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Catalytic Action of Azolium Salts. VI.[1] Preparation of Benzoins and Acyloins by Condensation of Aldehydes Catalyzed by Azolium Salts

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Benzoins 4 (2-hydroxyethanones substituted with aryl groups at the 1- and 2-positions) were prepared by self-condensation of aromatic aldehydes 3 using catalytic amounts of azolium salts 1 and 2 in excellent yields.

1,3-Dimethylbenzimidazolium iodide (2) was an effective catalyst for the preparation of acyloins 6 (2-hydroxyethanones substituted with alkyl groups at the 1- and 2-positions) by self-condensation of aliphatic aldehydes 5. On the other hand, an attempt at the condensation of hexanal (5d) catalyzed by 1,3-dimethylimidazolium iodide (1) failed to yield the acyloin 6d, and instead the aldol-type condensed product 8d was obtained.

Keywords benzoin; acyloin; 1,3-dimethylbenzimidazolium iodide; 1,3-dimethylimidazolium iodide, aldehyde; self-condensation

In the previous paper, we reported that 1,3-dimethylimidazolium iodide (**1**) and 1,3-dimethylbenzimidazolium iodide (**2**) were effective catalysts for preparation of aroylheteroarenes.[2] An intermediate A, which is formed between an aromatic aldehyde **3** and the ylide, is a key intermediate in the aroylation system. The ylide is generated by expulsion of C^2-hydrogen of the azolium salt **1** or **2**. Moreover, the key intermediate A corresponds to the mandelonitrile anion A′, which is formed between aromatic aldehyde and cyanide ion.[3,4] Our study of the catalytic action of azolium salts led us to consider that the behavior of the azolium salts **1** and **2** or the azolium ylide is similar to that of hydrogen cyanide or cyanide ion.[2] We therefore wished to clarify the degree of similarity between the azolium ylide and cyanide ion.

Benzoins **4** (2-hydroxyethanones substituted with aryl groups at the 1- and 2-positions) are important starting materials in organic synthesis. Among several preparative methods of benzoins,[5] self-condensation of aromatic aldehydes **3** is an easy and simple procedure. Namely, two molecules of aromatic aldehyde **3** condense in the presence of a catalyst, resulting in the formation of benzoins **4**. It is well known that cyanide ion catalyzes the condensation.[5] Several other effective catalysts have been reported; for example, thiazolium salts,[6] imidazolium salts,[7] benzimidazolium salts,[7] and electron-rich olefins.[8] Although it was reported that imidazolium salts and benzimidazolium salts can be used as catalysts, no details were given.[7] In order to clarify the degree of similarity between cyanide ion and the azolium ylide, the catalytic action of the azolium salts **1** and **2** for the condensation was reexamined. In addition, we succeeded in preparing acyloins **6** by self-condensation of aliphatic aldehydes **5** in the presence of benzimidazolium salts **2**. In the present paper, we report the above results in detail.

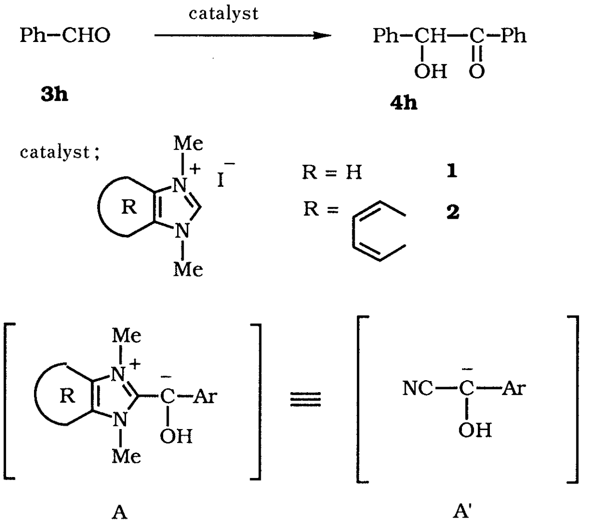

Chart 1

The self-condensation of benzaldehyde (**3h**) in the presence of the azolium salt **1** or **2** was carried out under various conditions. As shown in Table I, in the presence of strong bases, such as sodium hydride (NaH), sodium hydroxide (NaOH), and DBU (1,8-diazabicyclo[5.4.0]-7-undecene), benzoin (**4h**) was obtained in good yield by use of the azolium salt **2** as a catalyst. A similar result was observed in the condensation catalyzed by **1**. In the presence of NaH or NaOH, the condensation proceeded to give benzoin (**4h**) in good yield.

Preparation of various benzoins **4** by the self-con-

TABLE I. Self-Condensation on Benzaldehyde (**3h**) Catalyzed by Azolium Salt **1** or **2**

Solvent[a]	Catalyst	Base[b]	Benzoin (**4h**), yield (%)
THF	**1**	NaH	78
THF	**1**	DBU	7 (75)[c]
THF	**1**	TEA	— (97)[c]
THF	**2**	NaH	85
THF	**2**	DBU	82
THF	**2**	TEA	Trace (90)[c]
MeOH	**1**	NaOH	54
MeOH	**1**	DBU	— (85)[c]
MeOH	**1**	TEA	— (98)[c]
MeOH	**2**	NaOH	79
MeOH	**2**	DBU	68
MeOH	**2**	TEA	Trace (92)[c]

a) THF = tetrahydrofuran. *b*) DBU = 1,8-diazabicyclo[5.4.0]-7-undecene, TEA = triethylamine. *c*) Recovery of benzaldehyde (**3h**).

densation of aromatic aldehydes **3** catalyzed by the azolium salt **1** or **2** was examined. In the presence of the azolium salt **1** or **2**, the condensations of fluoro (**3c**), chloro (**3e**), bromo (**3g**), methyl (**3j**), and methoxy (**3k**) *para*-substituted benzaldehydes proceeded to give the corresponding benzoins **4** in good yields, as shown in Chart 2 and Table II. The condensation of *p*-nitrobenzaldehyde (**3l**) having a strong electron-accepting group and *p*-*N*,*N*-dimethylaminobenzaldehyde (**3n**) having a strong electron-donating group failed to proceed in a manner similar to that with cyanide ion.[4a] A similar result was observed in the reaction with *p*-cyanobenzaldehyde (**3m**). *p*-Cyanobenzoic acid and *p*-cyanobenzyl alcohol were formed in the reaction of **3m** catalyzed by **1** in MeOH. The products might be generated by Cannizzarro reaction. In the case of *ortho*-substituted benzaldehydes (**3a**, **3d**, **3i**), the condensation proceeded with difficulty in comparison with that of *para*-substituted benzaldehydes because of the steric hindrance, but the benzoins were obtained in low yields.

Next, the catalytic condensation was applied to aliphatic aldehydes **5**. In the presence of DBU, two molecules of hexanal (**5d**) condensed in the presence of a catalytic amount of **2** in refluxing dioxane to give the acyloin **6d**, whereas the reaction in the presence of **1** as a catalyst afforded **8d**, which was the aldol-type condensed product. In the presence of **2**, several acyloins **6** (2-hydroxyethanones having aliphatic groups at the 1- and 2-positions) were produced in good yields, as shown in Chart 3.

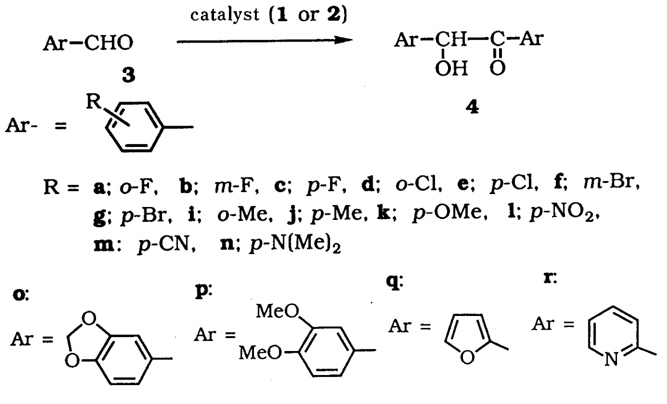

Chart 2

To our knowledge, among the catalysts which can be used for the benzoin condensation, only thiazolium salt catalyzes the formation of acyloins **6** by self-condensation of aldehydes.[9] In general, acyloins are prepared by condensation of esters with Na.[10] The discovery of a new catalyst or a new method for preparation of acyloins should be very useful in organic synthesis. The oxidation

Table II. Preparation of Benzoins **4** by Self-Condensation of Arenecarbaldehydes **3** Catalyzed by Azolium Salts **1** and **2**

Aldehyde	Catalyst	Reaction conditions		Benzoin	
		Time (h)	Method[a]		Yield (%)
3a	**2**	1	B	**4a**	37
3b	**2**	1	B	**4b**	99
3c	**2**	1	B	**4c**	67
3d	**1**	1	A	**4d**	43
3e	**1**	1	A	**4e**	67
3e	**2**	1	A	**4e**	87
3e	**2**	2	B	**4e**	99
3e	**2**	2	C	**4e**	82
3f	**1**	1	A	**4f**	80
3f	**2**	1	B	**4f**	82
3g	**2**	1	A	**4g**	75
3g	**2**	2	C	**4g**	76
3i	**1**	1	A	**4i**	38
3j	**2**	1	B	**4j**	94
3j	**2**	1	A	**4j**	78
3k	**1**	1	A	**4k**	81
3k	**2**	1	A	**4k**	90
3k	**2**	1.5	B	**4k**	71
3k	**2**	1.5	C	**4k**	95
3l	**2**	1	D	**4l**	—[b]
3m	**2**	2.5	D	**4m**	—[c]
3n	**2**	1	A	**4n**	—[d]
3o	**1**	2	A	**4o**	66
3o	**2**	1	A	**4o**	68
3o	**2**	2	C	**4o**	81
3p	**2**	2	C	**4p**	85
3q	**2**	1	B	**4q**	96
3r	**2**	0.15	D	**4r**	66
3r	**2**	1	E	**4r**	70

a) Method A: THF/NaH, Method B: THF/DBU, Method C: dioxane/DBU, Method D: MeOH/NaOH Method E: MeOH/TEA. *b*) Gave *p*-nitrobenzyl alcohol (11%) and *p*-nitrobenzoic acid (33%). *c*) Gave *p*-cyanobenzyl alcohol (21%) and *p*-cyanobenzoic acid (32%). *d*) Recovered starting **3n** (24%).

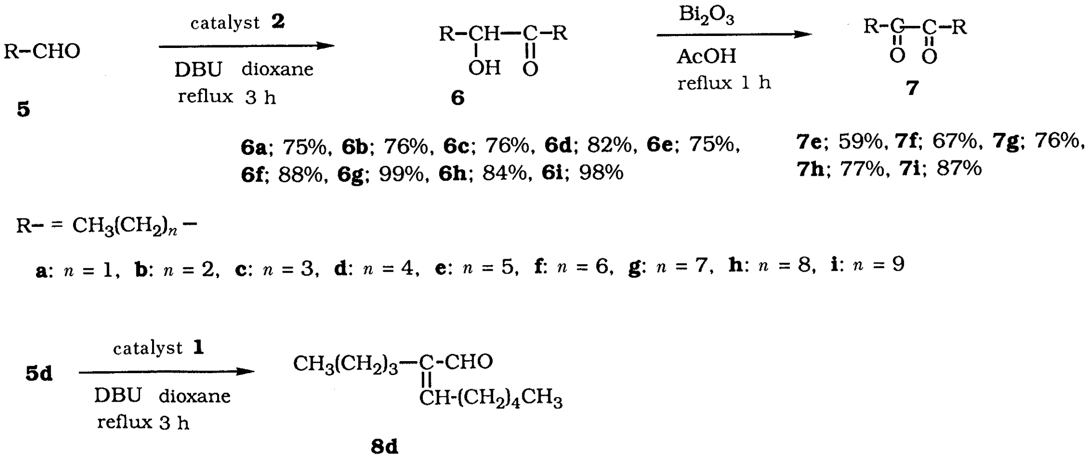

Chart 3

of the acyloins **6** with Bi_2O_3 led to the 1,2-diketones **7** in good yields.

By use of the azolium salts **1** and **2** as catalysts, a preparative method of benzoins **4** was established and several benzoins **4** were prepared in good yields. Moreover, acyloins **6** were produced by similar condensation of aliphatic aldehydes **5** catalyzed by **2** in the presence of DBU. The azolium salts **1** and **2** are useful and safe catalysts for the condensation of aldehydes in comparison with cyanide ion.

Experimental

All melting points are uncorrected. IR spectra were recorded on a JASCO A-102 diffraction grating IR spectrometer. ^1H-NMR spectra were measured at 60 MHz on a JEOL PMX60SI NMR spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard, and coupling constants (J) are given in hertz (Hz). Column chromatography was carried out on SiO_2.

Benzoin Condensation; General Procedure Methods A, B, and C: A solution of an aromatic aldehyde (**3**, 20 mmol) and an azolium salt (**1** or **2**, 1 mmol) in 50 ml of THF or dioxane was treated with base (2 mmol of NaH or 1 ml of DBU), and the mixture was refluxed, then cooled to room temperature and concentrated to dryness under reduced pressure. H_2O was added to the residue. The mixture was extracted with $CHCl_3$, and the extract was dried over Na_2SO_4 and concentrated. The residue was passed through a column of SiO_2 with benzene then $CHCl_3$. The fraction eluted with $CHCl_3$ gave the benzoins **4**.

Methods D and E: A solution of an aromatic aldehyde (**3**, 20 mmol) and an azolium salt (**1** or **2**, 1 mmol) in 50 ml of MeOH was treated with base (1 ml of 50% NaOH or 1 ml of TEA), and the mixture was refluxed. The reaction mixture was concentrated under reduced pressure and H_2O was added to the residue. The mixture was extracted with $CHCl_3$. Work-up as described above gave the benzoins **4**. The yields and reaction conditions are shown in Tables I and II.

2,2′-Difluorobenzoin (**4a**): Colorless needles from petroleum benzin, mp 60—62 °C. *Anal.* Calcd for $C_{14}H_{10}F_2O_2$: C, 67.74; H, 4.06. Found: C, 67.62; H, 4.42.

3,3′-Difluorobenzoin (**4b**): Colorless needles from petroleum benzin, mp 73—76 °C. *Anal.* Calcd for $C_{14}H_{10}F_2O_2$: C, 67.74; H, 4.06. Found: C, 67.69; H, 4.20.

4,4′-Difluorobenzoin (**4c**): Colorless prisms from petroleum benzin, mp 80—82 °C. *Anal.* Calcd for $C_{14}H_{10}F_2O_2$: C, 67.74; H, 4.06. Found: C, 67.79; H, 4.30. IR (KBr) cm^{-1}: 3400 (OH), 1680 (CO). ^1H-NMR ($CDCl_3$) δ: 6.70—7.95 (10H, m, aromatic H), 5.82 (1H, s, $C\underline{H}(OH)$), 4.80 (1H, s, OH).

4,4′-Dibromobenzoin (**4g**): Colorless needles from petroleum benzin, mp 94—96 °C. *Anal.* Calcd for $C_{14}H_{10}Br_2O_2$: C, 45.44; H, 2.72. Found: C, 45.81; H, 2.87. IR (KBr) cm^{-1}: 3400 (OH), 1670 (CO). ^1H-NMR ($CDCl_3$) δ: 7.00—7.80 (8H, m, aromatic H), 5.80 (1H, s, $C\underline{H}(OH)$), 4.50 (1H, s, OH).

The structures of the other benzoins **4d**, **4e**, **4f**, **4h**, **4i**, **4j**, **4k**, **4o**, **4p**, **4q**, and **4r** were confirmed by spectral data, and by comparison of the melting points with those of authentic samples reported in the literature.[5a)]

Reaction of Hexanal (5d) in the Presence of 1 A solution of hexanal (**5d**, 2000 mg, 20 mmol), 1,3-dimethylimidazolium iodide (**1**, 224 mg, 1 mmol), and DBU (2 ml) in 30 ml of dioxane was refluxed in an oil bath for 3 h. The reaction mixture was concentrated and H_2O was added to the residue. The mixture was extracted with $CHCl_3$, and the extract was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was distilled under reduced pressure to give **8d** in quantitative yield (1980 mg).

8d: Colorless oil, bp 130—140 °C (20 mmHg). IR (liquid) cm^{-1}: 1680 (CO), 1620 (C=C). ^1H-NMR ($CDCl_3$) δ: 9.35 (1H, s, CHO), 6.45 (1H, t, J=6 Hz, $=C\underline{H}-CH_2$), 0.70—2.60 (20H, aliphatic H).

Preparation of Acyloins; General Procedure DBU (1 ml) was added to a solution of an aliphatic aldehyde (**5**, 20 mmol) and 1,3-dimethylbenzimidazolium iodide (**2**, 274 mg, 1 mmol) in dioxane (30 ml), and the mixture was refluxed for 3 h. The reaction mixture was concentrated under reduced pressure and H_2O was added to the residue. The mixture was extracted with $CHCl_3$, and the extract was dried over Na_2SO_4 and concentrated. The residue was distilled under reduced pressure to give the acyloins **6**.

The structures of the acyloins **6a**—**i** were confirmed by spectral data, and by comparison of the melting points or boiling points with those of authentic samples reported in the literature.[10)]

Oxidation of Acyloins with Bi_2O_3; General Procedure A mixture of acyloin (**6**, 3 mmol) and Bi_2O_3 (6 mmol) in acetic acid (20 ml) was refluxed for 1 h.[9b),11)] The reaction mixture was poured into ice-H_2O and the insoluble solid was removed by filtration. The solid was washed with $CHCl_3$, then the filtrate and washings were combined and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was passed through a short column of SiO_2 with $CHCl_3$ to give 1,2-dialkylated ethanedione **7**.

7,8-Tetradecanedione (**7e**): Slightly yellow scales from MeOH, mp 39—40 °C. *Anal.* Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 73.62; H, 11.52. IR (KBr) cm^{-1}: 1703 (CO). ^1H-NMR ($CDCl_3$) δ: 2.70 (t, J=6 Hz, $COC\underline{H}_2$), 0.50—1.80 (m, aliphatic H).

8,9-Hexadecanedione (**7f**): Slightly yellow scales from MeOH, mp 48—50 °C. *Anal.* Calcd for $C_{16}H_{30}O_2$: C, 75.54; H, 11.89. Found: C, 75.07; H, 11.96. IR (KBr) cm^{-1}: 1703 (CO). ^1H-NMR ($CDCl_3$) δ: 2.68 (*t*, J=6 Hz, $COCH_2$), 0.50—2.00 (m, aliphatic H).

9,10-Octadecanedione (**7g**): Pale yellow scales from MeOH, mp 56—58 °C. *Anal.* Calcd for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.06; H, 12.21. IR (KBr) cm^{-1}: 1702 (CO). ^1H-NMR ($CDCl_3$) δ: 2.70 (t, J=6 Hz, $COCH_2$), 0.65—1.70 (m, aliphatic H).

10,11-Icosanedione (**7h**): Pale yellow scales from MeOH, mp 57—59 °C. *Anal.* Calcd for $C_{20}H_{38}O_2$: C, 77.36; H, 12.34. Found: C, 77.09; H, 12.30. IR (KBr) cm^{-1}: 1702 (CO). ^1H-NMR ($CDCl_3$) δ: 2.71 (t, J=6 Hz, $COC\underline{H}_2$), 0.80—1.75 (m, aliphatic H).

11,12-Docosanedione (**7i**): Pale yellow scales from MeOH, mp 63—65 °C. *Anal.* Calcd for $C_{22}H_{42}O_2$: C, 78.05; H, 12.50. Found: C, 77.64; H, 12.57. IR (KBr) cm^{-1}: 1703 (CO). ^1H-NMR ($CDCl_3$) δ: 2.70 (t, J=6 Hz, $COCH_2$), 0.70—1.70 (m, aliphatic H).

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