minations showed the monocarboxylic amide derived from *trans*-1,4-ditosyloxycyclohexane and ethyl malonate to be 3-cyclohexene-1-carboxamide.

EXPERIMENTAL[7]

Ethyl 3-cyclohexene-1-malonate. One-tenth mole (16.0 g.) of ethyl malonate was added to a solution of 4.6 g. (0.2 mole) of sodium in 100 ml. of absolute ethanol. Most of the solvent was removed by distillation under reduced pressure on the steam bath and a suspension of 42.4 g. (0.1 mole) of *trans*-1,4-ditosyloxycyclohexane[5] in 350 ml. of anhydrous benzene was added. The mixture was refluxed with stirring for 20 hr., cooled, and poured into water. The benzene phase was washed with water, dried over anhydrous potassium carbonate, and the solvent distilled on the steam bath. The residual oily solid was extracted with hexane which left a residue of 6.5 g. of unchanged ditosylate. Evaporation of the hexane extract gave a pale yellow oil which was distilled slowly at a bath temperature not exceeding 145°. Following a forerun of 7.4 g. of recovered ethyl malonate there was obtained 3.3 g. (14%) of a colorless liquid, b.p. 86–95°/0.08 mm. For analysis it was redistilled yielding 2.4 g. b.p. 106–110°/0.2 mm., n_D^{25} 1.4580.

Anal. Calcd. for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.91; H, 8.48.

3-Cyclohexene-1-malonic acid. A solution of 2.2 g. of the dicarboxylic ester above in 20 ml. of 90% ethanol containing 4.0 g. of potassium hydroxide was refluxed for 4 hr. An equal volume of water was added and the solution was distilled to dryness under reduced pressure on the steam bath. The solid residue was taken up in 40 ml. of water and acidified slightly with dilute hydrochloric acid. The colorless plates which separated were extracted with ether and the extracts were dried over anhydrous calcium chloride. Evaporation of the solvent gave 1.6 g. (95%) of a solid melting with decomposition at 151–153°. Recrystallization from toluene gave 1.2 g. of colorless plates, m.p. 151–153° dec.

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.90; H, 6.53.

3-Cyclohexene-1-acetic acid. The above dicarboxylic acid (1.1 g.) was heated for 30 min. at a bath temperature of 180° when gas evolution ceased. Distillation of the residue under reduced pressure gave 0.45 g. (54%) of colorless liquid, b.p. 140–142°/15 mm. It was redistilled for analysis giving 0.35 g., b.p. 138–140°/13 mm., n_D^{25} 1.4802.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.70; H, 8.73.

3-Cyclohexene-1-acetamide. (a) The above monocarboxylic acid (0.30 g.) was dissolved in 2.0 ml. of chloroform and 0.3 ml. of thionyl chloride. The solution was allowed to stand overnight and refluxed for 1 hr. Chloroform and excess thionyl chloride were removed by distillation on the steam bath under reduced pressure and the residue of 3-cyclohexene-1-acetyl chloride was taken up in 10 ml. of anhydrous ether. A gentle stream of anhydrous gaseous ammonia was passed into the solution for 1 hr. The resulting suspension was evaporated and the solid residue was recrystallized from 15 ml. of boiling water. The colorless plates (0.19 g., 63%) which separated on cooling melted at 142–143°. Recrystallization from water gave 0.095 g., m.p. 141–142°.

Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.21; H, 9.32; N, 9.91.

(b) An ethereal solution of diazomethane was prepared by adding 25.0 g. (0.17 mole) of *N*-nitroso-*N*-methyl-*N'*-nitroguanidine ("Diazald") in small portions to a stirred mixture of 40 ml. of 50% aqueous potassium hydroxide and 250 ml. of ether with ice bath cooling. The ethereal layer was separated and dried for several hr. over solid potassium hydroxide. A solution of 7.25 g. (0.05 mole) of 3-cyclohexene-1-carbonyl chloride[8] in 30 ml. of anhydrous ether was added dropwise with stirring to the ice-cold solution of diazomethane. When the evolution of nitrogen ceased the solvent and excess diazomethane were distilled at room temperature under reduced pressure. The residual yellow liquid diazoketone was dissolved in a solution of 150 ml. of purified dioxane[9] and 40 ml. of concd. ammonia and warmed to 60°. Five milliliters of 10% aqueous silver nitrate solution, 0.5 g. of silver oxide, and 1 ml. of methanol were added. Heating at 55–60° with stirring was continued for 1 hr. when an aliquot no longer liberated nitrogen with concd. hydrochloric acid. The suspension was then acidified slightly with dilute hydrochloric acid, filtered, and the filtrates were evaporated to dryness under reduced pressure. Recrystallization of the solid residue from boiling water gave 4.9 g. (71%) of colorless plates, m.p. 139–141°. The analytical sample melted at 141–142° (from water).

Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.27; H, 9.26; N, 9.96.

Norbornane-7-carboxylic acid. This acid (m.p. 78.5–79.5°) was obtained by a modification of the method of Kwart and Kaplan[10] in 59% yield from carefully fractionated 7-bromonorcamphane (b.p. 58–59°/8 mm., n_D^{20} 1.5178). The hydrocarbon byproduct of the reaction (m.p. 108–110°, reported 107–109°[10] gave an elementary analysis corresponding to that calculated for 7,7'-binorcamphane and thus confirms the structural speculations of these authors.

Anal. Calcd. for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.62; H, 11.50.

Norbornane-7-carboxamide. A solution of 1.9 g. of norbornane-7-carboxylic acid in 15 ml. of chloroform and 1.5 ml. of thionyl chloride was allowed to stand at room temperature for 3 hr. and refluxed for 2 hr. The solvent and excess thionyl chloride were removed by distillation under reduced pressure and the residual pale yellow liquid was taken up in 25 ml. of anhydrous ether. The ice-cooled ethereal solution was saturated with anhydrous gaseous ammonia and the solvent was allowed to evaporate. Two crystallizations of the residue from boiling water gave 0.90 g. (48%) of large colorless, glistening plates, m.p. 198.5–199.5°, unchanged upon further recrystallization.

Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.05. Found: C, 68.91; H, 9.21; N, 10.00.

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(7) Melting points are uncorrected. Analyses and infrared spectra by Mr. E. R. Hoffman and staff of these laboratories.

(8) J. Gillois-Doucet, *Ann. chim.* (*Paris*), **10**, 497 (1955).

(9) L. F. Fieser, *Experiments in Organic Chemistry*, third ed., D. C. Heath and Co., Boston, 1955, p. 285, procedure (a).

(10) H. Kwart and L. Kaplan, *J. Am. Chem. Soc.*, **76**, 4072 (1954).

The Conversion of *o*-Alkoxycinnamic Acids to Coumarins[1,2]

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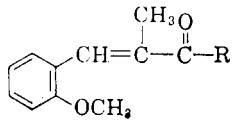
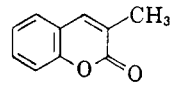
In connection with other work in progress in this laboratory it was necessary to to prepare *o*-

(1) This investigation was supported in part by a U.S. P.H.S. Research Grant (RG 6478) from the Division of General Medical Sciences, Public Health Service, and in part by a Grant-in-Aid from Eli Lilly & Co.

methoxy-α-methylcinnamoyl chloride (I). A mixture of thionyl chloride and *o*-methoxy-α-methylcinnamic acid (II) was refluxed and the excess thionyl chloride removed *in vacuo*. Distillation of the reaction mixture gave a white solid which did not behave as an acid chloride and in fact had the molecular formula, $C_{10}H_8O_2$. The molecular formula, melting point, infrared spectrum, and ultraviolet spectrum indicated that this material was 3-methylcoumarin (III). No depression of melting point was noted on admixture with an authentic sample of 3-methylcoumarin and the spectra were superimposable on those of the authentic material.



I. R = Cl
II. R = OH



III

The reaction of thionyl chloride with *o*-methoxy-α-methylcinnamic acid was repeated under identical conditions except that the crude product, after removal of the thionyl chloride, was distilled at a lower pressure and hence at a lower temperature. In this case a liquid, believed to be mainly *o*-methoxy-α-methylcinnamoyl chloride, was obtained. This liquid, which was never obtained in a completely pure condition, exhibited all of the properties expected for an acid chloride. Heating this acid chloride at 170° for a short time caused its complete conversion to 3-methylcoumarin. It is apparent, therefore, that the acid chloride is formed first and at a higher temperature cleavage of the ether occurs with cyclization.[3]

The cleavage of ethers by acid halides has been investigated from time to time[5] for many years. In most of these prior cases the cleavage was either intermolecular, or, if intramolecular, involved a rearranged product rather than a cyclic product. It was thus thought to be of interest to investigate to ether cleavage with coumarin formation further.[6,8]

A series of *o*-alkoxycinnamic acids with various substituents on the ring and in the *alpha* position were obtained commercially or prepared by standard literature methods and refluxed with thionyl chloride. After removal of the thionyl chloride, the temperature was raised and a solid sublimate collected. In all cases where a coumarin was obtained it was this sublimate. The results are presented in Table I.

In most cases the coumarin expected from ether cleavage was obtained although generally in small yield.[11] The low yields may be explained by the fact that only the *trans* acids were used while the *cis* form is the one favorable to cyclization.

To gain further confirmation of the acid chloride intermediate, 2,3-dimethoxycinnamic acid and thionyl chloride were treated and distilled at a low temperature to yield the acid chloride. Heating this acid chloride to 250° gave 8-methoxycoumarin.

The nature of the alkoxyl group appears to have little effect, as both *o*-ethoxy- and *o*-methoxycinnamic acid yielded coumarins although the yields were somewhat lower with the *o*-ethoxy group.

The use of cinnamic acids with an α-hydrogen, α-methyl, or α-ethyl all leads to coumarins with the appropriate substituent in the 3-position. The yields with the α-methyl and α-ethyl compounds were much higher than those in the unsubstituted cases and it is possible that this is because the energy difference between the *cis* and *trans* forms differ much less than for unsubstituted (no α- and β-substituents) cinnamic acids. No 3-cyanocoumarin could be isolated when *o*-methoxy-α-cyanocinnamic acid was treated with thionyl chloride. This cyano acid chloride was quite stable and only darkened slightly on heating to high temperatures.

7- and 8-Methoxycoumarins were formed in about the same yield as coumarin itself indicating little if any effect of substituents in the 3- and 4-positions of the cinnamic acid. The yields of 6-chloro-, 6-methyl-, and 6-methoxycoumarin, however, were from two to three times greater than the yield of coumarin itself while no 6-nitrocoumarin could be isolated by this method. These results indicate that an electron donating group *para* to the point of ether cleavage (and ring closure) enhances the reaction while an electron withdrawing group in the *para* position retards it.

(2) Presented in part before the Southeastern Regional Meeting of the American Chemical Society, November 3–5, 1960. A preliminary report was presented at the Florida Section of the A.C.S. Meeting-in-Miniature, May 13, 1960.

(3) It should be noted that the ether cleavage in this series apparently can occur only in an intramolecular manner with cyclization as *p*-methoxy-α-methylcinnamic acid gives only the expected cinnamoyl chloride[4] in good yield.

(4) W. Baker, *J. Chem. Soc.*, 176 (1949).

(5) See D. S. Noyce and H. I. Weingarten, *J. Am. Chem. Soc.*, **79**, 3093 (1957) for leading references.

(6) It should be noted that coumarin has been previously obtained from 2-methoxycinnamic acid by treatment with hydrogen bromide,[7] however, this involves an ether cleavage by the hydrogen bromide rather than by an acid chloride.

(7) L. Bert, *Compt. rend.*, **214**, 230 (1942).

(8) After most of this work was completed, the conversion of 2-carboxy-2′-methoxy-4′-nitrobiphenyl by polyphosphoric acid to 7-nitro-3,4-benzocoumarin through a facile splitting of the methoxy group was reported.[9] Again this did not involve an acid chloride. Preliminary studies of the reaction of *o*-methoxycinnamic acid with polyphosphoric acid[10] indicate that coumarin is not formed. The product of this reaction will be investigated further at a later date.

(9) H. Pan and T. L. Fletcher, *J. Org. Chem.*, **25**, 1106 (1960).

(10) F. D. Popp and W. E. McEwen, *Chem. Revs.*, **58**, 321 (1958); *idem., Trans. Kansas Acad. Sci.*, **63**, 169 (1960).

(11) The residue in the reaction vessel after sublimation was in every case dark tarry material which did not yield any identifiable products.

TABLE I

PREPARATION OF COUMARINS BY ETHER CLEAVAGE

Acid or Acid Chloride	M.P.	M.P., Lit.	Cyclization Product	M.P.	M.P., Lit.	Yield, %
o-Methoxcinnamic acid[a]	188–189	182–183[b]	Coumarin	69.5–70	67–67.5[c]	4
o-Ethoxycinnamic acid	131–132	133–134[d]	Coumarin	69–70	67–67.5[c]	4
2,3-Dimethoxycinnamic acid[a]	182–183	180[e]	8-Methoxycoumarin	88–89	87–89[f]	3
2,3-Dimethoxycinnamoyl chloride	81–82	[g]	8-Methoxycoumarin	88–89	87–89[f]	6
2,4-Dimethoxycinnamic acid[a]	182–183	184[h]	7-Methoxycoumarin	114–115	114[i]	3
2,5-Dimethoxycinnamic acid	146–148	147[j]	6-Methoxycoumarin	102–103.5	103[k]	12
o-Methoxy-α-methylcinnamic acid[a]	92–94[l]	102,[h] 107[m]	3-Methylcoumarin	88–89	90[n]	80
o-Methoxy-α-methylcinnamoyl chloride	B.p. 120/0.2	[o]	3-Methylcoumarin	88–89	90[n]	95
o-Ethoxy-α-methylcinnamic acid	131–132	130–133[p]	3-Methylcoumarin	88–89	90[n]	28
o-Methoxy-α-ethylcinnamic acid	107–108	105[q]	3-Ethylcoumarin	72–73	72[r]	48
o-Ethoxy-α-ethylcinnamic acid	113.5–114	[s]	3-Ethylcoumarin	72–73	72[r]	30
o-Methoxy-α-cyanocinnamic acid	211–212	211–212[t]	No coumarin[u]			
o-Methoxy-α-cyanocinnamoyl chloride	128	[v]	No coumarin[w]			
2-Methoxy-5-chlorocinnamic acid	203–204	191[h]	6-Chlorocoumarin	161–162	161–162[x]	8
2-Methoxy-5-nitrocinnamic acid	226	238[y]	No coumarin[z]			
2-Methoxy-5-methylcinnamic acid	114–115	[aa]	6-Methylcoumarin	74–76	73–74[bb]	9

[a] Obtained from Aldrich Chemical Co. [b] W. H. Perkin, *J. Chem. Soc.*, **31**, 414 (1866). [c] W. H. Perkin, *J. Chem. Soc.*, **21**, 56 (1856). [d] R. C. Gupta and K. C. Pandya, *J. Indian Chem. Soc.*, **25**, 148 (1948). [e] W. H. Perkin, Jr., and R. Robinson, *J. Chem. Soc.*, **105**, 2387 (1918). [f] M. Crawford and J. A. M. Shaw, *J. Chem. Soc.*, 3435 (1953). [g] *Anal.* Calcd. for $C_{11}H_{11}O_3Cl$: C, 58.29; H, 4.89. Found: C, 58.60; H, 4.99. [h] D. Chakravarti and B. Majumdar, *J. Indian Chem. Soc.*, **16**, 389 (1939). [i] F. Tiemann and C. L. Reimer, *Ber.*, **12**, 996 (1879). [j] H. Kauffman and K. Burr, *Ber.*, **40**, 2355 (1907). [k] F. Tiemann and W. H. M. Muller, *Ber.*, **14**, 1996 (1881). [l] All attempts to raise this m.p. by recrystallization of a commercial[a] or synthetic sample failed. [m] W. H. Perkin, *J. Chem. Soc.*, **39**, 429, 432 (1874). [n] W. H. Perkin, *J. Chem. Soc.*, **28**, 12 (1863). [o] Impossible to obtain completely free of traces of 3-methylcoumarin which formed during distillation. [p] G. Werner, *Ber.*, **28**, 2001 (1895). [q] W. H. Perkin, *J. Chem. Soc.*, **39**, 447 (1874). [r] T. Nakabayashi, E. Hori, and N. Okamurs, *J. Pharm. Soc. Japan*, **74**, 250 (1954). [s] *Anal.* Calcd. for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.86; H, 7.28. [t] W. Baker and C. S. Howes, *J. Chem. Soc.*, 119 (1953). [u] The acid chloride was the only product isolated. [v] *Anal.* Calcd. for $C_{11}H_8NO_2Cl$: C, 59.56; H, 3.64. Found: C, 59.54; H, 3.45. [w] Acid chloride recovered with slight decomposition. [x] A. Clayton, *J. Chem. Soc.*, **93**, 2022 (1906). [y] A. Schnell, *Ber.*, **17**, 1383 (1884). [z] Only decomposition products were obtained. [aa] *Anal.* Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.73; H, 6.46. [bb] T. J. Thompson and R. H. Edee, *J. Am. Chem. Soc.*, **47**, 2556 (1925).

In all cases the identity of the coumarins were checked by melting points and infrared and ultraviolet spectra and in most cases by comparison with authentic samples.

EXPERIMENTAL[12]

Reagents. The cinnamic acids used were obtained commercially or were prepared by standard literature methods. Reagent grade thionyl chloride was used.

o-Methoxy-α-methylcinnamic acid with thionyl chloride. A mixture of 4.0 g. of *o*-methoxy-α-methylcinnamic acid and 3.1 ml. of thionyl chloride was refluxed for 0.5 hr. and the excess thionyl chloride removed *in vacuo*. Benzene was added and the mixture was concentrated again. Distillation of the residue gave a white solid, b.p. 170–172° (approx. 60 mm.). Several recrystallizations from benzene or ether gave a solid, m.p., and mixed m.p. with 3-methylcoumarin, 88–89°.

Anal. Calcd. for $C_{10}H_8O_2$: C, 74.98; H, 5.03. Found: C, 75.07; 75.11; H, 5.22, 5.24.

This reaction was repeated under identical conditions. Distillation of the residue gave a liquid, b.p. 126° (2 mm.). This liquid was heated at 170° for 20 min. to yield 3-methylcoumarin, m.p. and mixed m.p. 88–89°.

General reaction of cinnamic acids with thionyl chloride. The cinnamic acid and thionyl chloride (0.6 ml. per g. of acid) were refluxed at 90° in a 3/4″ × 3″ Pyrex tube equipped with a cold-finger condenser. After 45 min., the temperature was raised to 225–250° for a 15- to 20-min. period. The coumarin was collected from the cold finger and recrystallized from an appropriate solvent.

2,3-Dimethoxycinnamoyl chloride. A mixture of 5.0 g. of 2,3-dimethoxycinnamic acid and 3.0 ml. of thionyl chloride was refluxed for 45 min. and the excess thionyl chloride removed *in vacuo* by treatment with benzene. Distillation of the residue gave a solid (90%) b.p. 156° (1 mm.); m.p. 81–82°.

Anal. Calcd. for $C_{11}H_{11}O_3Cl$: C, 58.29; H, 4.89. Found: C, 58.60; H, 4.99.

Heating this solid in the apparatus described above (250°) gave 8-methoxycoumarin, m.p. 88–89°.

o-Methoxy-α-cyanocinnamoyl chloride. Reaction of *o*-methoxy-α-cyanocinnamic acid and thionyl chloride in the general procedure described above gave a 23% yield of solid, m.p. 128°.

Anal. Calcd. for $C_{11}H_8NO_2Cl$: C, 59.56; H, 3.64. Found: C, 59.54; H, 3.45.

Heating this solid at 260° for extended periods of time did not yield any 3-cyanocoumarin.

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(12) Microanalyses by Spang Microanalytical Laboratory, Ann Arbor, Mich., and Drs. Weiler and Strauss, Oxford, England.

Action of Methylmagnesium Iodide on Water

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In connection with an investigation of the reaction of water with carbonyl compounds,[1] we had