors discussed above for the anthocyanin 2 are not restricted to this class of red flavylium salts. The group of 3-deoxyanthocyanidins, exemplified by apigeninidin (1), has been observed to react similarly in the presence of 6, although the lack of the C3 hydroxy makes the flavylium cation more resistant to photooxidation (Table VII).

Even simple flavyliums like the 4',7-dihydroxyflavylium chloride (18) perform in similar fashion. Table VIII shows the antagonistic photochemical effects on 18 of 6, 10, and 16, observed upon sunlight irradiation in 0.01 M citric acid solution, pH 2.8.

Table VIII. Effect of Copigments (500 ppm) on the Sunlight Fading of 4,7'-Dihydroxyflavylium Chloride (18) (20 ppm) in 0.01 M Citric Acid, pH 2.8[a]

copigment added	langleys							
	0	164	280	467	770	1377	1814	2317
6	100	100	97	94	86	75	61	46
none (control)	100	100	87	75	58	36	23	12
10	100	57	25	6	3	–	–	–
16	100	52	29	12	6	–	–	–

[a] Results expressed as percent color remaining at 458 nm with respect to 0 langley.

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N-Sulfinylated Derivatives of Methylcarbamate Esters

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Alkyl, aryl, and oxime carbamates react with thionyl chloride to give the corresponding N-chlorosulfinyl derivatives. This new reaction provided a useful intermediate for the synthesis of a large variety of new N-derivatized carbamates. N-(Chlorosulfinyl)carbamates reacted with alcohols and phenols to give N-[(alkyloxy)- and -(aryloxy)sulfinyl]carbamates, with alkane- and arenethiols to give N-[(alkanethio)- and -(arenethio)sulfinyl]carbamates, with carbamates to give either symmetrical or asymmetrical N,-N'-sulfinylbiscarbamates, with monosubstituted alkyl- or arylsulfonamides to give N-[[(alkyl- or -(arylsulfonyl)amino]sulfinyl]carbamates, and with trisubstituted sulfondiamides to give N-[[(amino-sulfonyl)amino]sulfinyl]carbamates. Application of these reactions to insecticidal methylcarbamates resulted in novel derivatives of high insecticidal activity but of a much lower mammalian toxicity as compared to the parent methylcarbamate insecticide.

During the course of a study concerned with the reaction between trimethyl phosphite and isopropyl N-(chlorosulfenyl)-N-methylcarbamate, it became necessary to prepare a sample of isopropoxy-N-methyliminoyl chloride (1). Since N-alkylamides are known to react with thionyl chloride to form the corresponding imidoyl chloride (Vaughan and Carlson, 1962), isopropyl methylcarbamate was reacted with thionyl chloride with the expectation that the carbamate would be converted to 1 according to
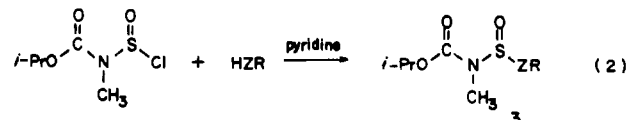

$$ \textit{i-PrO}\overset{O}{\overset{\|}{C}}NHCH_3 + SOCl_2 \longrightarrow \textit{i-PrO}\overset{Cl}{\overset{|}{C}}NCH_3 \qquad (1) $$
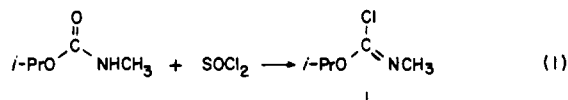
However, the reaction did not proceed according to the above equation and instead gave isopropyl N-(chloro-

sulfinyl)-N-methylcarbamate (2) in excellent yield.
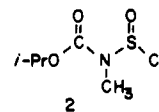
In the presence of pyridine, 2 reacted with a variety of nucleophiles, e.g., alcohols, mercaptans, etc., resulting in the displacement of the chloride ion and formation of the corresponding sulfinate derivative (3) according to

$$ \textit{i-PrO}\overset{O}{\overset{\|}{C}}\underset{CH_3}{N}\overset{O}{\overset{\|}{S}}Cl + HZR \xrightarrow{\text{pyridine}} \textit{i-PrO}\overset{O}{\overset{\|}{C}}\underset{CH_3}{N}\overset{O}{\overset{\|}{S}}ZR \qquad (2) $$

where Z = O, S, and N and R is a variety of different substituents. This paper is concerned with the synthesis of chlorosulfinyl intermediates of methylcarbamate esters, including methylcarbamate insecticides, and the reactions between the chlorosulfinyl intermediates and different kinds of nucleophilic agents. Preliminary data on the

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