Demethoxycarbonylation of Methyl 2,5- and Methyl 3,6-Dialkyl-1*H*-azepine-1-carboxylates: Formation and Characterization of 2*H*-, 3*H*- and 4*H*-Azepines

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Demethoxycarbonylation of methyl 2,5-di-*tert*-butyl-1*H*-azepine-1-carboxylate using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave 3*H*-azepines. Under similar conditions, methyl 3,6-di-*tert*-butyl-1*H*-azepine-1-carboxylate gave not only the 3*H*-azepine but also the isomerized 2*H*- and 4*H*-azepines. Application of the reaction to dimethyl and diisopropyl substituted 1*H*-azepines showed that bulky alkyl group substitution stabilizes the seven-membered azatriene system. The thermal behaviour of the di-*tert*-butyl substituted azepines is discussed.

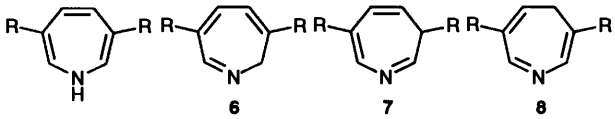
Effective deprotection of nitrogen atom-protected 1*H*-azepines is of interest in connection with the behaviour of 1*H*-azepine which can be regarded both as an anti-Hückel 8π-electron system and a nitrogen-containing seven-membered triene system.[1] A MNDO[2] molecular orbital calculation predicts that 3*H*-azepine is more stable than 1*H*-, 2*H*- (**6**) or 4*H*-azepine (**8**), related to 3*H*-azepine **7** by the thermally allowed, 1,5-hydrogen shift (Table 1). Owing to their instability, the chemical and physical properties of azepines have yet to be experimentally determined. The elegant conversion of methyl 1*H*-azepine-1-carboxylate into the 3*H*-azepine was accomplished by Vogel *et al.* with iodotrimethylsilane as a demethoxycarbonylating agent, the product being characterized by low-temperature NMR spectroscopy.[1b] Earlier, we reported the indirect conversion of methyl 2,5-**2a** and 3,6-di-*tert*-butyl-1*H*-azepine-1-carboxylates **3a** into the correspondingly substituted 3*H*-azepines **4a** and **7a** *via* 3*H*-cyclobuta[*b*]pyrrole derivatives such as **12**.[3] Nitta *et al.* have also reported the synthesis of 3-cyclohepta-2,4,6-trienyl-3*H*-azepine *via* an iron carbonyl complex of ethyl 1*H*-azepine-1-carboxylate and presented the first example of 1,5-hydrogen shift in the azepine ring system.[4]

We report here an alternative direct synthesis not only of 3*H*-azepines but also 2*H*- and 4*H*-azepines from methyl 2,5- **2a** and methyl 3,6-di-*tert*-butyl-1*H*-azepine-1-carboxylates **3a** by means of demethoxycarbonylation with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU), together with observations of the characteristic thermal behaviour of the seven-membered azatriene system.[5] Diisopropyl and dimethyl derivatives of methyl 1*H*-azepine-1-carboxylates **2b**, **c** and **3b**, **c** were also subjected to the demethoxycarbonylation described.

Results and Discussion

Preparation of Methyl 1H-*Azepine*-1-*carboxylate Derivatives* **2a–c** *and* **3a–c**.—The procedure for the preparation of the methyl 1*H*-azepine-1-carboxylate derivatives follows that reported by Hafner *et al.*[1a] and Lwowski *et al.*[6] *p*-Di-*tert*-butylbenzene **1a**, *p*-diisopropylbenzene **1b** and *p*-xylene **1c** were heated with methyl azidoformate (0.2–0.5 equiv.) at 125 °C, respectively (see Scheme 1). Careful separation of each reaction mixture by preparative medium-pressure liquid-chromatography (MPLC) gave methyl 2,5-disubstituted and 3,6-disubstituted 1*H*-azepine-1-carboxylates **2a–c** and **3a–c** in each case. Product identities were established by comparison of authentic data for 2,5-di-*tert*-butyl-,[3,7] 3,6-di-*tert*-butyl-,[3,7] 2,5-dimethyl-,[8] and 3,6-dimethyl-1*H*-azepines[9] for **2a**, **3a**, **2c** and **3c**, respectively. The hitherto unknown 2,5-diisopropyl- and 3,6-diisopropyl-1*H*-azepine-1-carboxylates **2b** and **3b** were identified by comparing their ^{1}H NMR and electronic spectra with those of the analogous 1*H*-azepine derivatives **2a**, **c** and **3a**, **c**.

Table 1 Calculated MNDO relative energies (ΔH_fs) for 2H-, 3H- and 4H-azepines based on H_f of 1H-azepine

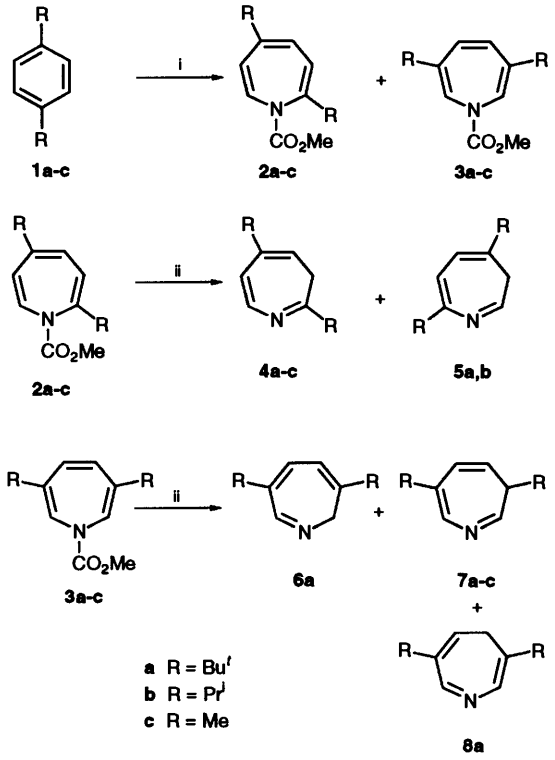


	1*H*-azepine	2*H*-azepine (6)	3*H*-azepine (7)	4*H*-azepine (8)
	ΔH_f/kJ mol^{-1}[a]			
R = H	0.0	−17.2	−47.5	−20.8
R = Bu^t	0.0	−20.2	1.1[b] −16.3[b]	−15.9

[a] The MNDO calculations were performed by complete geometry optimizations for all the compounds. For 1*H*-azepine, a plane of symmetry passing through nitrogen and the centre of the C-4 and C-5 double bond is maintained during optimization sequence. [b] The two relative energies were calculated for the two isomers, the structure of which are shown below, of 3,6-di-*tert*-butyl-3*H*-azepine **A** and **B** (upper for **A** and lower for **B**).

Demethoxycarbonylation with DBU.—A solution of methyl 1*H*-azepine-1-carboxylate derivative and DBU in dry nitrogen-purged xylene was refluxed under a nitrogen stream for 5–6 h. After cooling, the reaction mixture was introduced into a silica gel column in order to eliminate the excess of DBU and the polymeric compounds formed. From this eluent, the demethoxycarbonylated products were obtained by preparative MPLC on a silica gel column (see Scheme 1).

(*a*) *Di-*tert*-butyl derivatives.* The reaction of methyl 2,5-di-*tert*-butyl-1*H*-azepine-1-carboxylate **2a** gave 2,5- **4a** and 4,7-di-*tert*-butyl-3*H*-azepines **5a**. Under similar conditions, methyl 3,6-di-*tert*-butyl-1*H*-azepine-1-carboxylate **3a** gave 3,6-di-*tert*-butyl substituted 2*H*- **6a**, 3*H*- **7a**, and 4*H*-azepine **8a**. The azepines **4a** and **7a** were identical with those previously reported.[3] The new 4,7-di-*tert*-butyl-3*H*-azepine **5a** was readily



Scheme 1 *Reagents and conditions:* i, N_3CO_2Me, 125 °C; ii, DBU, xylene

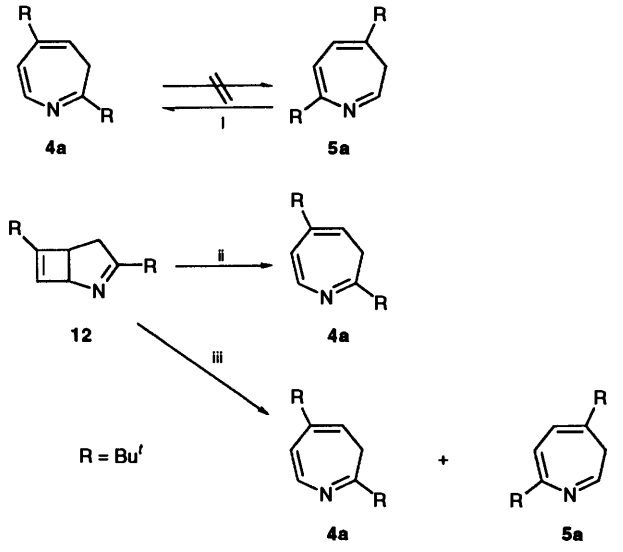
characterized by comparing the values of the coupling constants (Hz) for its AB-quartet ($J_{5,6}$ 6.7) and their chemical shifts ($\delta_{5\text{-H}}$ 6.14 and $\delta_{6\text{-H}}$ 6.06) with those of **4a** ($J_{6,7}$ 8.5, $\delta_{6\text{-H}}$ 6.28 and $\delta_{7\text{-H}}$ 7.28). The structure of 3,6-di-*tert*-butyl-2*H*- **6a** and 3,6-di-*tert*-butyl-4*H*-azepines **8a** were also elucidated by reference to the ^1H and ^{13}C NMR spectra of the previously obtained 3*H*-azepines **4a**, **5a** and **7a**. Assignments of the ^1H and ^{13}C NMR spectra for all the di-*tert*-butylazepines (see Table 2) were based on ^1H-COSY and ^1H–^{13}C correlation (HETCOR) measurements.

Use of *N*-ethoxycarbonyl derivatives instead of **2a** or **3a**, gave complete recovery of the starting materials no reaction having occurred. With the *N*-methoxycarbonyl derivatives, the reaction initially proceeds by effective demethylation of the methoxycarbonyl group with the strong base (DBU),[10] followed by decarboxylation to give 3*H*-azepines.

(*b*) *Diisopropyl derivatives.* With methyl 2,5-diisopropyl-1*H*-azepine-1-carboxylate **2b**, reaction gave the 2,5- **4b** and 4,7-diisopropyl-3*H*-azepines **5b**, analogously to **2a**, use of the 3,6-diisopropyl isomer **3b** as starting material gave 3,6-diisopropyl-3*H*-azepine **7b** with no simultaneous formation of 2*H*- and 4*H*-azepine isomers; it thereby differed from the reaction with the correspondingly substituted di-*tert*-butyl-1*H*-azepine **3a**.

(*c*) *Dimethyl derivatives.* Labile 2,5-dimethyl- **4c** and 3,6-dimethyl-3*H*-azepines **7c** were also obtained from methyl 2,5-dimethyl- **2c** and methyl 3,6-dimethyl-1*H*-azepine-1-carboxylates, **3c**, respectively. In order to purify the dimethyl derivatives, the reaction mixture was passed through the silica gel column at −2 °C to prevent the degradation of the dimethyl-3*H*-azepine formed. Although the solution of dimethyl-3*H*-azepines is stable for at least 6 h even at room temperature, the solvent-free compounds became dark brown with degradation or polymerization within 30 min at room temperature.

Thermal Behaviour of Azepines **4a**, **5a**, **6a** *and* **7a**.—In connection with the simultaneous formation of **4a** and **5a** from 1*H*-azepine **2a**, we examined the possibility of thermal isomerization between **4a** and **5a**. The reason for the formation of **4a** and **5a** might be considered to be a thermally allowed 1,5-hydrogen shift between the two. Under the demethoxycarbonylation conditions employed, neither **4a** nor **5a** gave the complementary isomers **5a** and **4a**, respectively. However, when a benzene solution of **5a** was heated in a sealed glass tube for 2 h at 175 °C, the previously reported temperature at which the 1,5-hydrogen shift occurs in a cycloheptatriene system,[11] the isomer **4a** was obtained only in 9% yield. On the other hand, the isomerization from **4a** to **5a** was not observed under these conditions (see Scheme 2). Earlier, we reported the results



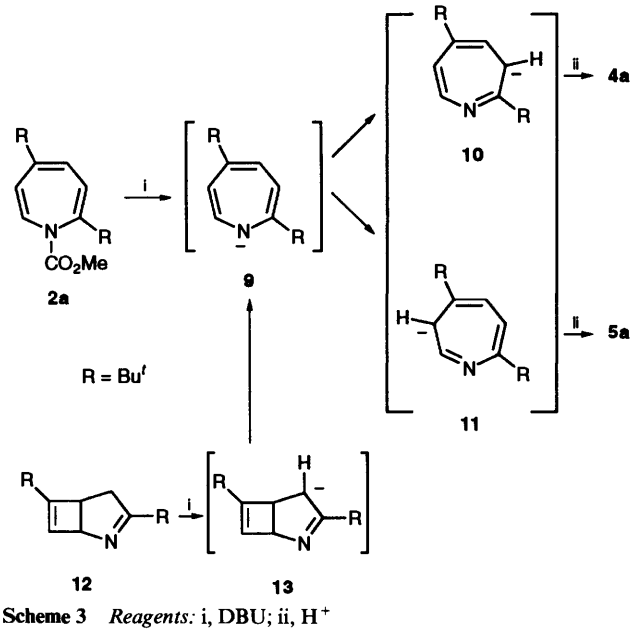
Scheme 2 *Reagents and conditions:* i, 175 °C; ii, C_6H_6, 125 °C; iii, DBU, xylene

of a kinetic study in which the thermal reaction of 2,4-di-*tert*-butyl-3a,5a-dihydro-3*H*-cyclobuta[*b*]pyrrole **12** in benzene at 150 °C gave 3*H*-azepine **4a** as a single product by a disrotatory cyclobutene ring-opening mechanism.[3] When a xylene solution of **12** and DBU was heated to reflux for 4 h, ring-opening also occurred to give the 3*H*-azepines **4a** and **5a** simultaneously in a similar ratio to that obtained from the demethoxycarbonylation reaction of **2a** (see Scheme 2). This indicates that the mechanism for the isomerization of cyclobuta[*b*]pyrrole **12** using DBU is different from that of the thermal isomerization. It can be considered that the cyclobutene ring-opening proceeds *via* an allylic DBU-deprotonated anion **13** forming the anion **9** (see Scheme 3). The same products and in a comparable ratio in both the reaction of **12** and **3a** implies a common intermediate leading to **4a** and **5a**. The results obtained suggest that the simultaneous formation of the 3*H*-azepine isomers **4a** and **5a** is not the result of a 1,5-hydrogen shift but rather arises from the competitive prototropy of the intermediate 1*H*-azepine or its anion **9** under the demethoxycarbonylation conditions presented (see Scheme 3).

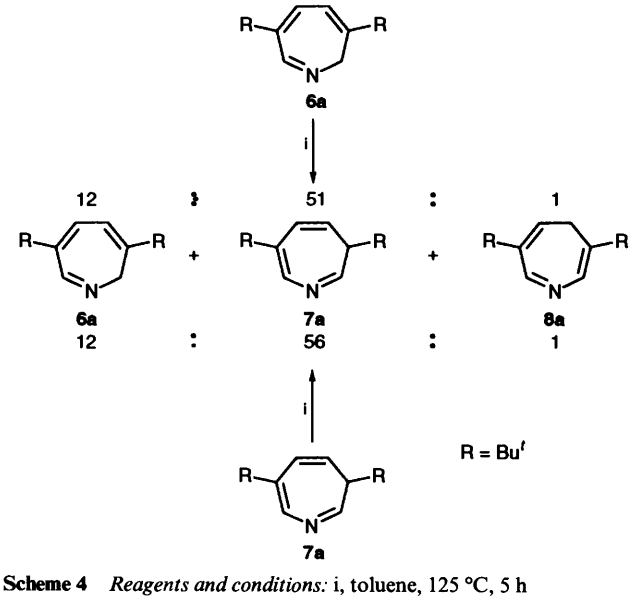
In contrast, the 1,5-hydrogen shift was observed between 3,6-di-*tert*-butylazepines **6a**, **7a** and **8a**. When heated at 125 °C in toluene for 5 h, 2*H*- **6a** or 3*H*-azepines **7a** were converted quantitatively into an azepine mixture consisting of 2*H*- **6a**, 3*H*- **7a** and 4*H*-azepines **8a** (12 : 51 : 1 from 2*H*-azepine **6a** or 12 : 56 : 1 from 3*H*-azepine **7a**) (see Scheme 4). This result shows that the distribution of azepine isomers is proportional to their relative thermal stabilities as they interconvert *via* the thermally allowed 1,5-hydrogen shift, although the MNDO calculated H_f values (see Table 1) are not reflected in the observed distribution ratios. The difference in the thermal behaviour between 2,5- or 4,7-di-*tert*-butylazepines and 3,6-di-*tert*-butylazepines and between

Table 2 ^1H (500 MHz) and ^{13}C (125 MHz) NMR data for ring protons and carbons of azepines **4–8a** in $CDCl_3$

		δ											
		C-2	C-3	C-4	C-5	C-6	2-H	3-H	4-H	5-H	6-H	7-H	J/Hz
2*H*-form	**6a**	52.2	150.6	119.1	128.6	158.7	3.5	—	6.09	6.60	—	7.91	$J_{4,5}$ 6.2 $J_{5,7}$ 1.9
3*H*-forms	**4a**	164.0	32.4	110.0	147.3	139.7	—	1.1 3.6	5.03	—	6.28	7.28	$J_{3,4}$ 7.0 $J_{6,7}$ 8.5
	5a	136.4	35.1	136.8	118.6	160.1	6.50	1.1 3.6	—	6.14	6.06	—	$J_{2,3}$ 5.0 $J_{5,6}$ 6.7
	7a	139.6	54.3	116.5	125.5	135.4	6.46	0.79	5.17	6.43	—	7.44	$J_{2,3}$ 4.8 $J_{3,4}$ 5.9 $J_{3,5}$ 1.7 $J_{4,5}$ 9.4 $J_{5,7}$ 1.9
4*H*-form	**8a**	130.7	140.9	26.4	125.6	160.1	6.73	—	2.05	5.54	—	8.55	$J_{4,5}$ 7.3 $J_{5,7}$ 2.1



Scheme 3 *Reagents:* i, DBU; ii, H^+



Scheme 4 *Reagents and conditions:* i, toluene, 125 °C, 5 h

3,6-di-*tert*-butylazepine and 3,6-diisopropylazepine is not as yet clear.

Conclusions

Efficient demethoxycarbonylation of dimethyl, diisopropyl and di-*tert*-butyl substituted *N*-methoxycarbonyl-1*H*-azepines **2a–c** and **3a–c** occurs when they are heated in xylene with DBU. The introduction of a bulky alkyl group into the 3*H*-azepine ring stabilizes the system and permits its isolation and further treatment. The evidence presented relating to the thermal behaviour of 3,6-di-*tert*-butyl substituted azepine indicates that the thermally allowed 1,5-hydrogen shift occurs to give an isomerized azepine mixture. Further efforts to clarify the features of the seven-membered azatriene system are underway in our laboratory.

Experimental

M.p.s were determined with a Yanagimoto micromelting point apparatus and are uncorrected. Silica gels HF_{254} (Merck) for TLC and Woelm 32–63 for preparative MPLC were used. IR spectra were recorded on a JASCO FT-IR 5000 spectrophotometer. ^1H and ^{13}C NMR were measured on a Varian XL-200 or XL-500 spectrometer. *J* Values are given in Hz. Electronic spectra were recorded on a Hitachi 288 spectrophotometer. Mass spectrometry was performed on a JEOL JMS-DX300 mass spectrometer coupled to the JMA-3100 data analysis system at the Department of Chemistry, College of Liberal Arts and Science, Okayama University. Elemental analyses were performed on a Yanagimoto MT-2 CHN-corder. The molecular orbital (MNDO) calculation was carried out on a NEC ACOS-2000 computer of Okayama University Computer Center.

Preparation of Methyl 2,5- *and Methyl* 3,6-*Diisopropyl*-1H-*azepine*-1-*carboxylates* **2b** *and* **3b**.—Methyl azidoformate (15 g, 0.15 mol) was added dropwise, with efficient stirring, to hot *p*-diisopropylbenzene **1b** (50 g, 0.31 mol) at 130 °C over 90 min, and the resulting solution was stirred at this temperature until the evolution of nitrogen ceased. After cooling excess of **1b** was removed from the brownish residue (26 g) by distillation under reduced pressure. The new residue was chromatographed (ethyl acetate–hexane 85 : 15, v/v) on silica gel to give a yellow oil (11.5 g). From 5.0 g of the yellow oil, 1*H*-azepines **2b** (950 mg, 6.5%) a pale yellow oil (Found: C, 71.5; H, 9.2; N, 6.0. $C_{14}H_{21}NO_2$ requires C, 71.5; H, 9.0; N, 5.95%); ν_{max}(neat)/cm^{-1} 1722, 1648 and 1635; λ_{max}(cyclohexane)/nm 215 (log ε/dm^3 mol^{-1} cm^{-1} 4.27) and 292 (3.20); δ_H(200 MHz, $CDCl_3$) 1.10 (12 H, br d, *J* 7.2), 2.39 (1 H, hept, *J* 7.2), 2.89 (1 H, br hept, *J* 7.2), 3.62 (3 H, s) and 5.8 (4 H, m); *m/z* 235 (M^+) and 220, and **3b** (790 mg, 5.4%), a pale yellow oil (Found: C, 71.7; H, 9.3; N, 6.0. $C_{14}H_{21}NO_2$ requires C, 71.5; H, 9.0; N, 5.95%); ν_{max}(neat)/cm^{-1}

1722, 1665 and 1637; λ_{max}(cyclohexane)/nm 215 (log ε/dm^3 mol^{-1} cm^{-1} 4.30) and 240 (sh, 3.40); δ_H(200 MHz, $CDCl_3$) 1.04 (12 H, d, *J* 7.2), 2.37 (2 H, hept, *J* 7.2), 3.67 (3 H, s), 5.71 (2 H, br s) and 6.07 (2 H, s); *m/z* 235 (M^+) and 220, were obtained by means of MPLC using ethyl acetate–hexane (1 : 10) as eluent.

Synthesis of 2,5- *and* 4,7-*Di*-tert-*butyl*-3H-*azepines* **4a** *and* **5a**.—A solution of 1*H*-azepine **2a** (2.0 g, 7.6 mmol) and DBU (12 g, 78 mmol) in nitrogen-purged dry xylene (12 cm^3) was refluxed under a nitrogen stream for 6 h. After cooling, the reaction mixture was introduced into a silica gel column and eluted with ethyl acetate–hexane (1 : 4). The eluent was concentrated and chromatographed again on silica gel (Woelm 32–63) by MPLC to give 3*H*-azepines **4a** (843 mg, 54%), colourless needles, m.p. 20.5–21 °C, and **5a** (343 mg, 22%), colourless needles, m.p. 41–42 °C (Found: C, 82.0; H, 11.1; N, 7.0. $C_{14}H_{23}N$ requires C, 81.9; H, 11.3; N, 6.8%); ν_{max}(KBr)/cm^{-1} 1595 (C=N); λ_{max}(EtOH)/nm 237 (log ε/dm^3 mol^{-1} cm^{-1} 3.76); δ_H(500 MHz, $CDCl_3$) 1.10 (1 H, br s), 1.13 (9 H, s), 1.20 (9 H, s), 3.60 (1 H, br s), 6.06 (1 H, d, *J* 6.7), 6.14 (1 H, d, *J* 6.7) and 6.50 (1 H, t, *J* 5.0); δ_C(125 MHz, $CDCl_3$) 29.5 (q), 29.7 (q), 35.1 (t), 35.2 (s), 36.4 (s), 108.9 (d), 118.6 (d), 136.4 (d), 136.8 (s) and 160.1 (s).

Synthesis of 3,6-*Di*-tert-*butyl*-2H-, 3H- *and* 4H-*azepines* **6a**, **7a** *and* **8a**.—Similarly, a solution of 1*H*-azepine **3a** (2.74 g, 10.4 mmol) and DBU (15.8 g, 104 mmol) in nitrogen-purged dry xylene (17 cm^3) gave 3*H*-azepine **7a** (988 mg, 46%) as colourless prisms, m.p. 57.5–58.5 °C, 4*H*-azepine **8a** (27 mg, 1.3%), a pale yellow oil (Found: C, 82.1; H, 11.3; N, 6.7. $C_{14}H_{23}N$ requires C, 81.9; H, 11.3; N, 6.8%); ν_{max}(neat)/cm^{-1} 1603 (C=N); λ_{max}(EtOH)/nm 241 (log ε/dm^3 mol^{-1} cm^{-1} 3.37) and 313 (3.09); δ_H(500 MHz, $CDCl_3$) 1.10 (18 H, s), 2.05 (2 H, d, *J* 7.3), 5.54 (1 H, dt, *J* 2.1 and 7.3), 6.73 (1 H, s) and 8.55 (1 H, d, *J* 2.1); δ_C(125 MHz, $CDCl_3$) 26.4 (t), 29.5 (q), 29.8 (q), 33.7 (s), 34.6 (s), 125.6 (d), 130.7 (d), 140.9 (s) and 160.1 (s), and 2*H*-azepine **6a** (241 mg, 11%) as colourless plates, m.p. 68.5–69 °C (Found: C, 81.9; H, 11.55; N, 6.8. $C_{14}H_{23}N$ requires C, 81.9; H, 11.3; N, 6.8%); ν_{max}(KBr)/cm^{-1} 1620 (C=N); λ_{max}(EtOH)/nm 246 (log ε/dm^3 mol^{-1} cm^{-1} 3.67) and 302 (3.38); δ_H(500 MHz, $CDCl_3$) 1.17 (9 H, s), 1.22 (9 H, s), 3.50 (2 H, br), 6.09 (1 H, d, *J* 6.2), 6.60 (1 H, dd, *J* 6.2 and 1.9) and 7.91 (1 H, d, *J* 1.9); δ_C(125 MHz, $CDCl_3$) 29.3 (q), 30.5 (q), 34.8 (s), 35.7 (s), 52.2 (t), 119.1 (d), 128.6 (d), 150.6 (s) and 158.7 (s) in this sequence.

Synthesis of 2,5- *and* 4,7-*Diisopropyl*-3H-*azepines* **4b** *and* **5b**.—A solution of 1*H*-azepine **2b** (460 mg, 2.0 mmol) and DBU (3 g, 20 mmol) in nitrogen-purged dry xylene (4 cm^3) was refluxed under a nitrogen stream for 5 h and then worked up by the above described treatment for **4a** and **5a** to give 3*H*-azepines **4b** (157 mg, 45%), a pale yellow oil (Found: C, 81.1; H, 10.5; N, 7.75. $C_{12}H_{19}N$ requires C, 81.3; H, 10.8; N, 7.9%); ν_{max}(neat)/cm^{-1} 1610 (C=N); λ_{max}(EtOH)/nm 237 (log ε/dm^3 mol^{-1} cm^{-1} 3.59) and 260 (3.62); δ_H(500 MHz, $CDCl_3$) 1.1 (1 H, m), 1.02 (6 H, d, *J* 6.8), 1.11 (6 H, d, *J* 6.8), 2.43 (1 H, hept, *J* 6.8), 2.56 (1 H, hept, *J* 6.8), 4.93 (1 H, t, *J* 6.6), 6.09 (1 H, d, *J* 8.4) and 7.25 (1 H, d, *J* 8.4); δ_C(125 MHz, $CDCl_3$) 21.0 (q), 33.4 (d), 33.8 (t), 37.2 (d), 110.1 (d), 116.8 (d), 140.0 (s), 145.0 (s) and 160.5 (s), and **5b** (47 mg, 13%), a pale yellow oil (Found: C, 81.1; H, 10.7; N, 7.8. $C_{12}H_{19}N$ requires C, 81.3; H, 10.8; N, 7.9%); ν_{max}(neat)/cm^{-1} 1591 (C=N); λ_{max}(EtOH)/nm 238 (log ε/dm^3 mol^{-1} cm^{-1} 3.88) and 280sh (3.45); δ_H(500 MHz, $CDCl_3$) 1.0 (1 H, m), 1.06 (6 H, d, *J* 6.8), 1.13 (6 H, d, *J* 6.8), 2.49 (1 H, hept, *J* 6.8), 2.64 (1 H, hept, *J* 6.8), 3.4 (1 H, br), 5.99 (1 H, d, *J* 6.3), 6.07 (1 H, d, *J* 6.3) and 6.49 (1 H, t, *J* 4.9); δ_C(125 MHz, $CDCl_3$) 22.2 (q), 22.3 (q), 34.7 (d), 35.6 (d), 36.1 (t), 110.8 (d), 120.0 (d), 134.1 (s), 136.6 (d) and 157.7 (s), were obtained.

Synthesis of 3,6-*Diisopropyl*-3H-*azepine* **7b**.—A solution of 1*H*-azepine **3b** (230 mg, 0.98 mmol) and DBU (1.7 g, 110 mmol) in nitrogen-purged dry xylene (2 cm^3) was refluxed for 5 h, after which the reaction mixture was treated as described before. MPLC gave 3*H*-azepine **7b** (74 mg, 43%), as a pale yellow oil (Found: C, 80.1; H, 11.0; N, 7.7. $C_{12}H_{19}N$ requires C, 81.3; H, 10.8; N, 7.9%); ν_{max}(neat)/cm^{-1} 1583 (C=N); λ_{max}(EtOH)/nm 230 (log ε/dm^3 mol^{-1} cm^{-1} 3.61) and 266 (sh, 3.44); δ_H(500 MHz, $CDCl_3$) 0.85 (1 H, m), 1.08 (3 H, d, *J* 6.8), 1.11 (3 H, d, *J* 6.8), 1.12 (3 H, d, *J* 6.8), 1.18 (d, 3 H, *J* 6.8), 2.13 (1 H, m), 2.59 (1 H, hept, *J* 6.8), 5.07 (1 H, dd, *J* 9.1 and 5.7), 6.27 (1 H, ddd, *J* 9.1, 1.7 and 1.7), 6.30 (1 H, d, *J* 4.9) and 7.32 (1 H, d, *J* 1.7); δ_C(125 MHz, $CDCl_3$) 20.5 (q), 20.8 (q), 23.4 (q), 23.7 (q), 28.4 (d), 33.9 (d), 51.9 (d), 118.1 (d), 125.7 (d), 136.8 (s), 136.9 (d) and 139.7 (d).

Synthesis of 2,5-*Dimethyl*-3H-*azepine* **4c**.—The dark brown reaction mixture obtained from the reaction of 1*H*-azepine **2c** (143 mg, 0.80 mmol) and DBU (1.21 g, 8.0 mmol) was heated to reflux in nitrogen-purged dry xylene (2 cm^3) solution for 5 h. The reaction mixture was cooled and introduced into a silica gel column, which was operated in a refrigerator room maintained at −2 °C, and eluted with ethyl acetate–hexane (1 : 4). Evaporation at 0 °C of the eluent under reduced pressure gave a labile 3*H*-azepine **4c** (43 mg, 44%), as a pale yellow oil; ν_{max}(neat)/cm^{-1} 1605 (C=N); λ_{max}(EtOH)/nm 235 (log ε/dm^3 mol^{-1} cm^{-1} 3.53) and 250 (3.55); δ_H(500 MHz, $CDCl_3$) 1.88 (3 H, s), 2.0 (2 H, br), 2.12 (3 H, s), 4.99 (1 H, t, *J* 6.8), 5.99 (1 H, d, *J* 8.3) and 7.15 (1 H, d, *J* 8.3); δ_C(125 MHz, $CDCl_3$) 21.0 (q), 20.9 (q), 26.3 (q), 37.2 (t), 112.5 (d), 119.2 (d), 135.5 (d), 139.7 (s) and 151.6 (s).

Synthesis of 3,6-*Dimethyl*-3H-*azepine* **7c**.—A solution of 1*H*-azepine **3c** (103 mg, 0.56 mmol) and DBU (860 mg, 5.7 mmol) in nitrogen-purged dry xylene (2 cm^3) when treated as described above gave the 3*H*-azepine **7c** (17.1 mg, 25%), as a pale yellow oil; ν_{max}(neat)/cm^{-1} 1605 (C=N); λ_{max}(EtOH)/nm 232 (log ε/dm^3 mol^{-1} cm^{-1} 3.64) and 250 (3.49); δ_H(500 MHz, $CDCl_3$) 1.2 (1 H, m), 1.52 (3 H, d, *J* 6.5), 2.05 (3 H, s), 4.88 (1 H, dd, *J* 8.9 and 5.3), 6.13 (1 H, dd, *J* 8.9 and 1.8), 6.20 (1 H, d, *J* 6.2) and 7.29 (1 H, s); δ_C(125 MHz, $CDCl_3$) 15.9 (q), 21.1 (q), 38.8 (d), 120.6 (d), 126.5 (d), 128.4 (d), 139.1 (s) and 141.7 (s), a compound more labile than **4c**.

Reaction of 2,4-*Di*-tert-*butyl*-3a,5a-*dihydro*-3H-*cyclobuta*-[b]*pyrrole* **12** *with DBU*.—A solution of 2,4-di-*tert*-butyl-3a,5a-dihydro-3*H*-cyclobuta[*b*]pyrrole **12** (57 mg, 0.28 mmol) and DBU (100 mg, 0.66 mmol) in dry xylene (1 cm^3) was refluxed under a nitrogen stream for 4 h. After cooling, a similar procedure to the demethoxycarbonylation of **2a** gave 3*H*-azepines **4a** (30 mg, 52%) and **5a** (10 mg, 18%).

Thermal Isomerization Reaction of 3,6-*Di*-tert-*butyl*-2H- and 3H-*azepines* **6a** *and* **7a**.—The respective xylene (1.5 cm^3) solutions of 2*H*-azepine **6a** (100 mg, 0.49 mmol) and 3*H*-azepine **7a** (100 mg, 0.49 mmol) were refluxed for 5 h under a nitrogen stream, and the resulting reaction mixtures were chromatographed on silica gel (Woelm 32–64) by MPLC. Compound **6a** and **7a** gave mixtures of **6a** (18 mg), **7a** (76 mg) and **8a** (1.5 mg), and **6a** (17 mg), **7a** (78 mg) and **8a** (1.4 mg), respectively.

Acknowledgements

We thank the SC-NMR Laboratory of Okayama University for the 500 and 200 MHz ^{1}H NMR and 125 and 50 MHz ^{13}C NMR measurements.

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Paper 4/00709C
Received 4*th February* 1994
Accepted 7*th March* 1994