

Nucleophilic Reactions of 5-*tert*-Butyl-2-methoxy-3*H*-azepine with Alkoxides and Alkyllithium Reagents

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The reaction of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) with sodium alkoxides gave 2-alkoxy-3*H*-azepine derivatives **3**–**6** by nucleophilic transetherification. The treatment of **2a** with *tert*-butyllithium also yielded 2,5-di-*tert*-butyl-3*H*-azepine (**7**); however, the reaction of **2a** and methyllithium gave the expected 5-*tert*-butyl-2-methyl-3*H*-azepine (**8**) along with unexpected 5-*tert*-butyl-2,2-dimethyl-2,3-dihydro-1*H*-azepine (**9**), but also 5,5′-di(*tert*-butyl)-2,2′-methylenedi(3*H*-azepine) (**11**), the structure of which was found to be tautomerized 5-*tert*-butyl-2-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidenemethyl)-3*H*-azepine (**12**). The energy profile for the observed tautomerization is discussed based on ab initio DFT calculations and kinetic measurements.

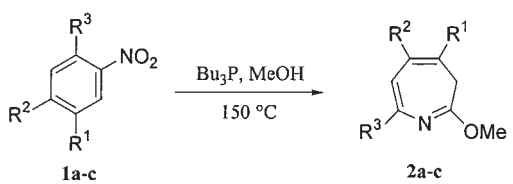
The parent 3*H*-azepine was first reported by E. Vogel et al. based on low-temperature NMR spectroscopy, and was found to be very unstable under ambient conditions.[1] The synthesis of stabilized 3*H*-azepines having an alkoxy or amino group at the 2-position on the ring has been well studied by means of an intramolecular ring-enlargement of the phenyl nitrene intermediate in nucleophilic media (i.e. amines or alcohols). However, the reaction of these 3*H*-azepines[2] has not necessarily been sufficiently explored. Although it has been known that the alkoxy group of the 2-alkoxy-3*H*-azepine derivative is displaced by alkylamines or carbanions from active methylene compounds,[3] a nucleophilic substitution reaction with the alkoxide ion has never been reported, so far. In order to explore the synthesis of stabilized 3*H*-azepines having an imidate conjugation with various alkoxy groups at the 2-position of 3*H*-azepines, we report here on the reaction of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) with sodium alkoxide in corresponding alcoholic media.

On the other hand, synthesis of 3*H*-azepines without any imidate and amidine conjugation on the ring was rarely explored.[4] Alkyl and/or aryl substituted 3*H*-azepines have been reported by Hassner et al.[5] and Göckel et al.[6] by means of a *hetero*-Diels–Alder reaction between highly strained small-ring olefins and appropriate dienes. Nitta et al. have also reported on the synthesis of 3-(2,4,6-cycloheptatrienyl)-3*H*-azepine from an iron carbonyl complex of ethyl 1*H*-azepine-1-carboxylate.[7] Recently, we reported a convenient procedure for preparing stable di-*tert*-butyl-3*H*-azepines by a direct demethoxycarbonylation reaction of methyl di-*tert*-butyl-1*H*-azepine-1-carboxylates under relatively drastic conditions using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[8] We employed the reaction of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) with alkyllithium reagents as an attempt to obtain 2,5-dialkyl-3*H*-azepines under more moderate reaction conditions and in more improved yields. A part of this work was recently reported as a preliminary communication.[9]

Results and Discussion

General synthetic methods for 2-alkoxy- and 2-alkylamino-3*H*-azepines have been known, that is, the thermolysis or photolysis of phenyl azide derivatives in the presence of alcohols[10] or alkylamines,[11] and the reduction of nitrobenzenes with phosphines in the presence of alcohols[12] or alkylamines.[13] In this work, the reduction method was applied for the synthesis of 2-methoxy-3*H*-azepines using 4-*tert*-butylnitrobenzene, 2-*tert*-butylnitrobenzene, and 2,5-di-*tert*-butylnitrobenzene (**1a**, **1b** and **1c**).

A solution of **1a** and tributylphosphine in methanol was heated in a sealed tube at 150 °C for 24 h. Subsequent distillation under reduced pressure of the reaction mixture gave 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) in 74% yield. The observed ^{1}H NMR signals for the olefinic ring protons at δ 5.15 (td, $J = 6.8$, 1.0 Hz, C4-H), 6.15 (dd, $J = 8.8$, 1.0 Hz, C6-H), and 6.94 (d, $J = 8.8$ Hz, C7-H) suggest the structure of **2a**. Similar procedures for 2-*tert*-butylnitrobenzene (**1b**) and 2,5-di-*tert*-butylnitrobenzene (**1c**) gave 7-*tert*-butyl-2-methoxy-3*H*-azepine (**2b**, 58%) and 4,7-di-*tert*-butyl-2-methoxy-3*H*-azepine (**2c**, 46%), respectively (Scheme 1). Olefinic protons of **2b** were observed at δ 5.24 (td, $J = 9.1$, 6.6 Hz, C4-H), 5.94 (d, $J = 5.7$ Hz, C6-H), and 6.18 (dd, $J = 9.1$, 5.7 Hz, C5-H) and those of **2c** were observed at δ 5.78 (d, $J = 6.2$ Hz, C6-H) and 5.97 (d, $J = 6.2$ Hz, C5-H). Olefinic signals for **2b** and **2c** suggest a lack of C7-H which would appear near to 6.9 ppm. Therefore, a *tert*-butyl group is considered to be situated at the C7-position on the respective 3*H*-azepine ring in both case. Three individual vicinal couplings for all ring protons,



1a-c **2a-c**

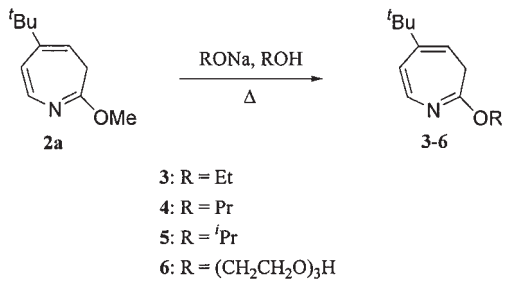
a: R^1 = H, R^2 = ^{t}Bu, R^3 = H
b: R^1 = H, R^2 = H, R^3 = ^{t}Bu
c: R^1 = ^{t}Bu, R^2 = H, R^3 = ^{t}Bu

Scheme 1.

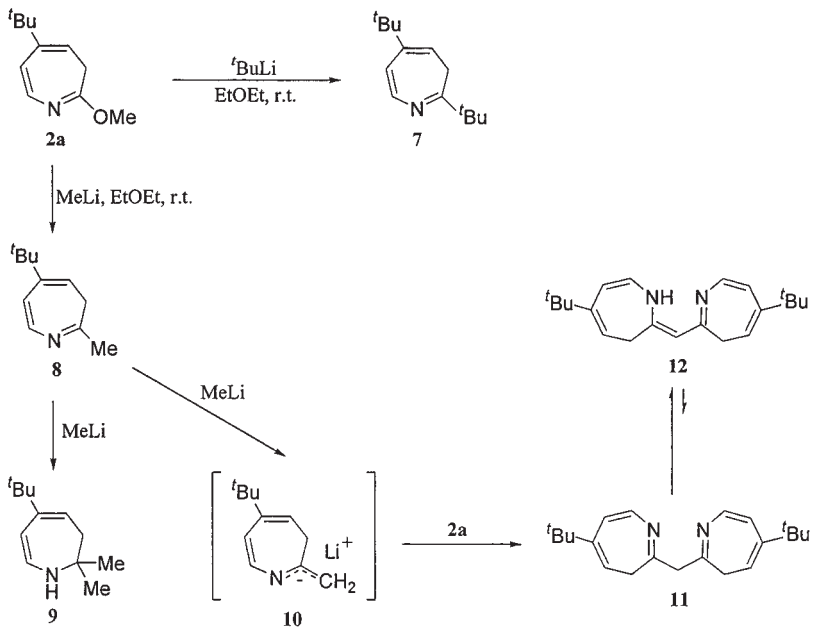
including the methylene group (C3-H_2) of **2b**, support the 2-methoxy-7-*tert*-butyl substitution pattern of the 3*H*-azepine ring; thus, the doublet signal at δ 2.57 (J = 6.6 Hz, 2H) is assigned to C3-H_2. In the case of **2c**, C3-H_2 is observed as a broad singlet signal at δ 2.59, and C4-H is omitted by the substitution of a *tert*-butyl group. Interestingly, no other possible structural isomer of 3*H*-azepine was formed from either nitrobenzene **1b** or **1c** under the reaction conditions.

To examine a behavior against alkoxide bases, 3*H*-azepine **2a** was employed. When a solution of **2a** and sodium ethoxide in ethanol was heated at under reflux temperature for 24 h, a transetherification reaction took place to produce 5-*tert*-butyl-2-ethoxy-3*H*-azepine (**3**) in 94% yeild. A similar procedure for **2a** with propoxide, isopropoxide and 2-[2-(2-hydroxyethoxy)ethoxy]ethoxide gave 5-*tert*-butyl-2-propoxy-3*H*-azepine (**4**, 95%), 5-*tert*-butyl-2-isopropoxy-3*H*-azepine (**5**, 92%), and 5-*tert*-butyl-2-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}-3*H*-azepine (**6**, 48%), respectively (Scheme 2). All of these compounds gave satisfactory analytical and spectroscopic data. The presented transetherification reaction is considered to be a formal nucleophilic displacement reaction of alkoxide.

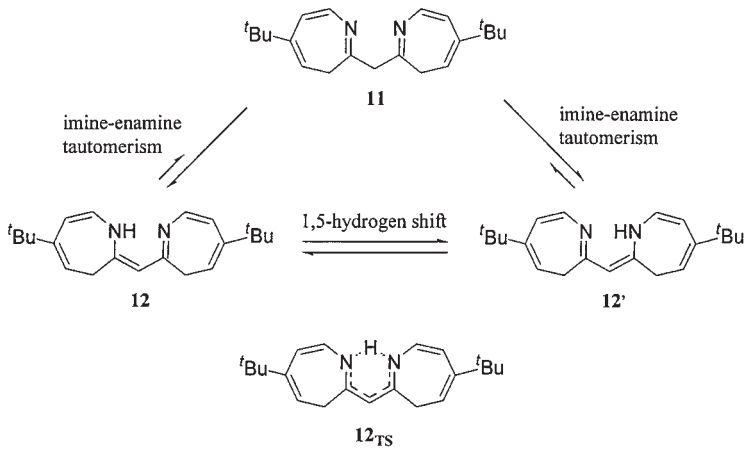
Previously, we reported on the synthesis of 2,5-di-*tert*-butyl-3*H*-azepine (**7**) by a demethoxycarbonylation reaction of methyl 2,5-di-*tert*-butyl-1*H*-azepine-1-carboxylate, which was obtained by the thermal degradation of methyl azidoformate in *p*-di-*tert*-butylbenzene.[8] In order to develop an alternative synthesis of **7**, a solution of **2a** in dry ether was treated with 1.5 molar amounts of *tert*-butyllithium at room temperature with stirring. Di-*tert*-butyl derivative **7** was obtained from the organic layer in 44% yield after quenching the reaction mixture with ice-water (Scheme 3). This procedure improved the total yield of 3*H*-azepine from benzene derivative by 10 or more times compared to a previously reported demethoxycarbonylation method.[4,8] To obtain a 2-methyl-3*H*-azepine derivatives under similar conditions, the reaction of **2a** with methyllithium was planned. Streef et al. reported that the reaction of 2-diethylamino-5-phenyl-3*H*-azepine with methyllithium resulted in the formation of 2-methyl-5-phenyl-3*H*-azepine.[14] When methyllithium was used as a nucleophile under similar conditions to substitute the methoxy group of **2a** with methanide, the expected 5-*tert*-butyl-2-methyl-3*H*-azepine (**8**) was obtained in 12% yield along with unexpected 5-*tert*-butyl-2,2-dimethyl-2,3-dihydro-1*H*-azepine (**9**) and 5-*tert*-butyl-2-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidenemethyl)-3*H*-azepine (**12**) as yellow needles in 37% and 25% yields, respectively (Scheme 3). The cyclic enamine structure of **9** was confirmed by the $\nu_{N\text{-}H}$ band at 3295 cm^{-1} in the IR spectrum and three olefinic proton signals at δ 4.63 (dd, J = 10.0, 1.7 Hz, 1H), 5.37 (td, J = 6.8, 1.7 Hz, 1H), 6.12 (dd, J = 10.0, 6.2 Hz, 1H) in ^{1}H NMR spectrum. The formation of **9** is able to explain a secondary attack of methanide to **8**, although such a sequential attack of 2-methylpropan-2-ide is prohibited, probably due to a steric hindrance. The molecular formula for the yellow solid was confirmed to be $C_{21}H_{30}N_2$ by HRMS (FAB), which showed m/z 311.2483 [$(M + H)^+$ calcd for $C_{21}H_{31}N_2$: 311.2487]. Therefore, 5,5′-di(*tert*-butyl)-2,2′-methylenedi(3*H*-azepine) (**11**) produced by another sequential reaction between the anion **10** generated from **8** and the starting 3*H*-azepine **2a** was expected based on the molecular formula and a symmetric structure suggested by the ^{1}H and ^{13}C NMR spectra. However, ^{1}H NMR signals at δ 4.42 (s, 1H) and 12.0 (br, 1H, D_2O exchangeable) and a ^{13}C NMR signal at δ 93.9 (d) were not able to be assigned to the structure **11**. A



Scheme 2.



Scheme 3.



Scheme 4.

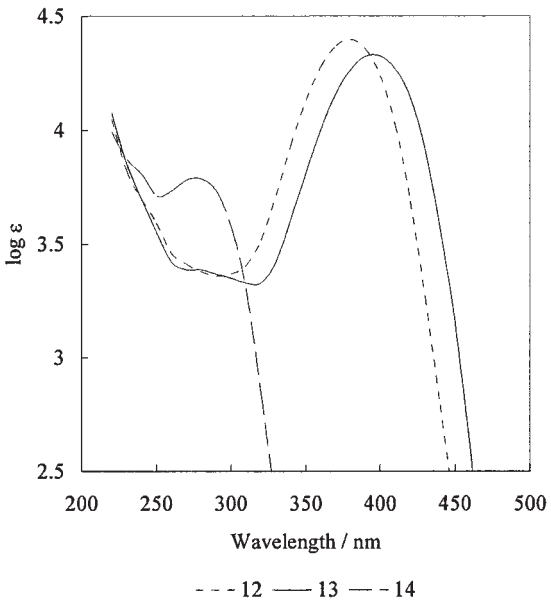
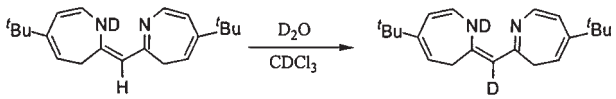


Fig. 1. Electronic spectra of **12**, **13** and **14** in ethanol.

satisfactory assignment for the observed symmetrical ^{1}H and ^{13}C NMR spectra is only possible when a tautomeric vinamidine **12** and its degenerate structure **12′** are interconverting with a faster rate than the NMR time scale via an intramolecular hydrogen bond (Scheme 4). A similar symmetric property in the NMR spectrum was also reported for more simple vinamidines.[15] An IR stretching band $\nu_{N\text{-}H}$ at 3046 cm^{-1} indicates the existence of an effective hydrogen bond; further the electronic spectrum also does not suggest a 3*H*-azepine ring, but an extended vinamidine conjugation by the λ_{max} at 380 nm (Fig. 1).

The prolonged H–D exchange reaction of **12** in $CDCl_3$ in the presence of excess D_2O resulted in not only a sudden disappearance of the signal at δ 12.0 (N–H), but also a gradual decreasing of the signal at δ 4.42 (center =CH–). A kinetic measurement for the latter H–D exchange rate was performed based on the signal intensity at δ 4.42 (Table 1). An Arrhenius plot showed a good linear correlation, which was represented by $\ln k = -8978/T + 21.56$, and gave kinetic parameters of $E_a = 74.7$ kJ/mol, $A = 2.30 \times 10^9$ s^{-1}, $\Delta H^{\ddagger} = 72.2$ kJ/mol, and $\Delta S^{\ddagger} = -74.0$ J/mol (Fig. 2). This should be attributed to imine-enamine

Table 1. Rate Constants k and Half-Lifes for the Imine–Enamine Tautomerism between **12** and **12′** in $CDCl_3$ at the Indicated Temperatures T



T/°C	$k^{a)}$/s^{-1}	$t_{1/2}{}^{a)}$/s	$r^{b)}$
22	1.43×10^{-4}	4848	0.9996
26	2.13×10^{-4}	3252	0.9996
30	3.05×10^{-4}	2268	0.9996
35	5.21×10^{-4}	1332	0.9983

a) k and $t_{1/2}$ were determined by plots of $\ln c/c_0$ versus t. b) r are the respective linear correlation coefficients.

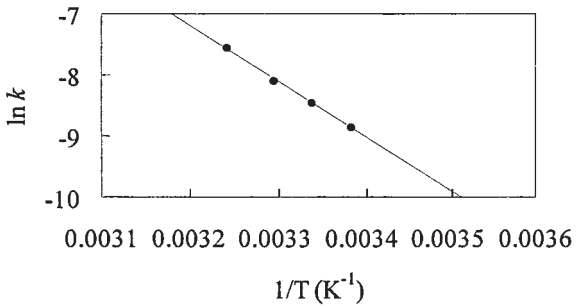


Fig. 2. The Arrhenius plot for the data of Table 1. The straight line is represented by $\ln k = -8978/T + 21.56$. Thus $E_a = 74.7$ kJ/mol, $A = 2.30 \times 10^9$ s^{-1}, $\Delta H^{\ddagger} = 72.2$ kJ/mol, and $\Delta S^{\ddagger} = -74.0$ J/mol. The respective linear correlation coefficient $r = 0.9991$.

tautomerizm by 1,3-prototropy via 2,2′-methylenedi(3*H*-azepine) **11**; however, the dominant path for an interconversion between **12** and **12′** is not ascribed to the imine-enamine tautomerizm because of a too moderate rate to understand the symmetrical ^{1}H and ^{13}C NMR spectra.

To obtain a theoretical background for the energies between **11**, vinamidine **12**, and transition state $\mathbf{12_{TS}}$, which is illustrated in Scheme 4, for the interconversion, calculations were performed using the Gaussian98 computer program.[16] A density functional method was employed using B3LYP[17] and the 6-31G*[18] basis set. All energies calculated here include zero-point energy corrections according to a reported scale factor.[19] The calcu-

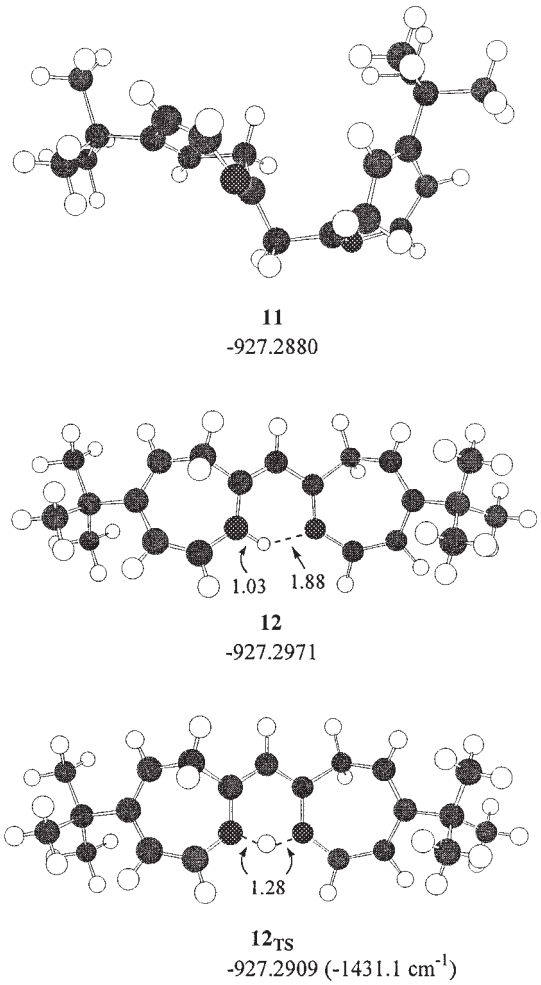


Fig. 3. Calculated structures for **11**, **12** and $\mathbf{12_{TS}}$. Atomic distances are in angstroms. Energies at B3LYP/6-31G* are in Hartrees. The value in parenthesis is a single imaginary frequency.

lated DFT energies for **11**, **12**, and $\mathbf{12_{TS}}$ based on the B3LYP/6-31G* levels were −927.2880, −927.2971, and −927.2909 Hartrees, respectively. The optimized structure for **11**, **12**, and $\mathbf{12_{TS}}$ are shown in Fig. 3 along with partial geometric parameters. Hexagonally arranged atoms including a methyne bridge across each azepine ring of **12** and $\mathbf{12_{TS}}$ are arranged in a plane. The calculated internuclear distances between the central hydrogen (N–H) and both sides of the nitrogen atom of **12** are 1.03 and 1.88 Å. In the transition structure $\mathbf{12_{TS}}$, the hydrogen is located on a C_2 symmetry axis with an internuclear distance of 1.28 Å. The calculation suggests that the methylenedi(3*H*-azepine) structure **11** is less stable than vinamidine structure **12** by 23.8 kJ/mol. Additionally, an optimized transition state $\mathbf{12_{TS}}$ of an interconversion between **12** and **12′** is more stable than **11** by 7.5 kJ/mol. The activation energy (E_a) for an interconversion by a 1,5-hydrogen shift between nitrogen atoms is estimated to be 16.3 kJ/mol. The energy profile of the degenerate interconversion between **12** and **12′**, and tautomerization between **11** and **12** is shown in Fig. 4. In conclusion, the rapid interconversion between **12** and **12′** should not be attributed to an imine-enamine tautomerism, but due dominantly to a direct hydrogen shift between two nitrogen atoms in the vinamidine conjugate system.

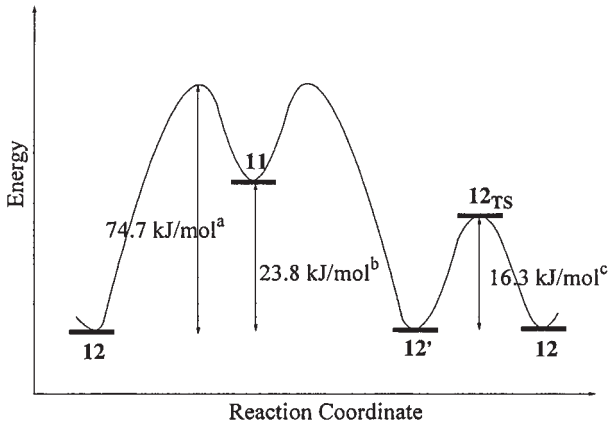
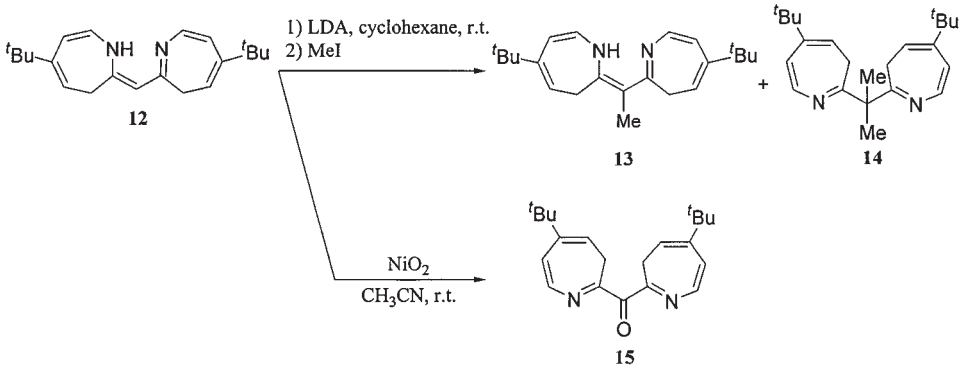


Fig. 4. Energy profile for **11**, **12**, and $\mathbf{12_{TS}}$. a) Arrhenius activation energy of imine-enamine tautomerism between **11** and **12**. b) Calculated energy difference between **11** and **12**. c) Calculated barrier of 1,5-hydrogen shift.

In order to explore the chemical properties of the newly occurred vinamidine **12**, a methylation reaction using methyl iodide was examined under basic conditions. Vinamidine **12** was found to resist against deprotonation under the conditions of an alkoxide base, because no product was obtained by a sequential treatment with sodium ethoxide and with methyl iodide. When lithium diisopropylamide (LDA) was added into a cyclohexane solution of **12**, the solution turned red, and the color then disappeared upon adding an excess amount of methyl iodide. After the mixture was stirred at room temperature for additional 3 hours, water was added. Two kinds of methylated compounds, 5-*tert*-butyl-2-[1-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidene)-ethyl]-3*H*-azepine (**13**) and 5,5′-di-*tert*-butyl-2,2′-(1-methyl-ethane-1,1-diyl)di-3*H*-azepine (**14**), were obtained from the organic layer in 27 and 40% yields, respectively (Scheme 5). The structure of **13** is considered to be methyl vinamidine, whose methyne proton at the center of the molecule was displaced by a methyl group. The ^{1}H- and ^{13}C-NMR signals of a seven-membered ring displayed a very similar pattern to that of **12**. An introduced methyl group is observed at δ_H 1.95 (s, 3H) and δ_C 15.3 (q). The electronic spectrum also suggests that compound **13** conserves the vinamidine conjugation by λ_{max} at 395 nm (Fig. 1). In contrast, compound **14** shows λ_{max} at 279 nm, which is attributed to the conjugation of 3*H*-azepine (cf. λ_{max} of **8** is 250 nm), and m/z 339 $[M + H]^+$ in MS (FAB). These data suggest that **14** is produced by secondary occurring methylation to the anionic species from **13**, and has a 1-methylethane-1,1-diylbisazepine structure. The ^{1}H-NMR signal assigned to methyl groups on a methylene bridge is observed at δ 1.25 (s, 6H). Signals for three olefinic protons are observed at δ 4.88 (br, 2H), 6.34 (dd, J = 8.8, 1.2 Hz, 2H), and 7.38 (d, J = 8.8 Hz, 2H), which are similar to those of monocyclic compound **8**. We next examined the behavior of **12** under the oxidation conditions using nickel peroxide (NiO_2), which has been known to be an effective dehydrogenation agent for nitrogen heterocycles.[20,21] A solution of **12** in acetonitrile was stirred at room temperature with freshly prepared NiO_2. After removing NiO_2 by filtration, an unexpected 5,5′-di-*tert*-butyl-2,2′-carbonyldi-3*H*-azepine (**15**) was obtained in quantitative yield. The structure of **15** was confirmed based on the $\nu_{C=O}$ IR band at 1676 cm^{-1}, olefinic proton signals at δ 5.24



Scheme 5.

(td, $J = 6.5$, 1.5 Hz, 2H), 6.61 (dd, $J = 8.5$, 1.5 Hz, 2H), and 7.59 (d, $J = 8.5$ Hz, 2H) in ^{1}H NMR, and m/z 325.2283 [(M + H)$^+$ calcd for $C_{21}H_{29}N_2O$: 325.2280] in HRMS (FAB). The signal pattern for olefinic protons obviously suggests a 2,5-disubstituted 3*H*-azepine. Although a dehydrogenation reaction could not be observed, the methyne bridge of the vinamidine **12** was found to be effectively oxidized to carbonyl by the action of NiO_2.

Conclusions

The nucleophilic reaction of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) with an appropriate alkoxide took place effectively at the 2-position of the ring. When bulky alkyllithium was used as a nucleophile, a similar displacement occurred to give a 2-alkyl-3*H*-azepine derivative as a single product. On the other hand, the reaction of **2a** with methyllithium gave not only 2-methyl-3*H*-azepine **8**, but also 2,2-dimethyl derivative **9** and methylene-di(3*H*-azepine) **11**, which tautomerized into the thermodynamically more stable vinamidine **12**.

We thank the SC-NMR Laboratory of Okayama University for ^{13}C and ^{1}H NMR spectral measurements.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-200 and/or XL-500 spectrometer. Infrared spectra were recorded on a JASCO FT-IR 5000 spectrophotometer. Fast Atom Bombardment (FAB) mass spectra were recorded on a Micromass 70-SE. GCMS were recorded on a JEOL JMS-DX300 mass spectrometer coupled to the JMA-3100 data analysis system. High Resolution Mass Spectra (HRMS) were obtained from the above instruments. Elemental analyses were performed on a PERKIN ELMER CHNS/O Analyzer 2400. Melting Points were measured on a Yanagimoto micromelting point apparatus and are uncorrected. UV-visible absorption was recorded on a Hitachi 288 spectrophotometer. Thin-layer chromatography (TLC) was performed on Silica gels HF_{254} (Merck). The molecular orbital calculations were carried out on a NEC SX5 computer system of Okayama University Computer Center.

5-*tert*-Butyl-2-methoxy-3*H*-azepine (2a): A solution of 4-*tert*-butylnitrobenzene (**1a**) (20.0 g, 112 mmol) and tributylphosphine (49.8 g, 246 mmol) in methanol (100 mL) was heated in a sealed tube at 150 °C for 24 hours, after which it was evaporated using a rotary evaporator under reduced pressure to remove the methanol. Distillation of the residue afforded 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (bp 54.0–56.0 °C/6.7 hPa, 14.8 g, Y = 74%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 9H), 2.59 (d, $J = 6.8$ Hz, 2H), 3.71 (s, 3H), 5.15 (td, $J = 6.8$, 1.0 Hz, 1H), 6.15 (dd, $J = 8.8$, 1.0 Hz, 1H), 6.94 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 30.0 (q), 32.5 (t), 34.5 (s), 54.4 (q), 110.1 (d), 115.5 (d), 137.4 (d), 148.6 (s), 154.8 (s); IR (neat) 2968, 1628, 1332, 1253, 1183 cm^{-1}; UV-vis (EtOH) λ_{max} 254 nm (log $\varepsilon = 3.68$); MS (FAB) m/z 180 [M + H]$^+$; Found: C, 73.77; H, 9.64; N, 7.67%. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81%.

7-*tert*-Butyl-2-methoxy-3*H*-azepine (2b): A solution of 2-*tert*-butylnitrobenzene (**1b**) (10.0 g, 55.8 mmol) and tributylphosphine (24.9 g, 123 mmol) in methanol (70 mL) was heated in a sealed tube at 150 °C for 24 hours, after which it was evaporated using a rotary evaporator under reduced pressure to remove the methanol. Distillation of the residue afforded 7-*tert*-butyl-2-methoxy-3*H*-azepine (**2b**) (bp 54.0–56.0 °C/5.3 hPa, 5.81 g, Y = 58%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18 (s, 9H), 2.57 (d, $J = 6.6$ Hz, 2H), 3.69 (s, 3H), 5.24 (td, $J = 9.1$, 6.6 Hz, 1H), 5.94 (d, $J = 5.7$ Hz, 1H), 6.18 (dd, $J = 9.1$, 5.7 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.6 (q), 32.9 (t), 37.3 (s), 54.1 (q), 106.6 (d), 114.6 (d), 127.8 (d), 148.9 (s), 158.7 (s); IR (neat) 2958, 1638, 1317, 1261, 1207, 1166 cm^{-1}; UV-vis (EtOH) λ_{max} 254 nm (log $\varepsilon = 3.61$); MS (FAB) m/z 180 [M + H]$^+$; Found: C, 74.04; H, 9.65; N, 7.95%. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81%.

4,7-Di-*tert*-butyl-2-methoxy-3*H*-azepine (2c): A solution of 2,5-di-*tert*-butylnitrobenzene (**1c**) (20.0 g, 85.0 mmol) and tributylphosphine (37.9 g, 187 mmol) in methanol (100 mL) was heated in a sealed tube at 150 °C for 48 hours, after which it was evaporated using a rotary evaporator under reduced pressure to remove the methanol. Distillation of the residue afforded 4,7-di-*tert*-butyl-2-methoxy-3*H*-azepine (**2c**) (bp 69.0–72.0 °C/2.7 hPa, 9.23 g, Y = 46%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.12 (s, 9H), 1.17 (s, 9H), 2.59 (brs, 2H), 3.68 (s, 3H), 5.78 (d, $J = 6.2$ Hz, 1H), 5.97 (d, $J = 6.2$ Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.8 (q), 29.6 (q), 33.5 (t), 36.1 (s), 37.0 (s), 53.8 (q), 106.9 (d), 118.3 (d), 138.2 (s), 150.6 (s), 156.8 (s); IR (neat) 2960, 1638, 1317, 1272, 1261, 1185 cm^{-1}; UV-vis (EtOH) λ_{max} 257 nm (log $\varepsilon = 3.76$); MS (FAB) m/z 236 [M + H]$^+$; Found: C, 76.78; H, 10.55; N, 5.96%. Calcd for $C_{15}H_{25}NO$: C, 76.55; H, 10.71; N, 5.95%.

5-*tert*-Butyl-2-ethoxy-3*H*-azepine (3): A solution of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (500 mg, 2.79 mmol) and sodium ethoxide (8.4 mmol) in ethanol (40 mL) was refluxed for 24 hours, after which it was evaporated in vacuo. Water was added to residue, after which it was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated in vacuo. A chromatographic treatment of a residue on silica gel (hexane:ethyl acetate = 9:1) gave 5-*tert*-butyl-2-ethoxy-3*H*-azepine (**3**) (505 mg, Y = 94%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 9H), 1.26 (t, $J = 7.2$ Hz, 3H), 2.54 (d, $J = 6.8$ Hz, 2H), 4.12 (q, $J = 7.2$ Hz, 2H), 5.15 (td, $J = 6.8$,

1.4 Hz, 1H), 6.13 (dd, J = 8.6, 1.4 Hz, 1H), 6.92 (d, J = 8.6 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.0 (q), 29.9 (q), 32.8 (t), 34.4 (s), 62.7 (t), 110.0 (d), 115.0 (d), 137.5 (d), 148.4 (s), 153.9 (s); IR (neat) 2968, 1626, 1325, 1251, 1183, 1029 cm^{-1}; UV-vis (EtOH) λ_{max} 254 nm ($\log \varepsilon$ = 3.77); MS (FAB) m/z 194 $[M + H]^+$; Found: C, 74.59; H, 9.94; N, 7.12%. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25%.

5-*tert*-Butyl-2-propoxy-3*H*-azepine (4): A solution of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (300 mg, 1.67 mmol) and sodium propoxide (5.0 mmol) in 1-propanol (7 mL) was refluxed for 24 hours, after which it was evaporated in vacuo. Water was added to the residue, after which it was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated in vacuo. A chromatographic treatment of the residue on silica gel (hexane:ethyl acetate = 9:1) gave 5-*tert*-butyl-2-propoxy-3*H*-azepine (**4**) (330 mg, Y = 95%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, J = 7.2 Hz, 3H), 1.06 (s, 9H), 1.61 (tq, J = 7.2, 6.8 Hz, 2H), 2.50 (d, J = 6.7 Hz, 2H), 3.98 (t, J = 6.8 Hz, 2H), 5.11 (td, J = 6.7, 1.4 Hz, 1H), 6.09 (dd, J = 8.8, 1.4 Hz, 1H), 6.88 (d, J = 8.8 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.3 (q), 21.8 (t), 29.9 (q), 32.8 (t), 34.4 (s), 68.6 (t), 110.0 (d), 115.0 (d), 137.5 (d), 148.4 (s), 154.1 (s); IR (neat) 2968, 1624, 1323, 1249, 1183 cm^{-1}; UV-vis (EtOH) λ_{max} 254 nm ($\log \varepsilon$ = 3.70); MS (FAB) m/z 208 $[M + H]^+$; Found: C, 75.12; H, 10.19; N, 6.92%. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76%.

5-*tert*-Butyl-2-isopropoxy-3*H*-azepine (5): A solution of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (500 mg, 2.79 mmol) and sodium isopropoxide (8.4 mmol) in 2-propanol (40 mL) was refluxed for 24 hours, after which it was evaporated in vacuo. Water was added to the residue, after which it was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated in vacuo. A chromatographic treatment of the residue on silica gel (hexane:ethyl acetate = 9:1) gave 5-*tert*-butyl-2-isopropoxy-3*H*-azepine (**5**) (530 mg, Y = 92%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 9H), 1.19 (d, J = 6.3 Hz, 6H), 2.51 (d, J = 7.4 Hz, 2H), 4.99 (hept, J = 6.3 Hz, 1H), 5.12 (td, J = 7.4, 1.2 Hz, 1H), 6.12 (dd, J = 8.8, 1.2 Hz, 1H), 6.92 (d, J = 8.8 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.5 (q), 30.0 (q), 33.4 (t), 34.5 (s), 69.2 (d), 109.8 (d), 114.6 (d), 137.5 (d), 148.5 (s), 152.6 (s); IR (neat) 2968, 1620, 1365, 1317, 1249, 1183 cm^{-1}; UV-vis (EtOH) λ_{max} 254 nm ($\log \varepsilon$ = 3.44); MS (FAB) m/z 208 $[M + H]^+$; Found: C, 75.10; H, 10.16; N, 6.51%. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76%.

5-*tert*-Butyl-2-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}-3*H*-azepine (6): A solution of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (500 mg, 2.79 mmol) and sodium 2-[2-(2-hydroxyethoxy)ethoxy]ethoxide (17.0 mmol) in triethylene glycol (40 mL) was heated at 80 °C for 24 hours. Water was added to the solution, after which it was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated in vacuo. A chromatographic treatment of the residue on silica gel (hexane:ethyl acetate = 9:1) gave 5-*tert*-butyl-2-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}-3*H*-azepine (**6**) (397 mg, Y = 48%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 9H), 2.58 (d, J = 6.6 Hz, 2H), 3.45 (brs, 1H), 3.66–3.75 (m, 10H), 4.25 (t, J = 4.7 Hz, 2H), 5.15 (t, J = 6.6 Hz, 1H), 6.15 (d, J = 8.6 Hz, 1H), 6.90 (d, J = 8.6 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.8 (q), 32.4 (t), 34.4 (s), 61.5 (t), 66.0 (t), 69.1 (t), 70.2 (t), 70.4 (t), 72.4 (t), 110.2 (d), 115.4 (d), 137.0 (d), 148.3 (s), 153.7 (s); IR (neat) 3400, 2966, 1624, 1323, 1251, 1183, 1125, 1069 cm^{-1}; UV-vis (EtOH) λ_{max} 254 nm ($\log \varepsilon$ = 3.52); HRMS (FAB) m/z calcd for $C_{16}H_{28}NO_4$ $[M + H]^+$ 298.2018, found 298.2017; Found: C, 64.84; H, 8.91; N, 4.92%. Calcd for $C_{16}H_{27}NO_4$: C, 64.62; H, 9.15; N, 4.71%.

2,5-Di-*tert*-butyl-3*H*-azepine (7): A solution of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (500 mg, 2.79 mmol) in 100 mL of anhydrous diethyl ether was treated with 1.5 molar amounts of *tert*-butyllithium (1.7 M in pentane) (1 M = 1 mol dm^{-3}) at room temperature. The solution was stirred at room temperature for 3 hours, after which water was added to quench the reaction. The solution was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated in vacuo. A chromatographic treatment of the residue on silica gel (hexane:ethyl acetate = 9:1) gave 2,5-di-*tert*-butyl-3*H*-azepine (**7**) (254 mg, Y = 44%) as colorless prisms. Mp 20.5–21.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.10 (brs, 1H), 1.14 (s, 9H), 3.57 (brs, 1H), 5.03 (t, J = 7.0 Hz, 1H), 6.28 (d, J = 8.2 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.7 (q), 30.3 (q), 32.4 (t), 34.4 (s), 38.1 (s), 110.0 (d), 115.9 (d), 139.7 (d), 147.3 (s), 164.0 (s); IR (neat) 2968, 1609, 1499, 1464, 1365, 1112, 853, 791 cm^{-1}; UV-vis (EtOH) λ_{max} 235 ($\log \varepsilon$ = 3.53) and 250 (3.55); GCMS m/z 205 ($[M]^+$, 54.1%); Found: C, 81.78; H, 11.35; N, 6.47%. Calcd for $C_{14}H_{23}N$: C, 81.89; H, 11.29; N, 6.82%.

Reaction of 5-*tert*-Butyl-2-methoxy-3*H*-azepine (2a) with Methyllithium. A solution of 5-*tert*-butyl-2-methoxy-3*H*-azepine (**2a**) (500 mg, 2.79 mmol) in 100 mL of anhydrous diethyl ether was treated with 2.2 molar amounts of methyllithium (1.14 M in diethyl ether) at room temperature. The solution was stirred at room temperature for 5 hours, after which water was added to quench the reaction. The solution was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated in vacuo. A chromatographic treatment of the residue on silica gel (hexane:ethyl acetate = 9:1) gave 5-*tert*-butyl-2-methyl-3*H*-azepine (**8**) (54 mg, Y = 12%) as a colorless oil, 5-*tert*-butyl-2,2-dimethyl-2,3-dihydro-1*H*-azepine (**9**) (183 mg, Y = 37%) as a colorless oil, and 5-*tert*-butyl-2-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidenemethyl)-3*H*-azepine (**12**) (112 mg, Y = 25%) as yellow needles.

5-*tert*-Butyl-2-methyl-3*H*-azepine (8): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.11 (s, 9H), 2.17 (s, 3H), 2.20 (brs, 2H), 5.11 (td, J = 6.8, 1.0 Hz, 1H), 6.30 (dd, J = 8.7, 1.0 Hz, 1H), 7.24 (d, J = 8.7 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.2 (q), 30.1 (q), 34.4 (s), 37.0 (t), 109.3 (d), 116.6 (d), 140.2 (d), 148.2 (s), 153.1 (s); IR (neat) 2968, 1622, 1429, 1367, 847, 795, 526 cm^{-1}; UV-vis (EtOH) λ_{max} 250 (sh) nm ($\log \varepsilon$ = 3.49); HRMS (FAB) m/z calcd for $C_{11}H_{18}N$ $[M + H]^+$ 164.1439, found 164.1411.

5-*tert*-Butyl-2,2-dimethyl-2,3-dihydro-1*H*-azepine (9): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.07 (s, 6H), 1.09 (s, 9H), 2.08 (d, J = 6.8 Hz, 2H), 3.80 (brs, 1H), 4.63 (dd, J = 10.0, 1.7 Hz, 1H), 5.37 (td, J = 6.8, 1.7 Hz, 1H), 6.12 (dd, J = 10.0, 6.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.9 (q), 30.0 (q), 35.2 (s), 42.6 (t), 55.7 (s), 94.5 (d), 113.0 (d), 132.0 (d), 148.3 (s); IR (neat) 3295, 2966, 1756, 1464, 1365, 1160 cm^{-1}; MS (FAB) m/z 180 $[M + H]^+$; Found: C, 79.91; H, 11.32; N, 8.28%. Calcd for $C_{12}H_{21}N$: C, 80.38; H, 11.81; N, 7.81%.

5-*tert*-Butyl-2-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidenemethyl)-3*H*-azepine (12): Mp 151.0–151.5 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.09 (s, 18H), 2.63 (d, J = 6.8 Hz, 4H), 4.42 (s, 1H), 5.24 (td, J = 6.8, 1.2 Hz, 2H), 5.85 (dd, J = 9.0, 1.2 Hz, 2H), 6.83 (d, J = 9.0 Hz, 2H), 12.0 (brs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.9 (q), 34.7 (s), 36.2 (t), 93.9 (d), 113.4 (d), 114.1 (d), 134.8 (d), 148.6 (s), 155.4 (s); IR (KBr) 3046, 2954, 1620, 1586, 1547, 1499, 1429, 1365, 1334, 1311, 1114, 764 cm^{-1}; UV-vis (EtOH) λ_{max} 380 nm ($\log \varepsilon$ = 4.40); HRMS (FAB) m/z calcd for $C_{21}H_{31}N_2$ $[M + H]^+$ 311.2487, found 311.2483; Found: C, 81.36; H, 9.82; N, 9.08%. Calcd for $C_{21}H_{30}N_2$: C, 81.24; H, 9.74; N, 9.02%.

Reaction of 12 with LDA and Methyl Iodide. Two molar amounts of LDA (1.5 M in cyclohexane) were added to a solution of 5-*tert*-butyl-2-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidenemethyl)-3*H*-azepine (**12**) (700 mg, 2.26 mmol) in 40 mL of anhydrous cyclohexane at room temperature under stirring. After 20 minutes, methyl iodide (1.12 mL, 18.0 mmol) was added. The solution was

stirred at room temperature for 3 hours, after which water was added. As the mixture was separated into two phases, a cyclohexane layer was obtained. The organic layer was dried over $MgSO_4$ and evaporated in vacuo. Methanol was added to the residue and washed with methanol. Filtration of the precipitate gave 5-*tert*-butyl-2-[1-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidene)ethyl]-3*H*-azepine (**13**) (139 mg, Y = 27%) as yellow needles. A chromatographic treatment of the filtrate on silica gel (hexane:ethyl acetate = 19:1) gave 5,5′-di-*tert*-butyl-2,2′-(1-methylethane-1,1-diyl)di-3*H*-azepine (**14**) (306 mg, Y = 40%) as yellow prisms.

5-*tert*-Butyl-2-[1-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidene)ethyl]-3*H*-azepine (13): Mp 126.0–127.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.10 (s, 18H), 1.95 (s, 3H), 2.68 (d, J = 7.5 Hz, 4H), 5.28 (td, J = 7.5, 1.5 Hz, 2H), 5.86 (dd, J = 8.5, 1.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3 (q), 30.1 (q), 32.7 (t), 34.6 (s), 111.4 (d), 112.4 (d), 116.9 (s), 134.5 (d), 149.2 (s), 155.1 (s); IR (KBr) 3044, 2966, 1618, 1578, 1491, 1365, 1301, 1180, 774 cm^{-1}; UV-vis (EtOH) λ_{max} 395 nm (log ε = 4.33); MS (FAB) m/z 325 $[M + H]^+$; Found: C, 81.23; H, 9.99; N, 8.40%. Calcd for $C_{22}H_{32}N_2$: C, 81.43; H, 9.94; N, 8.63%.

5,5′-Di-*tert*-butyl-2,2′-(1-methylethane-1,1-diyl)di-3*H*-azepine (14): Mp 51.0–52.0 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08 (s, 18H), 1.25 (s, 6H), 1.45 (brs, 2H), 3.33 (brs, 2H), 4.88 (brs, 2H), 6.34 (dd, J = 8.8, 1.2 Hz, 2H), 7.38 (d, J = 8.8 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.6 (q), 30.2 (q), 33.6 (t), 34.4 (s), 50.1 (s), 111.7 (d), 116.5 (d), 139.8 (d), 147.3 (s), 159.4 (s); IR (KBr) 2966, 1601, 1464, 1365, 1267, 1116, 1089, 1038, 791 cm^{-1}; UV-vis (EtOH) λ_{max} 279 nm (log ε = 3.80); MS (FAB) m/z 339 $[M + H]^+$; Found: C, 81.83; H, 10.19; N, 8.07%. Calcd for $C_{23}H_{34}N_2$: C, 81.60; H, 10.12; N, 8.28%.

5,5′-Di-*tert*-butyl-2,2′-carbonyldi-3*H*-azepine (15): Nickel peroxide was added to a solution of 5-*tert*-butyl-2-(5-*tert*-butyl-2,3-dihydro-1*H*-azepin-2-ylidenemethyl)-3*H*-azepine (**12**) (50 mg, 0.161 mmol) in 30 mL of acetonitrile at room temperature for 24 hours under stirring. The reaction solution was filtrated to remove nickel peroxide and 5,5′-di-*tert*-butyl-2,2′-carbonyldi-3*H*-azepine (**15**) as yellow oil (53 mg, Y = 99%) was obtained by evaporation of the filtrate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (s, 18H), 5.24 (td, J = 6.5, 1.5 Hz), 6.61 (dd, J = 8.5, 1.5 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), methylene protons were not observed; ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.2 (q), 32.1 (t), 34.8 (s), 112.3 (d), 120.5 (d), 139.4 (d), 146.2 (s), 148.6 (s), 191.5 (s); IR (neat) 2968, 1676, 1603, 1357, 1265, 1050, 797 cm^{-1}; UV-vis (EtOH) λ_{max} 270 (sh) nm (log ε = 3.52), 334 (sh) nm (log ε = 3.31); HRMS (FAB) m/z calcd for $C_{21}H_{29}N_2O$ $[M + H]^+$ 325.2280, found 325.2283.

References

1 E. Vogel, H. J. Altenbach, J. M. Drossard, H. Schmickler, and H. Stegelmeier, *Angew. Chem., Int. Ed. Engl.*, **19**, 1016 (1980).

2 R. J. Sundberg, B. P. Das, and R. H. Smith, Jr., *J. Am. Chem. Soc.*, **91**, 658 (1969); E. Leyva and R. Sagredo, *Tetrahedron*, **60**, 7367 (1998); C. G. Younger and R. A. Bell, *J. Chem. Soc., Chem. Commun.*, **1992**, 1359; C. J. Shields, D. R. Chrisope, G. B. Schuster, A. J. Dixon, M. Poliakoff, and J. J. Turner, *J. Am. Chem. Soc.*, **109**, 4723 (1987).

3 S. Bátorit, R. Gompper, J. Meier, and H. U. Wagner, *Tetrahedron*, **44**, 3309 (1988).

4 K. Satake, R. Okuda, M. Hashimoto, Y. Fujiwara, I. Watadani, H. Okamoto, M. Kimura, and S. Morosawa, *J. Chem. Soc., Chem. Commun.*, **1991**, 1154; K. Satake, R. Okuda, M. Hashimoto, Y. Fujiwara, H. Okamoto, M. Kimura, and S. Morosawa, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 1753; K. Satake, K. Takaoka, M. Hashimoto, H. Okamoto, M. Kimura, and S. Morosawa, *Chem. Lett.*, **1996**, 1129.

5 D. J. Anderson and A. Hassner, *J. Am. Chem. Soc.*, **93**, 4339 (1971); A. Hassner and D. J. Anderson, *J. Org. Chem.*, **39**, 3070 (1974).

6 U. Göckel, U. Hartmannsgruber, A. Steigel, and J. Sauer, *Tetrahedron Lett.*, **21**, 595 (1980).

7 M. Nitta, K. Shibata, and H. Miyano, *Heterocycles*, **29**, 253 (1989).

8 K. Satake, R. Okuda, M. Hashimoto, Y. Fujiwara, H. Okamoto, M. Kimura, and S. Morosawa, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 1753.

9 K. Satake, Y. Kubota, H. Okamoto, and M. Kimura, *Heterocycles*, **57**, 223 (2002).

10 Y. Ohba, S. Kubo, M. Nakai, A. Nagai, and M. Yoshimoto, *Bull. Chem. Soc. Jpn.*, **59**, 2317 (1986); R. Purvis, R. K. Smalley, H. Suschitzky, and M. A. Alkhader, *J. Chem. Soc., Perkin Trans. 1*, **1984**, 249.

11 R. Huisgen, D. Vossius, and M. Appl, *Chem. Ber.*, **91**, 1 (1958); R. Huisgen and M. Appl, *Chem. Ber.*, **91**, 12 (1958); W. V. E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966); E. Meyer and G. Griffin, *Angew. Chem.*, **79**, 648 (1967); *Angew. Chem., Int. Ed. Engl.*, **6**, 634 (1967); B. A. DeGraff, D. W. Gillespie, and R. J. Sundberg, *J. Am. Chem. Soc.*, **96**, 7791 (1974); R. J. Sundberg and R. W. Heintzelman, *J. Org. Chem.*, **39**, 2546 (1974); S. E. Carroll, B. Nay, E. F. V. Scriven, and H. Suschitzky, *Tetrahedron Lett.*, **18**, 943 (1977); E. Leyva, M. S. Platz, G. Persy, and J. Wirz, *J. Am. Chem. Soc.*, **108**, 3783 (1986).

12 M. Masaki, K. Fukui, and J. Kita, *Bull. Chem. Soc. Jpn.*, **50**, 2013 (1977).

13 F. R. Atherton and R. W. Lambert, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 1079.

14 J. W. Streef, H. C. van der Plas, and A. van Veldhuizen, *Recl. Trav. Chim. Pays-Bas.*, **103**, 225 (1984).

15 R. Knorr and A. Weiß, *Chem. Ber.*, **114**, 2104 (1981).

16 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, "Gaussian 98, Revision A.7," Gaussian, Inc., Pittsburgh PA, 1998.

17 A. D. Becke, *J. Chem. Phys.*, **98**, 5648 (1993); C. Lee, W. Yang, and R. G. Parr, *Phys. Rev. B*, **37**, 785 (1988).

18 P. C. Hariharan and J. A. Pople, *Theor. Chim. Acta.*, **28**, 213 (1973).

19 C. W. Bauschlicher, Jr. and H. Partridge, *J. Chem. Phys.*, **103**, 1788 (1995); M. W. Wong, *Chem. Phys. Lett.*, **256**, 391 (1996); A. P. Scott and L. Radom, *J. Phys. Chem.*, **100**, 16502 (1996).

20 S. Tanaka, K. Satake, A. Kiyomine, T. Kumagai, and T. Mukai, *Angew. Chem., Int. Ed. Engl.*, **27**, 1061 (1988); K. Satake, D. Nakoge, and M. Kimura, *Heterocycles*, **48**, 433 (1998).

21 M. Nitta, Y. Lino, E. Hara, and T. Kobayashi, *J. Chem. Soc., Perkin Trans. 1*, **1989**, 51.