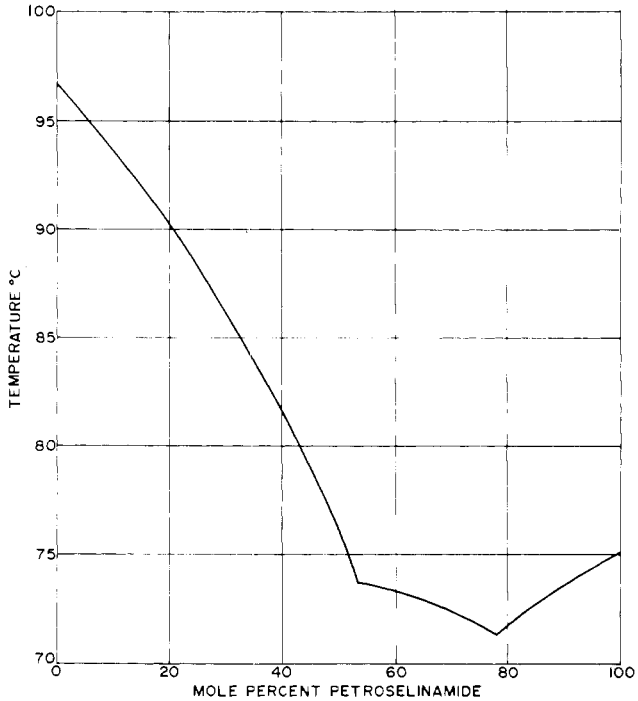


Figure 1. Binary freezing-point diagram for petroselaidamide with petroselinamide.

laidamide: N, 4.98. Found: N, 4.97, 4.98; fp 96.81 °C.

Freezing points were determined by the static method.[11] For each composition, weighed amounts of the two amides were sealed in a glass tube. A glass bead was included to ensure efficient stirring as the sample tubes were turned end over end in a constant-temperature water bath. Two temperatures a few tenths of a degree apart were found, one at which the last crystals disappeared and the other at which a few crystals remained undissolved after prolonged agitation. The freezing point was taken as the mean of these two temperatures, corrected for both thermometer calibration and emergent stem.

The X-ray long- and short-spacing measurements were made by the powder method of O'Connor et al.[12] A General Electric XRD-5 diffractometer was used to obtain X-ray diffractions by the direct-measurement technique with a chart recorder. The instrument was equipped with a copper target X-ray tube and a 0.0007 in. thick nickel filter. Divergence and antiscattering slits were used. The X-rays were generated at 30 kVp and 15 mA from 0 to 12.5°, 2θ, and 36 kVp and 16 mA from 12.5 to 50°, 2θ.

Results and Discussion

The freezing-point data for the binary system are summarized in Table I and represented in Figure 1. The two isomeric amides form an incongruently melting 1:1 molecular compound with a peritectic at 73.7 °C (53.8% petroselinamide) and a eutectic at 71.4 °C (78.0%). Thus, the binary freezing-point behavior of the *cis*- and *trans*-6-octadecenamides parallels that of the *cis*- and *trans*-9-octadecenamides.[10] Both binary systems exhibit the formation of a 1:1 molecular compound with an incongruent melting point and a eutectic.

The X-ray diffraction patterns indicate that the petroselinamide has a long-spacing value of 40.8 Å and short spacings at 4.33, 3.86, and 3.45 Å. The corresponding values for the petroselaidamide are 49.3 and 4.10, 3.52, and 3.08 Å.

Acknowledgment

The authors thank Gene Sumrell for assistance with the manuscript.

Literature Cited

(1) Placek, L. L. *J. Am. Oil Chem. Soc.* **1963**, *40*, 319.
(2) Novak, A. F.; Fisher, M. J.; Fore, S. P.; Dupuy, H. P. *J. Am. Oil Chem. Soc.*, **1964**, *41*, 503.
(3) Mod, R. R.; Skau, E. L.; Fore, S. P.; Magne, F. C.; Novak, A. F.; Dupuy, H. P.; Ortego, J. R.; Fisher, M. J. U.S. Patent 3 285 812, 1966.
(4) Steele, W.; Jenkin, H. M. *Proc. Soc. Exp. Biol. Med.* **1977**, *155*, 405.
(5) Jenkin, H. M. German Patent 2 305 553, 1973. *Chem. Abstr.* **1975**, *83*, 108631.
(6) Placek, L. L.; Dollear, F. G. *J. Am. Oil Chem. Soc.* **1962**, *39*, 347.
(7) Placek, L. L.; Dollear, F. G.; Sumrell, G. *J. Am. Oil Chem. Soc.* **1967**, *44*, 431.
(8) Mod, R. R.; Harris, J. A.; Skau, E. L. *J. Chem. Eng. Data* **1968**, *13*, 115.
(9) Roe, S. T.; Scanlon, J. T.; Swern, D. *J. Am. Chem. Soc.* **1949**, *71*, 2215.
(10) Mod, R. R.; Magne, F. C.; Skau, E. L. *J. Chem. Eng. Data* **1960**, *5*, 478.
(11) Magne, F. C.; Skau, E. L. *J. Am. Chem. Soc.* **1952**, *74*, 2628.
(12) O'Connor, R. T.; Mod, R. R.; Murray, M. D.; Skau, E. L. *J. Am. Chem. Soc.* **1955**, *77*, 892.

Received for review May 29, 1979. Accepted July 9, 1979. Names of companies or commercial products are given solely for the purpose of providing specific information; their mention does not imply recommendation or endorsement by the U.S. Department of Agriculture over others not mentioned.

Synthesis of Isomeric Methyl- and Dimethyl-Substituted 4-Benzylidene-2-phenyloxazolin-5-ones and Ring-Opened Derivatives

Everton S. Nicholas and David J. Phelps*

Department of Chemistry, Saint Mary's University, Halifax, Nova Scotia, Canada B3H 3C3

4-Benzylidene-2-phenyloxazolin-5-one and 15 mono- and dimethylated isomers as well as their ring-opened methyl ester and acid derivatives have been synthesized. Absorption spectroscopy indicates insignificant changes in the chromophore due to the methyl groups.

Because of the implication of cyclic species resembling oxazolinones in enzymatic reactions[1-3] and because oxazolinones themselves are able to acylate various enzymes,[4,5] recent attention has been given to the resonance Raman[6,7] and absorption spectroscopy[5-7] of these molecules. Due to work indicating significant changes in reactivity of various methyl isomers of furylacrylic and thienylacrylic acid acyl enzymes of α-chymotrypsin,[8] it was considered worthwhile to synthesize isomeric methylated oxazolinones for structure–activity relationship studies. It was also of interest to determine if any perturbation of the structure of these intense chromophores would result from the substitution of methyl groups for hydrogen.

The characteristic absorption spectrum of the (*Z*)-4-benzylidene bond[5,8] indicates that all of the oxazolinones synthesized were of the *Z* configuration. The λ_{max} and ϵ values

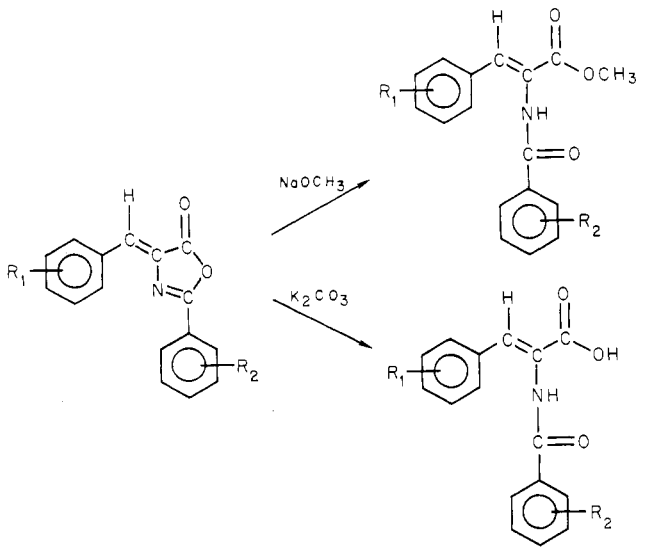
0021-9568/80/1725-0089$01.00/0

Table I. Melting Points and Yields of Synthetic Materials

substituents		oxazolinone		ester (2)		acid (3)	
R_1	R_2	yield,[a] %	mp (lit.)	yield,[a] %	mp (lit.)	yield,[a] %	mp (lit.)
H	H	60	165-166 (165-166[5])	89	140 (147-149[13])	58	229-231 (229-230[13])
o-CH_3	H	41	139 (134-135[9])	61	104-105	65	225-228
m-CH_3	H	56	125	58	120-121	54	210-212
p-CH_3	H	50	139-140 (140-141[10])	85	101-103	79	232
H	o-CH_3	40	95	64	105	76	204-207
H	m-CH_3	75	136 (130[11])	85	154-155	54	202-204
H	p-CH_3	63	185 (184-185[12])	54	165	81	261-263 (239-240[14])
o-CH_3	o-CH_3	34	140	71	96-97	73	198-200
o-CH_3	m-CH_3	55	148	91	109-110	84	225-227
o-CH_3	p-CH_3	36	159-160	84	122	54	240-241
m-CH_3	o-CH_3	55	103-104	55	114	76	215-217
m-CH_3	m-CH_3	62	114	78	134-135	65	194-195
m-CH_3	p-CH_3	69	148	52	123-125	32	212-214
p-CH_3	o-CH_3	52	155	81	133	81	225
p-CH_3	m-CH_3	71	153	81	118-119	81	233-235
p-CH_3	p-CH_3	22	181	78	119	30	227-230

[a] Recrystallized material.

Scheme I



(acetonitrile solvent) show no significant change for the 16 oxazolinones, indicating little electronic or steric effect on the chromophore by the methyl groups. Because the oxazolinones and the α-benzamidomethyl cinnamates are potential substrates for proteolytic enzymes and because the acids would be the presumed hydrolysis product, these molecules were made and characterized. The structures of the oxazolinones (**1**) the esters (**2**), and the acids (**3**) are given in Scheme I. The molecules were readily synthesized in good yields by the general methods given in the Experimental Section. Table I lists the yields and melting points of the various compounds. All new compounds gave the appropriate combustion analyses and nuclear magnetic resonance spectra.

Experimental Section

Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. All commercial chemicals were from Aldrich Chemical Co. Methylhippuric acids were synthesized by Schotten-Baumann benzoylations of glycine. Acetonitrile used for spectroscopy was Eastman Spectro Grade solvent. Absorption spectra were obtained with a Cary 219 UV/VIS spectrometer and nuclear magnetic resonance spectra on a Varian EM 360 spectrometer. Elemental analyses were performed by Mr. Hector Seguin of the National Research Council of Canada, Ottawa, Ontario. General experimental conditions for the three reactions are given below.

Oxazolinone Synthesis. The aldehyde (20 mmol), the acid (20 mmol), and $KHCO_3$ (0.4 g) were placed in a round-bottomed flask. Acetic anhydride (20 mL) was added and the mixture was warmed with stirring until everything had dissolved. The contents of the flask were then allowed to stir overnight at room temperature. Next day the yellow mixture was poured with stirring into 500 mL of hot (60 °C) water. The resultant solid was collected after 0.5 h, dried, and crystallized from 95% ethanol. The air-dried, crystallized, yellow solid was characterized by NMR, UV, and elemental analysis. See Table I for melting points and yields.

α-Benzamidocinnamic Acid Syntheses. The oxazolinone (0.35 g) was treated with acetone (25 mL), water (20 mL), and K_2CO_3 (0.25 g) at reflux until TLC ($CHCl_3$) showed no starting material remained (5–10 h). After rotary evaporation of the acetone, 1 N HCl (5–10 mL) was added and the resulting white solid collected and crystallized from 70% ethanol. The resultant white needles were characterized by UV and elemental analysis. See Table I for melting points and yields.

Methyl α-Benzamidocinnamate Syntheses. A 1 N solution of sodium methoxide was prepared by dissolving metallic sodium (2.3 g) in distilled methanol (100 mL). The oxazolinone (1 mmol) was dissolved or suspended in benzene (5 mL) and the sodium methoxide solution (1.1 mL) was added. After 0.5 h, 1 N HCl (1 mL) was carefully added. Upon rotary evaporation of the methanol, a white solid was formed. This was crystallized from 50% ethanol. The resultant white solid was characterized by UV and elemental analyses. See Table I for melting points and yields.

Literature Cited

(1) S. H. Yu and T. Viswanatha, *Eur. J. Biochem.*, **11**, 347 (1969).
(2) M. A. Coletti-Previero, C. Axelrud-Cavadore, and A. Previero, *FEBS Lett.*, 213, 218 (1970).
(3) P. R. Carey, R. G. Carriere, K. R. Lynn and H. Schneider, *Biochemistry*, **15**, 2387 (1976).
(4) J. DeJersey and B. Zerner, *Biochemistry*, **8**, 1967, 1975 (1969).
(5) K. Brocklehurst and K. Williamson, *Tetrahedron*, **30**, 351 (1974).
(6) K. Kumar, D. J. Phelps, and P. R. Carey, *Can. J. Chem.*, **56**, 232 (1978).
(7) D. J. Phelps, R. G. Carriere, K. Kumar, and P. R. Carey, *Can. J. Chem.*, **56**, 240 (1978).
(8) D. J. Phelps, B. A. E. MacClement, R. G. Carriere and P. R. Carey, manuscript in preparation.
(9) A. Masquestiau, Y. VanHaverbeke, and R. Muller, *Bull. Soc. Chem. Belg.*, **83**, 259 (1974).
(10) G. Stefanovic and M. Stefanovic, *J. Org. Chem.*, **21**, 161 (1956).
(11) A. M. Islam, A. M. Khalil, and M. S. El-Houseni, *Aust. J. Chem.*, **26**, 1701 (1973).
(12) M. Crawford and W. T. Little, *J. Chem. Soc.*, 729 (1959).
(13) H. E. Carter and W. C. Risser, *J. Biol. Chem.*, **139**, 255 (1941).
(14) R. Pfleger and G. Markert, *Ber. Deutsch Chem. Ges.*, **90**, 1482 (1957).

Received for review September 17, 1979. Accepted October 29, 1979.