The Acid-Catalyzed Rearrangement of 1-*N*-Allylindolines

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Zinc chloride-catalyzed rearrangement of 1-*N*-allylindoline and 1-*N*-(2-methylallyl)indoline proceeds readily in refluxing xylene to give 7-allylindoline and 7-(2-methylallyl)indoline in 73% and 86% yields, respectively. The reaction of 1-*N*-2-butenylindoline and zinc chloride give rise to the mixture of 7-(1-methylallyl)indoline, 7-(*cis*- and *trans*-1-methyl-1-propenyl)indoline, and 7-(*trans*-2-butenyl)indoline. On the other hand, the similar reaction of 1-*N*-(3-methyl-2-butenyl)indoline with zinc chloride led to the formation of a mixture of 1,2,5,6-tetrahydro-4,4-dimethyl-4*H*-pyrrolo[3,2,1-*ij*]quinoline and 7-(3-methyl-2-butenyl)indoline.

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Claisen rearrangements are of importance in view of synthetic and mechanistic aspects and have been utilized for various synthetic design. However, amino Claisen rearrangements are considerably less facile than those of their oxygen counterparts [1]. On the other hand, because of the very potent and diverse biological activity exhibited by various indole derivatives, this heterocyclic system has attracted considerable attention in chemistry, biology, and medicine, and by a variety of routes, some indole derivatives have been prepared from indolines [2]. Previously, the pyrolysis and acid-catalyzed rearrangement of 1-allylindoles have been reported by Patterson *et al.* [3] and Inada *et al.* [4], respectively. To our knowledge, a Claisen rearrangement of 1-*N*-allylindolines (**1**) has not been reported. Herein, we wish to report the acid-catalyzed rearrangement of **1** in connection with our interest in the synthesis of 7-alkylindoles. The experimental results for the rearrangement of **1** are summarized in Table 1.

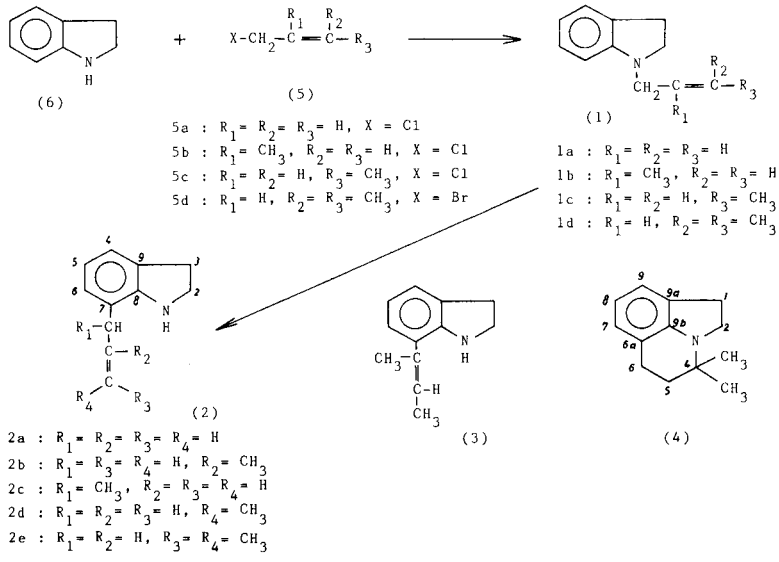
In the present work, it was found that a refluxing mixture of 1-*N*-allylindoline (**1a**) and zinc chloride in xylene gave rise to 7-allylindoline (**2a**) (entry 1-4). The rearrangement of **1a** in the presence of an equivalent of zinc chloride gives **2a** in only 23% yield (entry 1), however, in the presence of 3 or 4 equivalents of zinc chloride, **2a** was obtained in 86% yield (entry 3 and 4). In the presence of a Lewis acids such as aluminum chloride or boron trifluoride etherate in benzene, the reaction does not take place (entry 5 and 6).

Table 1
The Zinc Chloride Rearrangement of 1-*N*-Allylindolines **1**

Entry	1-*N*-Allylindolines **1**	$ZnCl_2$/ **1** mol ratio	Product (yield)
1	**1a**	1.15	**2a** (23%)
2	**1a**	2.30	**2a** (37%)
3	**1a**	3.0	**2a** (73%)
4	**1a**	4.0	**2a** (74%)
5	**1a**	$AlCl_3$	------
6	**1a**	BF_3•OEt_2	------
7	**1b**	3.0	**2b** (86%)
8	**1c**	3.0	**2c** (45%) **3** (15%) **2d** (8%)
9	**1d**	3.0	**4** (26%) **2e** (22%)

Furthermore, under the similar conditions, the zinc chloride catalyzed reaction of 1-*N*-(2-methylallyl)indoline

Scheme 1



(**1b**) produced only a [3,3]-sigmatropic product, 7-(2-methylallyl)indoline (**2b**) (entry 7). When 1-*N*-(*cis*- and *trans*-2-butenyl)indoline (**1c**) and zinc chloride were heated at 140° in xylene, 7-(1-methylallyl)indoline (**2c**) and 7-(1-methyl-1-propenyl)indoline (**3**), accompanied by a small amount of 7-(*trans*-2-butenyl)indoline (**2d**) which arose by arrangement without inversion of the allyl group, apparently by a cleavage process (entry 8). Compound **3** was probably derived from double bond isomerization of the initial [3,3]-sigmatropic product **2b**.

On the other hand, under similar conditions, the zinc chloride catalyzed rearrangement of 1-*N*-(3-methyl-2-butenyl)indoline (**1d**) proceed slowly to from a mixture of 1,2,5,6-tetrahydro-4,4-dimethyl-4*H*-pyrrolo[3,2,1-*ij*]quinoline (**4**) and 7-(3-methyl-2-butenyl)indoline (**2e**) (entry 9). In the reaction, compound **1d** apparently rearranged to **2e** without inversion of the allyl group, and compound **4** probably arose from **2e** by an acid-catalyzed cyclization.

EXPERIMENTAL

Infrared spectra were obtained on a Hitachi 260-10 spectrometer. The ^{1}H and ^{13}C nmr spectra were recorded on a Hitachi R-90H instrument. Chemical shifts are in ppm (δ) relative to tetramethylsilane as the internal standard. Electron impact mass spectra were recorded on a Hitachi RMU-6M mass spectrometer.

General Procedure for The Preparation of 1-*N*-Allylindolines **1**.

Under a nitrogen atmosphere, 0.24 mole of allyl halide **5** was added dropwise to indoline (**6**) (25 g, 0.21 mole) at 0-5°, and an additional 4 hour heating period at 60° followed. The reaction mixture was cooled to room temperature, quenched by addition of 200 ml of 5% sodium hydroxide solution, and then diluted with benzene (300 ml). The benzene layers were washed with brine and dried over anhydrous magnesium sulfate. After removal of the solvents, the reaction product **1a-d** was fractionately distilled under a reduced pressure.

1-*N*-Allylindoline (**1a**).

This compound was obtained from allyl chloride (**5a**) as a pale yellow oil in 87% yield, bp 128-129°/22 mm Hg; ir (neat): 1640, 940, 920 (CH_2=CH-), 750 cm^{-1} (*o*-disubstituted benzene ring); ^{1}H-nmr (deuteriochloroform): δ 2.85 (t, 2H, C_3-*H*), 3.23 (t, 2H, C_2-*H*), 3.60 (d, 2H, -N-C*H*$_2$-C=C), 5.18 (d-d, 2H, N-C-C=C*H*$_2$), 5.63-5.98 (m, 1H, -C-C*H*=C), 6.36-6.65 (m, 2H, C_5-*H* + C_6-*H*), 6.90-7.02 ppm (m, 2H, C_4-*H* + C_7-*H*); ms: m/z 159 (M$^+$).

Anal. Calcd. for $C_{11}H_{13}N$: C, 82.97; H, 8.23; N, 8.30; MW 159. Found: C, 82.92; H, 8.10; N, 8.71.

1-*N*-Methylallyl)indoline (**1b**).

This compound was obtained from methallyl chloride (**5b**) as a pale yellow oil in 86% yield, bp 108-110°/8 mm Hg; ir (neat): 1630, 895, 705 (-CH=CH_2), 740 cm^{-1} (*o*-disubstituted benzene ring); ^{1}H-nmr (deuteriochloroform): 1.75 (s, 3H, -C*H*$_3$), 2.89 (t, 3H, C_3-*H*), 3.24 (t, 2H, C_2-*H*), 3.51 (s, 2H, -N-C*H*$_2$-C=C-), 4.86 (d, 1H, -C=C*H*), 4.95 (d, 1H, -C=C*H*), 6.36-7.06 ppm (m, 4H, aromatic ring protons); ms: m/z 173 (M$^+$).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09; MW 173. Found: C, 83.09; H, 8.65; N, 8.02.

1-*N*-(2-Butenyl)indoline (**1c**).

This compound was obtained from 2-butenyl chloride (**5c**) as a pale yellow oil in 83% yield, bp 92-93°/2 mm Hg; ir (neat): 1640, 960 (*trans* -CH=CH-), 715 (*cis* -CH=CH-), 740 cm^{-1} (*o*-disubstituted benzene ring); ^{1}H-nmr (deuteriochloroform): δ 1.68 (d, 3H, -C*H*$_3$), 2.88 (t, 2H, C_3-*H*), 3.28 (t, 2H, C_2-*H*), 3.64 (d, 2H, -N-C*H*$_2$-C=C), 5.36-5.83 (m, 2H, -C*H*=C*H*-), 6.42-6.68 (m, 2H, C_5-*H* + C_6-*H*), 6.93-7.10 ppm (m, 2H, C_4-*H* + C_7-*H*); ms: m/z 173 (M$^+$).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09; MW 173. Found: C, 83.09; H, 8.65; N, 8.02.

1-*N*-(3-Methyl-2-butenyl)indoline (**1d**).

This compound was obtained from 3-methyl-2-butenyl bromide (**5d**) as a pale yellow oil in 59% yield, bp 108-110°/2 mm Hg; ir (neat): 1660, 840 (-C=CH-), 740 cm^{-1} (*o*-disubstituted benzene ring); ^{1}H-nmr (deuteriochloroform): δ 2.23 (s, 6H, -C*H*$_3$), 2.95 (t, 2H, C_3-*H*), 3.20 (t, 2H, -C_2-*H*), 3.55 (d, 2H, -C*H*$_2$-C=C-), 6.40-6.60 (m, 1H, -C-C*H*=C-Me$_2$), 6.93-7.16 ppm (m, 4H, aromatic ring protons); ms: m/z 187 (M$^+$).

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48; MW 187. Found: C, 83.23; H, 9.07; N, 7.38.

General Procedure for The Rearrangement of 1-*N*-Allylindolines **1**.

Under nitrogen atmosphere, a mixture of **1** (19 mmoles) and zinc chloride (57 mmoles) in xylene (20 ml) was refluxed with stirring for 4.5 hours. After cooling to room temperature, the reaction mixture was poured into 10% sodium hydroxide solution and extracted with xylene. The layer was washed with water and dried over anhydrous magnesium sulfate. After an evaporation of the solvents, the residue was purified by column chromatography using silica gel and hexane-benzene (3:1) or by distillation under a reduced pressure. The results are shown in Table 1.

The structures of the products were verified by elemental analyses, by their ^{1}H- and ^{13}C-nmr, and ir spectra.

7-Allylindoline (**2a**).

A pale yellow oil was obtained, bp 135-137°/20 mm Hg; ir (neat): 3380 (-NH), 1640, 995, 910 (-CH=CH_2), 750 cm^{-1} (*o*-disubstituted benzene ring); ^{1}H-nmr (deuteriochloroform): δ 2.93 (t, 2H, C_3-*H*), 3.17 (d, 2H, -N-C*H*$_2$-C=C-), 3.31-3.51 (m, 3H, -N*H* + C_2-*H*), 5.03 (d-d, 2H, -C=C*H*$_2$), 5.73-5.97 (m, 1H, -N-C-C*H*=C), 6.60-6.85 ppm (m, 3H, aromatic ring protons); ^{13}C nmr (deuteriochloroform): δ 29.9 (C_3), 36.1 (Ar-CH_2-), 46.9 (C_2), 115.4 (-C=CH_2), 118.6 (C_6), 120.2 (C_7), 122.4 (C_4), 127.3 (C_5), 128.9 (C_9), 136.0 (-CH=CH_2), 150.0 ppm (C_8); ms: m/z 159 (M$^+$).

Anal. Calcd. for $C_{11}H_{13}N$: C, 82.98; H, 8.23; N, 8.80; MW 159. Found: C, 82.87; H, 8.16; N, 8.69.

7-(2-Methylallyl)indoline (**2b**).

A pale yellow oil was obtained, bp 125-127°/15 mm Hg; ir (neat): 3400 (-NH), 1640, 885 (-C=CH_2), 750 cm^{-1} (1,2,3-trisubstituted aromatic ring); ^{1}H-nmr (deuteriochloroform): δ 1.67 (s, 3H, -C*H*$_3$), 2.93 (t, 2H, C_3-*H*), 3.15 (s, 2H, Ar-C*H*$_2$-C=C-), 3.42 (t, 2H, C_2-*H*), 3.67 (s, 1H, -N*H*), 4.75 (d-d, 2H, -C=C*H*$_2$), 6.52-6.98 ppm (m, 3H, aromatic ring protons); ^{13}C-nmr (deuteriochloroform): δ 22.0 (CH_3-C=C-), 29.8 (C_3), 40.7 (Ar-CH_2-), 46.9 (C_2), 111.2 (-C=CH_2), 118.6 (C_6), 120.0 (C_7), 122.4 (C_4), 128.0 (C_5), 128.9 (C_9), 143.5 (-C=CH_2), 150.2 ppm (C_8); ms: m/z 173 (M$^+$).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09; MW 173. Found: C, 83.02; H, 8.61; N, 7.98.

7-(1-Methylallyl)indoline (**2c**).

A pale yellow oil was obtained; ir (neat): 3380 (-NH), 1645, 990, 910 (-C=CH_2), 750 cm^{-1} (1,2,3-trisubstituted aromatic ring); ^{1}H-nmr (deuteriochloroform): δ 1.32 (d, 3H, -CH_3), 2.93 (t, 2H, C_3-*H*), 3.38 (m, 1H, Ar-C*H*-Me), 3.42 (t, 2H, C_2-*H*), 3.63 (s, 1H, -N*H*), 4.98 (m, 2H, -C=CH_2), 5.88 (m, 1H, Ar-C-C*H*=C), 6.65 (d, 1H, C_5-*H*), 6.83 (d, 1H, C_6-*H*), 6.92 ppm (d-d, 1H, C_4-*H*); ^{13}C-nmr (deuteriochloroform): δ 18.2 (-C-*C*H_3), 29.8 (C_3), 38.9 (Ar-*C*H-), 46.8 (C_2), 113.0 (-C=*C*H_2), 118.6 (C_6), 122.3 (C_4), 124.7 (C_5), 125.3 (C_9), 129.0 (C_7), 141.9 (-*C*=CH_2), 149.3 ppm (C_8); ms: m/z 173 (M^+).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09; MW 173. Found: C, 83.11; H, 8.66; N, 7.96.

7-(1-Methyl-1-propenyl)indoline (**3**).

A pale yellow oil was obtained; ir (neat): 3360 (-NH), 1645, 840, 820 (trisubstituted olefin), 765 cm^{-1} (1,2,3-trisubstituted aromatic ring); ^{1}H-nmr (deuteriochloroform): δ 1.72 (d, 3H, Ar-C=C-CH_3), 1.92 (s, 3H, Ar-C-CH_3), 2.92 (t, 2H, C_3-*H*), 3.37 (t, 2H, C_2-*H*), 3.72 (s, 1H, -N*H*), 5.67 (q, 1H, Ar-C=C*H*-), 6.64 (d, 1H, C_5-*H*), 6.84 (d, 1H, C_6-*H*), 6.92 ppm (d, 1H, C_4-*H*); ^{13}C-nmr (deuteriochloroform): δ 13.8 (Ar-C=C-*C*H_3), 16.1 (Ar-C-*C*H_3), 30.0 (C_3), 47.1 (C_2), 118.2 (Ar-C=*C*-), 122.4 (C_6), 122.8 (C_4), 125.6 (C_5), 126.5 (Ar-*C*=C-), 128.9 (C_9), 134.2 (C_7), 148.2 ppm (C_8); ms: m/z 173 (M^+).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09; MW 173. Found: C, 83.16; H, 8.56; N, 8.03.

7-(*trans*-2-Butenyl)indoline (**2d**).

A pale yellow oil was obtained; ir (neat): 3380 (-NH), 1620, 965 (*trans* -CH=CH-), 740 cm^{-1} (1,2,3-trisubstituted aromatic ring); ^{1}H-nmr (deuteriochloroform): δ 1.64 (d, 3H, -C=C-CH_3), 2.92 (t, 2H, C_3-*H*), 3.18 (d, 2H, Ar-CH_2-C=C-), 3.38 (t, 2H, C_2-*H*), 3.48 (s, 1H, -N*H*), 5.43-5.53 (m, 2H, -C*H*=C*H*-), 6.46 (d, 1H, C_5-*H*), 6.76 (d, 1H, C_6-*H*), 6.87 ppm (d, 1H, C_4-*H*); ^{13}C-nmr (deuteriochloroform): δ 17.7 (Ar=C=C-*C*H_3), 29.8 (Ar-*C*H_2-), 38.5 (C_3), 47.3 (C_2), 109.1 (-C=*C*-Me) 124.5 (Ar-CH2-*C*=C-), 125.1 (C_6), 126.7 (C_7), 126.9 (C_4), 129.4 (C_9), 130.9 (C_5), 149.5 ppm (C_8); ms: m/z 173 (M^+).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09; MW 173. Found: C, 83.05; H, 8.62; N, 7.93.

7-(3-Methyl-2-butenyl)indoline (**2e**).

A pale yellow oil was obtained; ir (neat): 3370 (-NH), 1640, 840 (trisubstituted olefin), 750 cm^{-1} (1,2,3-trisubstituted aromatic ring); ^{1}H-nmr (deuteriochloroform): δ 1.72 (s, 6H, -CH_3), 2.97 (t, 2H, C_3-*H*), 3.12 (d, 2H, Ar-CH_2-C=C-), 3.48 (t, 2H, C_2-*H*), 3.51 (s, 1H, -N*H*), 5.24 (t, 1H, -C-C*H*=C-Me), 6.61 (d-d, 1H, C_5-*H*), 6.83 (d, 1H, C_6-*H*), 6.95 ppm (d, 1H, C_4-*H*); ^{13}C-nmr (deuteriochloroform): δ 17.8 (-C=C-*C*H_3), 25.6 (-C=C-*C*H_3), 29.9 (C_3), 30.4 (Ar-*C*H_2-), 47.1 (C_2), 118.6 (Ar-C-*C*=C-), 121.8 (C_6), 122.1 (C_4), 122.4 (C_5), 126.8 (-C=*C*-Me$_2$), 128.7 (C_9), 132.7 (C_7), 149.7 ppm (C_8); ms: m/z 187 (M^+).

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48; MW 187. Found: C, 83.35; H, 9.10; N, 7.41.

1,2,5,6-Tetrahydro-4,4-dimethyl-4*H*-pyrrolo[3,2,1-*ij*]quinoline (**4**).

A pale yellow oil was obtained; ir (neat): 1600, 1580, 750 cm^{-1} (1,2,3-trisubstituted aromatic ring); ^{1}H-nmr (deuteriochloroform): δ 1.07 (s, 6H, -CH_3), 1.73 (t, 2H, C_1-*H*), 2.62 (t, 2H, C_5-*H*), 2.82 (t, 2H, C_6-*H*), 3.24 (t, 2H, C_2-*H*), 6.49 (d-d, 1H, C_8-*H*), 6.76 (d, 1H, C_7-*H*), 6.84 ppm (d, 1H, C_8-*H*); ^{13}C-nmr (deuteriochloroform): δ 22.3 (C_5), 23.3 (-*C*H_3), 28.4 (C_1), 37.0 (C_6), 46.8 (C_2), 50.9 (C_4), 117.1 (C_7), 117.6 (C_{9a}), 121.6 (C_9), 125.8 (C_8), 128.2 (C_{6a}), 148.2 ppm (C_{9b}); ms: m/z 187 (M^+).

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48; MW 187. Found: C, 83.28; H, 9.13; N, 7.39.

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