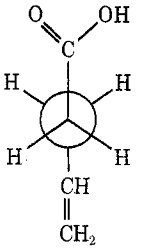
The values of the entropy of activation become more negative from the reaction of iodine with 2,2-diphenyl-4-pentenoic acid to the reaction of iodine with 4-pentenoic acid, while the values of the enthalpy of activation increase from the reaction of iodine with 4-pentenoic acid to the reaction of iodine with 2,2-diphenyl-4-pentenoic acid (Table III).

The formation of the complex between iodine and the acid probably occurs as a fast step in each of the systems studied.[12] The very high negative values of the entropy of activation indicate a high degree of order in the activated complex with respect to the reactants, which is as expected for a third-order electrophilic addition process.

The increase in the measured entropy of activation from the reaction of iodine with 2,2-diphenyl-4-pentenoic acid (−28 eu) to the reaction with 4-pentenoic acid (−59 eu) is at least partly explained by a conformation analysis of the acids. For the 4-pentenoic acid the more stable conformation should be the anti (I); for the 2-phenyl-4-pentenoic acid there are two stable conformations (IIa and IIb); for the 2,2-diphenyl-4-pentenoic acid there are three stable conformations (IIIa, IIIb, and IIIc). As the conformations IIb of the 2-phenyl-4-pentenoic acid, and IIIb and IIIc for the 2,2-diphenyl-4-pentenoic acid, are appropriate to the formation of the intermediate cyclic cations, there is an increase of the population of the appropriate conformation for the reaction from the 4-pentenoic acid to the 2,2-diphenyl-4-pentenoic acid.



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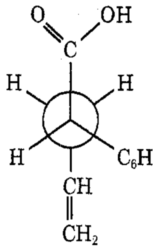
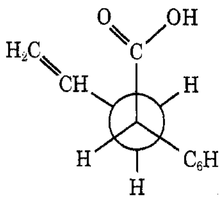
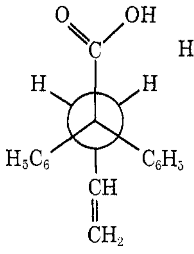


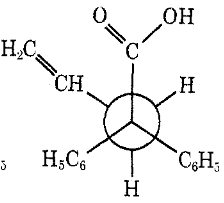
IIa



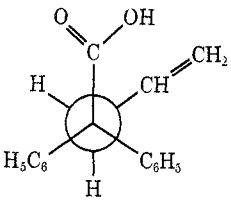
IIb



IIIa



IIIb



IIIc

The increasing values of the enthalpy of activation from 4-pentenoic acid to 2,2-diphenyl-4-pentenoic acid are consistent with the eclipsed conformation of the cyclic transition state, since repulsion between phenyl hydrogens and those β to the carbonyl group is expected to contribute to the energy of activation.

Registry No.—I, 591-80-0; II, 1575-70-8; III, 6966-03-6; iodine, 7553-56-2.

Acknowledgment.—The author is indebted to Dr. John M. Malin for helpful comments concerning this work.

Notes

Syntheses of Several 1,3-Thiazine Derivatives with Polyphosphate Ester

Masataka Yokoyama,* Yoshio Sawachi, and Toshiaki Isso

Department of Chemistry, Faculty of Science, Chiba University, Yayoi-cho, Chiba, Japan

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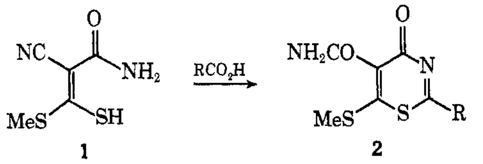
In previous work,[1] 3-alkylthio-2-cyano-3-mercaptoacrylamide (**1a**) and 3-alkylthio-2-cyano-3-mercaptothioacrylamide (**1b**) promised to be useful intermediates for synthesizing 4-keto-1,3-thiazine derivatives and 4-thioketo-1,3-thiazine derivatives, respectively.

It has been shown recently by Kanaoka and coworkers[2] that benzothiazoles can be obtained by condensation of *o*-mercaptoanilines and free carboxylic acids in the presence of polyphosphate ester (PPE). This suggested that a similar condensation of the mercaptoamides with acids and PPE might provide a good route to 1,3-thiazine derivatives.

Pursuing this possibility, we have found that reaction of the cyanoamide **1** with an aromatic acid and PPE in refluxing chloroform gives the 5-carbamoyl-6-methylthio-1,3-thiazin-4-ones (**2**) in 27–90% yield. The cyano thiazines could not be detected.



1 **2**

The structure **2** is consistent with analyses and spectral data. Mass spectral data for **2** show a P − 47 ion characteristic for the SCH_3 group.[3] The nmr spectrum (DMSO-d_6) of **2a** gives a singlet methyl signal at δ 2.65, a multiplet phenyl signal at 7.70, and a broad amino signal at 8.20, which disappears on deuterium exchange. Ir spectral data of **2a** show a very strong peak of the

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(1) (a) M. Yokoyama, *Bull. Chem. Soc. Jap.*, **44**, 1610 (1971); (b) M. Yokoyama, *J. Org. Chem.*, **36**, 2009 (1971).

(2) Y. Kanaoka, T. Hamada, and O. Yonemitsu, *Chem. Pharm. Bull.*, **18**, 587 (1970).

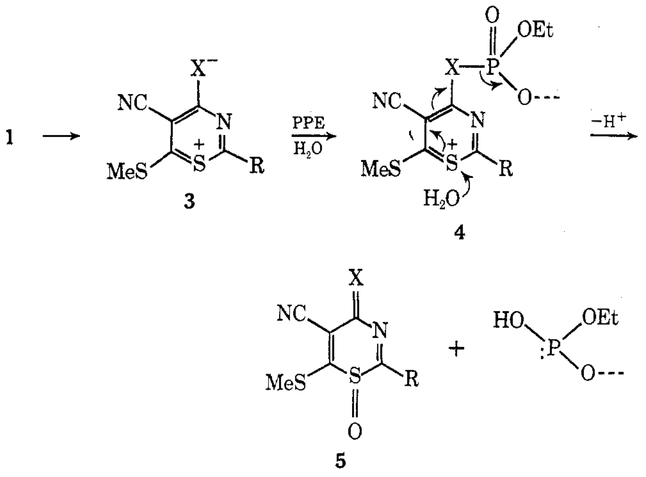
(3) Mass spectral data for 6-methylthio-2,3-dihydro-1,3-thiazin-4-one (thione) derivatives showed a P − 47 ion which was considered to be a fragment of the P − SCH_3 ion (see ref 1).

TABLE I

1	Carboxylic acid	Product	Time, min	Mp, °C	Yield, %
1a (X = O)	Benzoic acid	**2a**	60	222–223	90
	p-Hydroxybenzoic acid	**2b**	30	252–254	48
	p-Chlorobenzoic acid	**2c**	180	213–214	27
	β-Naphthoic acid	**2d**	60	211–212	67
	Furan-2-carboxylic acid	**2e**	180	279–280 dec	37
	Phenylacetic acid	**5f**	15	198–199	35
	Acetic acid	**5g**	30	195–196 dec	35
	Propionic acid	**5h**	60	155–156 dec	13
1b (X = S)	Benzoic acid	**5i**	10	232–233	53
	Furan-2-carboxylic acid	**5j**	20	134–135	56
	Acetic acid	**5k**	50	238–239	12

amide group and two characteristic peaks of the phenyl group at 1600 and 1510 cm^{-1}. The features of the uv spectrum of **2** are similar to those of 2-amino-6-methoxycarbonyl-1,3-thiazin-4-one and 2-acetylamino-6-methoxycarbonyl-1,3-thiazin-4-one.[4] These spectroscopic data show the presence of methylthio, carbamoyl, and phenyl groups. Their positions on the 1,3-thiazin-4-one ring are determined according to a possible cyclization reaction reported by Kanaoka, *et al.*[2]

In contrast to the reaction **1** → **2**, the reaction of **1** with aliphatic acids gave in low yields the 5-cyano-6-methylthio-1-oxo-1,3-thiazin-4-ones (**5**, X = O). These structures are supported by the appearance of an S=O stretching band at 1002–1010 cm^{-1} and a CN band at 2200–2230 cm^{-1}. The presence of an $SOCH_3$ group was ruled out by the absence of $P - SOCH_3$ and $SOCH_3$ ions (mass spectra).



Analogous 5-cyano-1-oxo products (**5**, X = S) were obtained from the thioamide (**1**, S replacing O) and either aromatic or aliphatic acids. These sulfoxides were obtained when the reaction were carried out in an inert atmosphere, suggesting that the S=O group arises by nucleophilic attack of water, resulting from the dehydration step, on the intermediate (**3**). The competition between attack of water on sulfur (**4**) or at the cyano group of **3** to give **2** appears to depend on both the group X and the electronic nature of R.

The thiazinium structure (**3**) makes a more important contribution with X = S because of poor 2p-3pπ overlap, and the reaction **4** → **5** is favored. When X = O, reaction **3** → **4** is important only when R is an electron-releasing group such as alkyl. When R is an electron-attracting group such as aryl, which cannot stabilize the thiazinium structure (**3**), hydration of the cyano thiazine intermediate occurred to give **2** instead of the reaction **3** → **4**.

Our attempt to isolate the cyano thiazine intermediate from the reaction mixture failed. Hydration of the cyano thiazine intermediate in the formation of **2** presumably involves coordination of PPE at the cyano group and attack of water to the nitrilium center instead of at sulfur. The 1-oxo-5-cyano compounds (**5**) were unaffected by heating with PPE in chloroform, but hydration to the amide occurred on heating in polyphosphoric acid.

Table I summarizes the results obtained by this method. The reaction rate for the formation of **5** generally exceeded the rate for **2**. In this experiment, two reactions to give **2** and **5** did not occur simultaneously.

Experimental Section[5]

Compounds **1a** and **1b** were prepared by our method.[1a,6] PPE was prepared by refluxing a mixture of 150 g of phosphorus pentoxide, 150 ml of diethyl ether, and 300 ml of chloroform until the solution was clear.[7] All other carboxylic acids, pure grade of Wako Chemicals, were used without further purification.

Preparation of 5-Carbamoyl-6-methylthio-2-phenyl-1,3-thiazin-4-one (2a).—A mixture of **1a** (3.5 g, 20 mmol), benzoic acid (2.5 g, 20 mmol), PPE (12 g), and chloroform (80 ml) was refluxed for 60 min. After evaporation of the solvent *in vacuo*, the red oily residue was treated with ice-water and neutralized with $NaHCO_3$. The red oil which was separated from the solution was crystallized from acetic acid–H_2O. The resulting orange powder (5 g) was recrystallized twice from acetic acid to give orange plates. Compounds **2b–5k** were prepared in the same method as mentioned above. Compounds **2** were generally isolated as yellow plates or needles and **5** as an orange powder.

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[4] E. Winterfeldt and J. M. Nelke, *Chem. Ber.*, **100**, 3671 (1967).

[5] Elemental analyses, uv, ir, nmr, and mass spectral data of compounds synthesized by this method will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-73-802. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

[6] T. Takeshima, M. Yokoyama, N. Fukada, and M. Akano, *J. Org. Chem.*, **35**, 2438 (1970).

[7] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 892.

In this reaction, the refluxing was allowed to continue until red oil appeared on the reaction mixture (the reaction had been completed at this point). Compound **5i** was synthesized by refluxing **1b** and benzoic acid in the dehydrated chloroform under nitrogen which was deoxygenated by using alkali pyrogallol and by crystallization of the resulting red oil with the absolute alcohol. Compound **2a** was also prepared in the same method as above. By employing the mild reaction conditions such as decreasing the amount of PPE, shortening the refluxing time, and increasing the amount of chloroform solvent, a small amount of **2** or **5** was collected together with the unreacted compound **1**, and the expected cyano thiazine derivatives could not be detected.

Nitrile Hydrolysis of 5-Cyano-6-methylthio-2-phenyl-1-oxo-1,3-thiazine-4-thione (5i).—A mixture of **5i** (1 g, 3.5 mmol) and polyphosphoric acid (PPA, 61 g) was heated at 80° for 3 hr. The reaction mixture was cooled and decomposed by adding ice–water (*ca.* 200 ml) and neutralized with KOH. The resulting brown crystals (0.8 g) were recrystallized from acetic acid to give brown plates: mp 223–224°; ir (KBr) 3440, 3400 (NH_2), 2920 (CH_3), 1640 (CO), 1580 (benzene ring), 1533 (hetero ring), 1444, 1415 (CH_3), 1119 (CS), 1002 cm^{-1} (SO); uv $\lambda_{max}^{99\% EtOH}$ 225 nm (log ϵ 4.14), 268 (4.29), 329 (3.78), 370 (4.48).

Anal. Calcd. for $C_{12}H_{10}N_2S_3O_2$: C, 46.43; H, 3.25; N, 9.03; mol wt, 310.42. Found: C, 46.51; H, 3.18; N, 8.98; mol wt, 310 (mass spectrum).

Registry No.—**1a**, 37614-61-2; **1b**, 29082-78-8; **2a**, 37614-62-3; **2b**, 37614-63-4; **2c**, 37614-64-5; **2d**, 37614-65-6; **2e**, 37614-66-7; **5f**, 37614-67-8; **5g**, 37614-68-9; **5h**, 37614-69-0; **5i**, 37614-70-3; **5j**, 37614-71-4; **5k**, 37614-72-5; benzoic acid, 65-85-0; *p*-hydroxybenzoic acid, 99-96-7; *p*-chlorobenzoic acid, 74-11-3; *β*-naphthoic acid, 93-09-4; furan-2-carboxylic acid, 88-14-2; phenylacetic acid, 103-82-2; acetic acid, 64-19-7; propionic acid, 79-09-4.

Transmission of Electronic Effects through the Cyclopropane Ring in Some Arylcyclopropanes

G. Montaudo and C. G. Overberger*

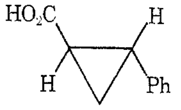
Department of Chemistry and the Macromolecular Research Center, University of Michigan, Ann Arbor, Michigan 48104

Received July 6, 1972

The possibility of electronic interaction between the cyclopropane ring and unsaturated groups has been of interest to several workers.[1–5] Some theoretical predictions[1] of Walsh for special geometric requirements for such interactions were tested[6] through the study of the ultraviolet spectra of a series of rigid arylcyclopropanes, but it was concluded that the steric relationship between a cyclopropane and benzene ring is of little consequence on the ultraviolet spectra.[6]

However, nmr evidence has been presented[7] showing that a conformation with the phenyl ring bisecting the three-membered ring is preferred in phenylcyclopropane. These results seem to imply that ultraviolet spectra are not sensitive to the relatively small conjugative effects in arylcyclopropanes.

This conclusion received indirect support by the recent report[8] that the ultraviolet and circular dichroism (CD) spectra of compounds I and II are very similar. In fact, this evidence was interpreted[8] as



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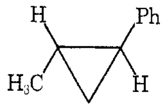
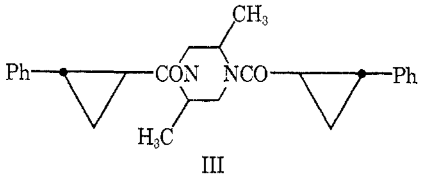


II

indicating that the carboxyl chromophore did not contribute significantly to the absorption, the latter being attributed exclusively to the benzene chromophore.

We report here additional evidence on the uv and CD spectra of compound I, which indicates some electronic interaction between the benzene and carboxyl chromophores in this molecule. This result suggests some transmission of electronic effects through the cyclopropane ring in arylcyclopropanes. These effects are also present in the diamide III, derived from the acid I.

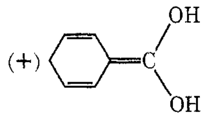


III

Results and Discussion

Relevant data on the uv, ORD, and CD spectra of compound I in tetramethylenesulfone (TMS) and methanesulfonic acid (MSA) are reported in Table I. The CD spectrum in TMS shows the typical vibrational structure of the ^1L_b benzene band in the 250–275-mμ region as well as a peak of higher intensity at 225 mμ which has been assigned[8] to the ^1L_a benzene transition. Although the TMS curve shows essentially the same features of the methanol spectrum previously reported,[8] a red shift is observed (Table I) in the MSA spectrum, with regard to the 225-mμ band.

This suggests that the 225-mμ band reflects an electronic interaction between the ^1L_a benzene transition and the carboxyl group, *via* the cyclopropane ring. In fact, red shifts of uv bands are known[9] to occur in aromatic carboxylic acids by addition of strong acids capable of protonating the carboxyl group, generating quinoid species such as IV absorbing at lower energy.[9]



IV

If the band at 225 mμ was entirely due to the ^1L_a benzene transition, it should not be drastically affected by the MSA addition. We have ascertained that phenylacetic acid shows a moderate blue shift in the corresponding uv absorption band in going from TMS (210 mμ) to MSA (204 mμ). However, the 280-mμ absorption of *trans*-cinnamic acid in TMS is shifted to about 325 mμ in MSA.

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[1] A. D. Walsh, *Trans. Faraday Soc.*, **45**, 179 (1949).

[2] L. S. Bartell, B. L. Carroll, and J. P. Guillory, *Tetrahedron Lett.*, 705 (1964); L. S. Bartell and J. P. Guillory, *J. Chem. Phys.*, **43**, 647 (1965).

[3] G. J. Karabatsos and N. Hsi, *J. Amer. Chem. Soc.*, **87**, 2864 (1965).

[4] R. Hoffmann, *Tetrahedron Lett.*, 3819 (1965), and references cited therein.

[5] M. Pelissier, A. Serafini, J. Devanneaux, J. F. Labarre, and J.-F. Tocanne, *Tetrahedron*, **27**, 3271 (1971), and references cited therein.

[6] A. L. Goodman and R. H. Eastman, *J. Amer. Chem. Soc.*, **86**, 908 (1964).

[7] G. L. Closs and R. A. Moss, *ibid.*, **86**, 4042 (1964); G. L. Closs and H. B. Klinger, *ibid.*, **87**, 3265 (1965).

[8] L. Verbit and Y. Inouye, *ibid.*, **89**, 5717 (1967).

[9] R. Stewart and K. Yates, *ibid.*, **82**, 4059 (1960).