Reactions of Salicylaldehyde with Some Conjugated Olefins

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Some condensation reactions of salicylaldehyde with various conjugated olefins, **1a, 1b, 1c, 2a, 2b, 2c,** and **3**, were studied. In the condensations with **1a, 1b,** and **1c** gave 2,2-dimethyl-2*H*-chromene derivatives *via* "3-2 cyclization", while the condensations with **2a, 2b, 2c,** and **3** gave 2-methyl-2*H*-chromen-2-yl)acetic acid derivatives *via* "3-4 cyclization".

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In our previous paper [1], the condensation of salicylaldehyde with ethyl 3-methyl-2-butenoate **1a** gave 2,2-dimethyl-2*H*-chromene **4**, ethyl 2,2-dimethyl-2H-chromen-3-carboxylate **5a**, and 3-isopropenycoumarin **6** in 35%, 1%, and 3%, respectively. In this reaction, chromene derivatives **4** and **5a** were probably derived from double nucleophilic attacks. One is an attack of the phenoxide ion to the C=C double bond, and the other is an attack of the resulting α carbanion to the C=O double bond of the aldehyde, and now we call this "3-2 cyclization". Coumarin **6** might be derived from another type of double nucleophilic attacks. One is an attack of the phenoxide ion to the C=O double bond of the ester, and the other is an attack of a carbanion formed deprotonation of the γ proton, and so we call this "1-2 cyclization". In this paper, similar condensations of salicylaldehyde with olefins having another electron-withdrawing group such as 3-methyl-2-butenonitrile **1b** or 4-methyl-3-penten-2-one **1c** and with olefins having one more electron-withdrawing group such as diethyl isopropylidenemalonate **2a**, ethyl 2-cyanol-3-methyl-2-butenoate **2b**, 2-acetyl-3-methyl-2-butenoate **2c**, or diethyl cyclohexylidenemalonate **3** will be compared.

The condensations were carried out under the similar conditions (stirring with potassium carbonate in DMF at 130° for 8 hours) and the results are summarized in Table 1. The condensations with **1b, 1c, 2b, 2c** mainly gave polymerized products and showed low yields. So, these were also carried out at 80° to prevent the polymerization, but this resulted in recovery of the starting materials. The condensation with olefins having two electron-withdrawing groups **2a, 2b, 2c and 3** mainly gave (2-methyl-2*H*-chromen-2-yl)acetyl derivatives **7a, 7b, 7c** and **10** as cyclized products. These were probably formed by another double nucleophilic attack, one is the attack of γ carbanion on the C=O double bond of the aldehyde and the other is the attack of the phenoxide ion on the C=C double bond, thus now we call this "4-3 cyclization". Thus the "3-2 cyclization", observed in **1a, 1b, 1c** was converted to the "4-3 cyclization" in **2a, 2b, 2c** or **3**. The existence of two electron-withdrawing groups increased the acidity of γ proton and the easily formed γ carbanion caused "4-3 cyclizations". The condensation with **3** also gave 3-(1-cyclohexenyl)coumarin **12**, which was probably derived from "1-2 cyclization".

The pmr spectra of these chromenes were summarized in Table 3. Two protons of the methylene group were observed as non-equivalent AB signals in **7a**, but observed as equivalent A_2 signals in **7b** and **7c**. It indicated that the ethoxycarbonyl group might be too bulky to rotate freely, but the cyano, and the acetyl groups might be small enough to rotate freely.

Table 1

Condensations of Salicylaldehyde with Conjugated Olefins

Conjugated Olefin	Reaction Temperature	Chromene "3-2 Cycl"	Chromene "4-3 Cycl"	Coumarin "1-2 Cycl"	Non-Cyclized Products
1a	130°	**4** (35%) **5a** (1%)		**6** (3%)	
1b	130°	**5b** (14%)			**8b** (8%) **9b** (3%)
	80°	**5b** (3%)			
1c	130°	**5c** (5%)	**7c** (1%)		
	80°	**5c** (3%)			**8c** (4%)
2a	130°		**7a** (35%)		**8a** + **9a** (2:1) (16%) **8a'** (9%) **9a'** (3%)
2b	130°		**7b** (4%)		**8b** (17%)
2c	130°		**7a** (2%) **7c** (8%)		**8a** (2%) **8c** + **9c** (3:1) (10%)
3	130°		**10** (6%)	**11** (2%)	**12** (10%)

Table 2

Some Physical Data and Elemental Analyses of New Compounds

Compound	Melting Point	IR (cm^{-1})	Mass M+ (m/z)	Elemental Analysis Found C (%)	Found H(%)	Found N(%)	Calcd. C (%)	Calcd. H(%)	Calcd. N(%)	
5b	147-151 (17 mmHg) [a]	2210	185	77.80	5.93	7.77	77.81	5.99	7.56	for $C_{12}H_{11}NO$
5c	128-147 (16 mm Hg) [a]	1660	202	77.15	7.08		77.20	6.98		for $C_{13}H_{14}O_2$
7a	139-142 (3 mm Hg) [a]	1730	232	72.44	7.07		72.39	6.94		for $C_{14}H_{16}O_3$
7b	183-185 (4 mm Hg) [a]	2250	185	77.55	5.76	7.44	77.81	5.99	7.56	for $C_{12}H_{11}NO$
7c	---------- [b]	1710	202	77.12	7.05		77.20	6.98		for $C_{13}H_{14}O_2$
8a	65-67	1670	232	72.62	6.92		72.36	6.94		for $C_{14}H_{16}O_3$
8a'	225-226 subl.	1640	204	70.57	5.67		70.57	5.92		for $C_{12}H_{12}O_3$
9a'	190-192 subl.	1675	204	70.68	5.97		70.57	5.92		for $C_{12}H_{12}O_3$
8b	141-143	2210	185	77.98	5.93	7.40	77.81	5.99	7.56	for $C_{12}H_{11}NO$
9b	115-117	2210	185	77.85	6.12	7.53	77.81	5.99	7.56	for $C_{12}H_{11}NO$
8c	142-143	1620	202	76.84	6.64		77.20	6.98		for $C_{13}H_{14}O_2$
10	180-194 (4 mm Hg) [a]	1720	262	75.13	7.48		74.97	7.40		for $C_{17}H_{20}O_3$
11	145-146.5	1695	226	79.33	6.37		79.62	6.24		for $C_{15}H_{14}O_3$
12	102.5-103.,5	1685	272	74.95	7.66		74.97	7.40		for $C_{17}H_{20}O_3$

[a] Boiling point. [b] Oil with no chance to measure the boiling point.

Table 3

PMR Spectral Data of New Chromenes, δ/ppm (J/Hz)

Compound	2-Me	2-CH_2	3-H	4-H	Ar-H	Others
5b	1.5 (s)	------	-------	[a]	6.7-7.3 (m)	
5c	1.5 (s)	------	------	[a]	6.5-7.3 (m)	2.3 (s)
7a	1.5 (s)	2.6 (d, 15) 2.7 (d, 15)	5.7 (d, 10)	6.3 (d, 10)	6.5-7.3 (m)	1.2 (t, 7) 4.1 (q, 7)
7b	1.6 (s)	2.6 (s)	5.6 (d, 10)	6.4 (d, 10)	6.7-7.3 (m)	
7c	1.5 (s)	2.6 (s)	5.7 (d, 10)	6.4 (d, 10)	6.6-7.2 (m)	2.1 (s)
10	1.6 (m)	2.4 (d, 13) 2.9 (d, 13)	2.3 (m)	6.1 (br s)	6.5-7.6 (m)	1.1 (t, 7) 3.8 (two q, 7) 1.6 (m)

[a] signals are hidden under the aromatic signals.

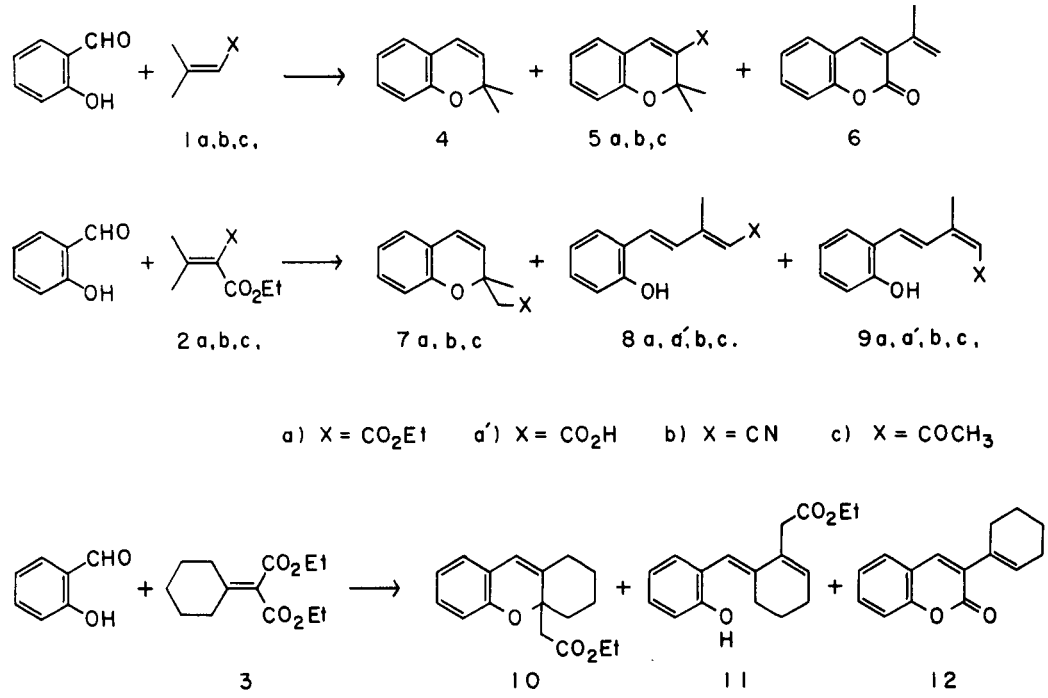
Table 4

PMR Spectral Data of Non-cyclized Products, δ/ppm (J/Hz)

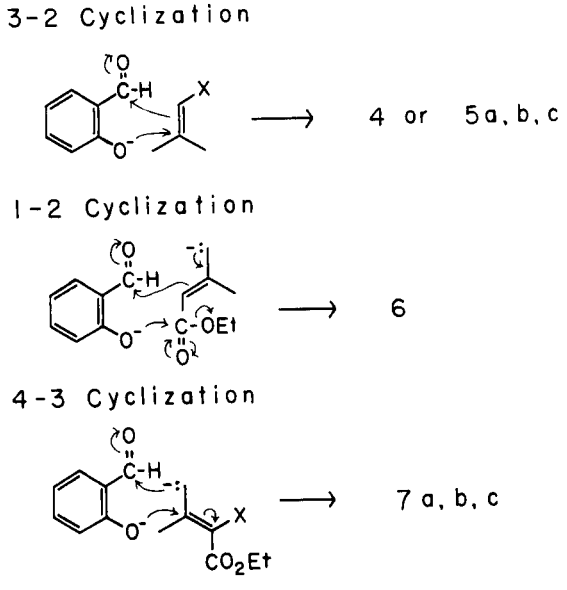
Compound	Solvent	α-H	β-Me	γ-H	δ-H	Ar-H	Others
8a	CCl_4	5.8 (s)	2.4 (s)	6.8 (s)		6.5-7.5 (m)	1.3 (t, 7) 4.2 (q, 7)
8a'	DMSO-d_6	5.9 (s)	2.3 (s)	6.8 (s)		6.7-7.6 (m)	9.8 (br s) 11.9 (br s)
9a [a]	CCl_4	5.6 (s)	2.1 (s)	8.3 (d, 16)	7.3 (d, 16)	6.7-7.7 (m)	1.2 (t, 7) 4.2 (q, 7)
9a'	DMSO-d_6	5.7 (s)	2.1 (s)	8.3 (d, 16)	7.3 (d, 16)	6.7-7.7 (m)	9.8 (br s) 12.0 (br s)
8b	acetone-d_6	5.5 (s)	2.3 (s)	6.9 (s)		6.7-7.6 (m)	
8c [a]	$CDCl_3$	6.3 (s)	2.4 (s)	[b]	[b]	6.7-7.7 (m)	2.3 (s)
9c [a]	$CDCl_3$	6.1 (s)	2.1 (s)	8.3 (d, 16)	[b]	6.7-7.7(m)	2.3 (s)

[a] Data obtained from a sample mixture. [b] Signals are hidden under the aromatic signals.

As shown in Table 1, some condensations gave non-cyclized products **8a**, **8b**, **8c**, **9a**, **9b**, **9c**, and **12**. In the condensation with **2a**, the esters **8a** and **9a** were obtained as a mixture, and the acids **8a'** and **9a'** were also obtained as a mixture and isolated after recrystallizations. Pure ester **8a** was derived from pure acid **8a'** by treating the silver salt of **8a'** with iodoethane without any isomerization. The ratio of **8a** and **9a** was determined by the ratio of the pmr signals. Wiley *et al.* [2] already reported the pmr spectra of the 3-methyl-5-phenylpenta-2,4-dienoic acids. They described that the carbonyl group deshielded the neibouring γ proton of the (2-*Z*) isomer and showed it was



observed at lower field (8.42 ppm). The γ protons also were observed around 8.3 ppm in our (2-*Z*) isomers, and those in our (2-*Z*) isomers were observed around 6.8 ppm. So, in the pmr spectra, the (2-*Z*) isomers exhibited δ and γ protons as two non-equivalent doublet signals at 7.3 and 8.3 ppm, while the (2-*E*) isomers had equivalent signals at about 6.8 ppm. These data are summarized in Table 4. The conversion of non-cyclized **8b** to cyclized chromene **7b** was effected by uv irradiation in acetonitrile.



EXPERIMENTAL

All melting points and boiling points are uncorrected. The ir spectra were taken on a Hitachi 260-50 spectrophotometer as liquid films or as potassium bromide disks. Mass spectra were recorded on a JEOL JMS-OISG-2 spectrometer. Some physical data and elemental analyses of the new compounds are summarized in Table 2. The pmr spectra were recorded on a JEOL PMX-60Si spectrometer, and the data of new chromenes and non-cyclized compounds are listed in Tables 3 and 4, respectively.

General Procedure for the Condensation of Salicylaldehyde with Conjugated Olefins **1b, 1c, 2a, 2b, 2c,** or **3**.

According to the procedure previously reported in our paper [1], a mixture of salicylaldehyde (*ca.* 10.0 mmoles), conjugated olefins **1b, 1c, 2a, 2b, 2c,** or **3** (*ca.* 10.0 mmoles), anhydrous potassium carbonate (4.0 g), and DMF (100 ml) was heated at 130° or 80° for 8 hours. After removing the solvent *in vacuo*, the mixture was diluted with water, acidified with 10% hydrochloric acid, and extracted with ether. The ether layer was washed with a 5% sodium hydroxide solution and a saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After removing the ether, the residual oil was chromatogramed on a silica-gel column. Oily cyclized chromenes **4, 5a, 5b, 5c, 7a, 7b, 7c,** or **10** were obtained as the fractions eluted by benzene. Crystalline non-cyclized **11** and coumarin **12** were also obtained as the fractions eluted by benzene and recrystallized from cyclohexane. These data are summarized in Tables 1-3. The alkaline washings were acidified with 10% hydrochloric acid and extracted with ether. After removing the ether, the crystalline residue was recrystallized to give pure acids **8a'** and **9a'** from ethyl acetate or pure nitriles **8b** and **9b** from benzene, and the oily residue was chromatographed on silica-gel to give a mixture of **8a** and **9a** as the fractions eluted with benzene, or **8a** and a mixture of **8c** and **9c** as the fractions eluted with hexane-ethyl acetate 3:1. Thus, the

geometrical isomers could not be isolated, and the ratios were determined from the pmr signals. The results are summarized in Table 1, and the data were listed in Tables 2 and 4.

Non-isomerized Conversion of **8b** to **7b**.

Pure (2*E*,4*E*)-acid **8a'** (123 mg, 0.603 mmole) was dissolved in 0.1*N* sodium hydroxide solution (6 ml) and diluted with distilled water (30 ml). To this solution was added a freshly prepared aqueous solution of silver nitrate (0.11 g, 0.64 mmole in 6 ml). The precipitate of silver salts was collected and washed well with distilled water, ethanol, and ether, and dried well under reduced pressure. A suspension of the silver salts in dry ether was treated with iodoethane (0.20 g, 1.3 mmoles) and refluxed for 70 hours. After removing silver iodide by filtration, the oily residue was obtained by evaporation and purified on a silica-gel column to give pure **8a** (38 mg, 27%).

Conversion of a Non-cyclized Nitrile **8b** to a Cyclized Nitrile **7b**.

A solution of **8b** (1.10 g, 5.95 mmoles) and benzil (1.34 g, 6.37 mmoles) (sensitizer) in acetonitrile (200 ml) was irradiated for 8 hours using an 100W high-pressure mercury lamp. After removing the solvent, the residue was chromatogramed to give **7b** (0.14 g, 12%) as the fractions eluted with chloroform. The starting material **8b** was recovered in 30% as the fractions eluted with benzene.

REFERENCES AND NOTES

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[2] R. H. Wiley, T. H. Crawford and C. E. Staples, *J. Org. Chem.*, **27**, 1535 (1962).