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The lithium 1,8-diazabicyclo[5.4.0]undec-6-ide (**1**) prepared from 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and *n*-butyllithium reacts with alkyl halides and carbonyl compounds such as benzophenone, acetophenone, and benzaldehyde to give 6-substituted DBU derivatives in good yields. The reaction behavior of 6-substituted DBU was also investigated.

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1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) has been used to various organic reactions [1] as strong organic base. However, the synthesis and reaction behavior of DBU derivatives have not been well investigated so far.

Previous communication from this laboratory has described that lithium 1,8-diazabicyclo[5.4.0]undec-6-ide (**1**), prepared from DBU and *n*-butyllithium, effectively functions as a carbon dioxide carrier [2]. In this paper, we wish to report the preparation and reactivity of various 6-substituted 1,8-diazabicyclo[5.4.0]undec-7-ene.

The reactions carried out in this work are shown in Scheme 1. The procedure is described for the reaction of **1** with carbonyl compound. DBU was treated with a molar equivalent of *n*-butyllithium in tetrahydrofuran (THF) at 0° under argon. The resulting N-C-C ambident anion **1** was then reacted with a molar equivalent of carbonyl compound. The aqueous acid and alkaline work-up of the reaction mixture afforded the corresponding adduct (**2**) in considerable yields. The yields of adduct are shown in Table 1. We have examined the thermal stability of **2** at the temperature higher than the melting point. For example, when the **2a** was gradually heated without solvent at 180° for 2 hours, benzophenone was obtained in 85% yield and DBU was recovered almost quantitatively. DBU derivatives, **2b** and **2c**, decomposed at 150° and 180° to give acetophenone and benzaldehyde, in 90% and 32%, respectively. Thus, the smooth C-C bond fission of **2** by moderate heating was elucidated (Scheme 2).

Scheme 1

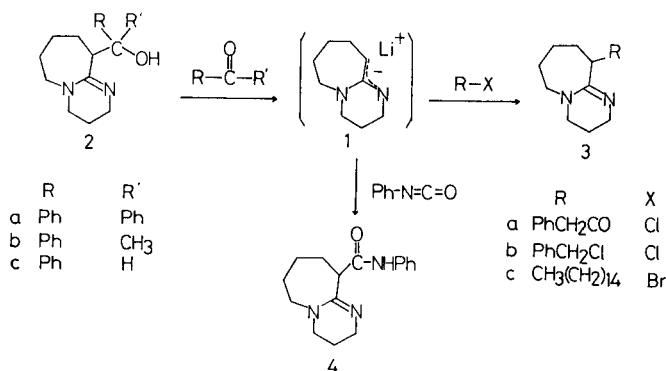


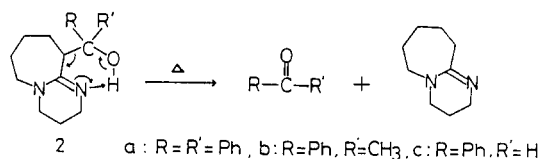
Table 1

Reaction of Ketone and Aldehyde with **1** [a]

R	R'	Reaction Time (hours)	Yield, % [b]
C ₆ H ₅	C ₆ H ₅	2	82
C ₆ H ₅	CH ₃	2	50
C ₆ H ₅	H	2	44

[a] The reactions were carried out at 0° in tetrahydrofuran under argon. [b] Yields of isolated products.

Scheme 2



When alkyl halide and acyl chloride were reacted with **1** under similar reaction conditions, 6-substituted 1,8-diazabicyclo[5.4.0]undec-7-ene (**3**) were obtained in the yields shown in Table 2.

Table 2

Reaction of Alkyl halide and Acyl chloride with **1** [a]

R	Substrate X	Reaction Time (hours)	Yield, % [b]
C ₆ H ₅ CH ₂ CO	Cl	2	45
C ₆ H ₅ CH ₂	Cl	10	38
CH ₃ (CH ₂) ₄	Br	29	75

[a] The reactions were carried out at 0° in tetrahydrofuran under argon.

[b] Yields of isolated products.

Tables 3 and 4 show the analytical and spectral data of compounds **2-4**. The keto-enol isomerization of **3a** was observed and the major isomer was ascribed to the enol form B (Scheme 3) based on ir and ¹H-nmr spectra.

Table 3

Melting Points, Boiling Points, and Analyses of 6-Substituted 1,8-Diazabicyclo[5.4.0]undec-7-enes 2-4

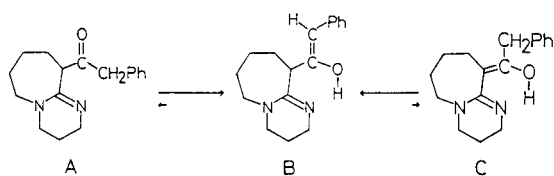
Compound	MP [°C] and/or BP [°C/mm Hg]	Molecular Formula	Analysis, %		
			C	H	N
2a	124-125	C ₂₂ H ₂₆ N ₂ O	79.00	7.84	8.38
			79.31	8.03	8.32
2b	95-96	C ₁₇ H ₂₄ N ₂ O	74.96	8.88	10.29
			74.88	9.12	10.09
2c	Oil	C ₁₆ H ₂₂ N ₂ O	74.38	8.58	10.84
			74.58	8.85	11.11
3a	66-70	C ₁₇ H ₂₂ N ₂ O	75.52	8.20	10.36
			75.13	8.60	10.20
3b	153-155/2	C ₁₆ H ₂₂ N ₂	79.29	9.15	11.56
			79.30	9.15	11.50
3c	166-168/3	C ₂₄ H ₄₆ N ₂	79.49	12.79	7.73
			79.46	12.82	7.69
4	128-129	C ₁₆ H ₂₁ N ₃ O	70.71	7.98	15.14
			70.82	7.80	15.48

Table 4

Spectral Data of 6-Substituted 1,8-Diazabicyclo[5.4.0]undec-7-ene 2-4

Compound	IR (cm ⁻¹) (potassium bromide)	¹ H-NMR (δ, ppm) (deuteriochloroform)	MS, m/e
2a	1605 (C=N)	1.06-1.92 (m, 8H, N-CH ₂ -CH ₂ -CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N), 2.55-4.00 (m, 7H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ CH-C=N), 6.65-7.40 (m, 10H, aromatic), 9.02 (brs, 1H, OH)	182, 152, 105, 77
2b	1610 (C=N)	1.1-2.3 (m, 11H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N, CH ₃), 2.5-4.0 (m, 7H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ CH-C=N), 6.9-7.6 (m, 5H, aromatic), 8.7 (brs, 1H, OH)	152, 120, 105, 77
2c	1610 (C=N)	0.8-2.1 (m, 8H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N), 2.35-3.85 (m, 7H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N), 4.65 (m, 1H, C ₆ H ₅ -CH ₂), 5.25 (d, OH), 7.0-7.5 (m, 5H, aromatic)	152, 106, 105, 77
3a	3220 (OH) 1710 (C=O, sh) 1610 (C=N)	0.75-3.75 (m, 15H, DBU-H), 4.25 (brs, 1H, OH), 7.0-7.8 (m, 6H, aromatic C ₆ H ₅ -CH=)	152, 91, 78, 18
3b	neat/1620 (C=N)	0.9-2.10 (m, 8H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N), 2.10-4.00 (m, 9H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N), C ₆ H ₅ CH ₂ , 7.08 (brs, 5H, aromatic)	242, 213, 151, 91, 18
3c	neat/1620 (C=N)	0.60-2.00 (m, 40H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N, CH ₃ (CH ₂) ₄), 2.90-3.50 (m, 6H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N)	362, 213, 151, 112, 70, 28, 18
4	3200 (NH) 1695 (C=O) 1600 (C=N)	1.1-2.7 (m, 9H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ -CH-C=N), 2.7-4.0 (m, 7H, N-CH ₂ CH ₂ CH ₂ -N, N-CH ₂ (CH ₂) ₃ CH-C=N, NH), 7.0-7.9 (m, 5H, aromatic)	152, 119, 93

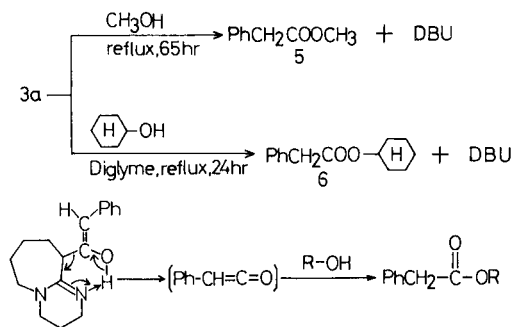
Scheme 3



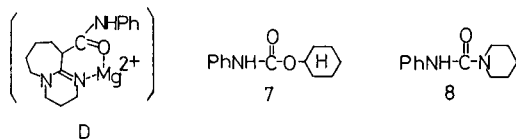
Namely, in the ir spectrum of **3a**, the carbonyl absorption appeared as shoulder at 1710 cm⁻¹. Whereas, the strong absorption of hydroxy group was recognized at

3220 cm⁻¹. In the ¹H-nmr spectrum, the methylene proton of benzyl group was not observed, but the hydroxy proton and olefinic protons were recognized at 4.25 and 7.0-7.8 ppm, respectively (See Table 4). From these data, we have considered the C-C bond fission at 6-position of B to be possible in a similar manner in Scheme 2. Therefore, we have examined the reaction of B with alcohols such as methanol and cyclohexanol under various conditions. Consequently, **5** and **6** of esters were obtained in 6% and 14%, respectively. On the basis of these results, we have deduced that the phenyl ketene intermediate should generate in the course of the reaction (See Scheme 4).

Scheme 4



The reaction of phenyl isocyanate with **1** gave the amide **4** in 41% yield. When cyclohexanol and piperidine were stirred with **4** at 150° in DMF, urethane and urea derivatives (**7** and **8**) were obtained in 22% and 25% yields, respectively. Whereas, when the reactions were carried out by adding magnesium chloride, the product, **7** and **8** were not obtained because of the formation of complex D.



Work is in progress to explore the applicability of **1** to other organic syntheses.

EXPERIMENTAL

Melting points were determined with a Yanagimoto melting point apparatus and are uncorrected. The ir spectra were recorded on a Hitachi 215 Grating infrared spectrometer. The ¹H-nmr spectra were obtained on a Hitachi Perkin-Elmer R-24 spectrometer (60 MHz). Chemical shifts are reported in ppm from TMS as an internal standard and are given in δ units. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6E instrument equipped with a solid sample injector; the ionizing voltage was 80 ev.

General Procedure for the Synthesis of **2**, **3**, and **4**.

To a cooled THF solution (0°) of 1,8-diazabicyclo[5.4.0]undec-7-ene (7.0 mmoles) was added dropwise a hexane solution of *n*-butyllithium (7.0 mmoles) with stirring under argon and stirred for 1 hour at 0°. To the resulting N-C-C ambident anion (**1**) was added dropwise a THF solution of substrate (7.0 mmoles). The reaction mixture was acidified with aqueous hydrochloric acid. The mixture was extracted several times with ether and the aqueous layer was alkalinized slowly with aqueous sodium hydroxide and extracted three times with 70 ml portions of ether. The ethereal layer was washed with water, dried over anhydrous magnesium sulfate, and condensed under reduced pressure. Recrystallization or distillation of the residue gave the products, **2**, **3**, and **4**, respectively. The yields, the melting points, the ¹H-nmr and elemental analyses of 6-substituted DBU (**2**, **3**, and **4**) are listed in Tables 1-4.

Reaction of **3a** with Methanol (**5**).

A solution of 200 mg (0.74 mmole) of **3a** in 10 ml of methanol was heated at reflux for 65 hours. After the excess methanol was removed *in vacuo*, the residue was chromatographed on a silica gel column, using chloroform as an eluent, to give 7 mg (6%) of **5**.

Reaction of **3a** with Cyclohexanol (**6**).

A solution of 200 mg (0.74 mmole) of **3a** and 740 mg (7.4 mmoles) of cyclohexanol in 15 ml of diglyme were heated at reflux for 24 hours. The reaction mixture was extracted with ether. After the removal of the ether, the residue was chromatographed on a silica gel column using chloroform as the eluent, to give 23 mg (14%) of **6**.

The products, **5** and **6** were identified by a comparison of their ir, ¹H-nmr, and mass spectra with those of the respective authentic specimens.

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