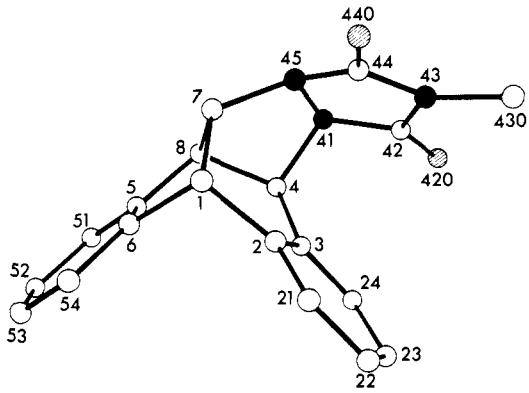


Figure 1. Perspective drawing of the urazole **15** with the labeling of the atoms corresponding to Tables I and II; white, black, and hatched spheres represent carbon, nitrogen, and oxygen atoms, respectively.

flections. In the range $3.0° \leq 2\theta \leq 55.0°$, 2307 reflections were obtained which were utilized for the structure determination. For the evaluation the SHELXTL system on a Eclipse S250 at the Max-Planck-Institut für Festkörperforschung was employed. The structure was solved by direct phase determination. The phases of 342 strong reflections were determined and on the resulting E map approximate positions of all C, N, and O atoms could easily be determined. Positional and thermal parameters could be refined by anisotropic least-squares cycles to $R = 0.067$. The positions of the hydrogen atoms were calculated geometrically and considered isotropically in all refinements.

Urazole **15** crystallizes orthorhombically in the space group *Pbca* with $a = 1499.2$ (2) pm, $b = 2397.4$ (4) pm, and $c = 847.9$ (1) pm. The unit cell contains $Z = 8$ formula units, the density was calculated to be 1.383 $Mg \cdot m^{-3}$. All atomic parameters are listed in Table II. The labeling of the atoms can be seen in Figure 1. Bond distances and bond angles are summarized in Table III.

Acknowledgment is made to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the National Institutes of Health, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for generous financial support. We thank Professor H. Hopf, University of Braunschweig, for measuring the ^{13}C NMR spectra for us.

Registry No. 1, 2734-13-6; **2**, 2199-28-2; **3**, 262-89-5; **4**, 17509-84-1; **9**, 82639-35-8; **10**, 82639-36-9; **14**, 78500-30-8; **15**, 82639-37-0; MTAD, 13274-43-6.

Electroorganic Chemistry. 62. Reaction of Iminium Ion with Nucleophile: A Versatile Synthesis of Tetrahydroquinolines and Julolidines

Tatsuya Shono,* Yoshihiro Matsumura, Kenji Inoue, Hiroshi Ohmizu, and Shigenori Kashimura

Contribution from the Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Sakyo, Kyoto 606, Japan. *Received February 4, 1982*

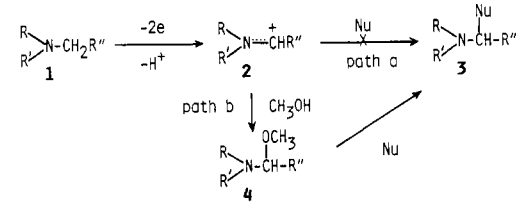
Abstract: A versatile synthetic method of tetrahydroquinolines and julolidines has been developed. The method involves the anodic oxidation of *N,N*-dimethylaniline in methanol to afford α-methoxylated or α,α'-dimethoxylated compounds and subsequent treatment of the products with Lewis acids in the presence of nucleophiles. Simple and electron-rich olefins such as alkenes, styrene, enol ethers, silyl enol ethers, enamines, and enol esters are usable as the nucleophiles. The intermediary formation of iminium ions from the methoxylated compounds is proposed as one of the key steps. The nucleophilic reaction of Grignard reagents with the methoxylated compounds in the presence of Lewis acid is also described.

Although anodic oxidation of amines or their derivatives (**1**) (Scheme I) has been known to be a versatile tool in generating iminium ion intermediates (**2**),[1] the trapping of **2** with carbanion or the like under conditions of anodic oxidation (path a) is almost impossible, since except cyanide ion,[2] the nucleophiles mentioned above are generally unstable under the reaction conditions.

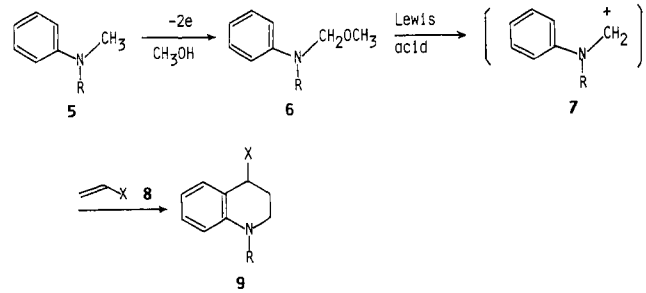
We have recently found, however, that **2** ($R' = CO_2CH_3$) can be trapped efficiently with a variety of nucleophiles when **2** is first trapped with methanol to give α-methoxylated carbamates (**4**, $R' = CO_2CH_3$) followed by regeneration of **2** from **4** with Lewis acid catalysts in the presence of nucleophiles (path b).[3] This concept of trapping and regeneration of iminium ion may be applicable to amines other than carbamates of aliphatic amines.

According to the above concept, we describe herein a versatile perparation of tetrahydroquinolines (**9**) and julolidines (**34** and **35**) starting from *N*-methyl-*N*-alkylanilines (**5**). Scheme II illustrates our method, which involves the anodic oxidation of **5** in methanol and subsequent treatment of the oxidized products (**6**) with Lewis acid to regenerate iminium ions (**7**) that can be

Scheme I



Scheme II



(1) For examples, see (a) Barnes, K. K.; Mann, C. K. *J. Org. Chem.* **1967**, *32*, 1474. (b) Barry, J. E.; Finkelstein, M.; Mayeda, E. A.; Ross, S. D. *Ibid.* **1974**, *39*, 2695. (c) Shono, T.; Hamaguchi, H.; Matsumara, Y. *J. Am. Chem. Soc.* **1975**, *97*, 4264.

(2) Chiba, T.; Takaya, Y. *J. Org. Chem.* **1977**, *42*, 2973.

(3) (a) Shono, T.; Matsumura, Y.; Tsubata, K. *J. Am. Chem. Soc.* **1981**, *103*, 1172. (b) Shono, T.; Matsumura, Y.; Tsubata, K.; Takata, J. *Chem. Lett.* **1981**, 1121. (c) Shono, T.; Matsumura, Y.; Tsubata, K. *Tetrahedron Lett.* **1981**, *22*, 2411. (d) *Ibid.* **1981**, *22*, 3249.

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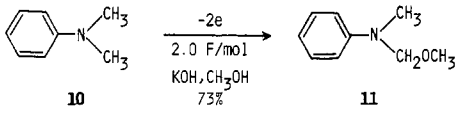
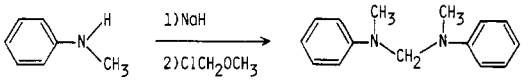
trapped in situ with a variety of electron-rich olefins (**8**) to yield **9**. The nucleophilic reaction of Grignard reagents with **6** is also described.

Results and Discussion

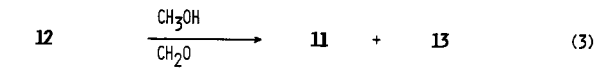
Synthesis of α-Methoxy- and α,α′-Dimethoxy-*N*,*N*-dialkylanilines. The iminium ion formed by the anodic oxidation of *N*,*N*-dimethylaniline (**10**) is easily trapped by methanol according to the method described in the literature.[4] Although the α-methoxylated compound (**11**) may be thought to be synthesized by the alkylation of *N*-metylaniline (**12**) with chloromethyl methyl ether or by the Mannich reaction[5] of **12** with formaldehyde and methanol, these methods were not satisfactory, as shown in eq 2 and 3.



10 11 (1)

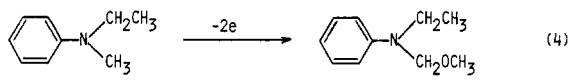


12 13 (2)



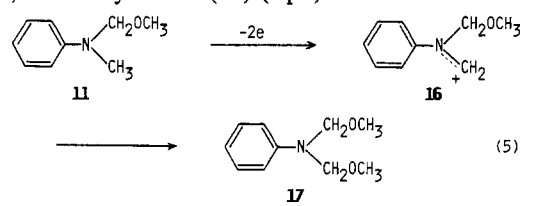
12 → 11 (32%) + 13 (31%) (3)

One of the advantages of the anodic method is its high regioselectivity as shown in the oxidation of *N*-ethyl-*N*-methylaniline (**14**), in which the methoxylation takes place at the methyl group exclusively.



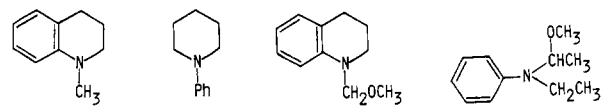
14 15 (4)

Further anodic oxidation of **11** yields a new iminium ion (**16**), which can easily be trapped by methanol to form α,α′-dimethoxy-*N*,*N*-dimethylaniline (**17**) (eq 5).



11 16 → 17 (5)

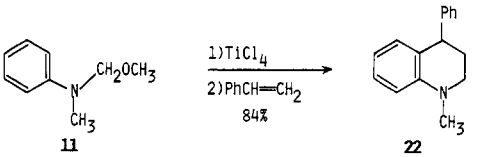
The anodic oxidation of *N*-methyltetrahydroquinoline (**18**) or



18 19 20 21

N-phenylpiperidine (**19**), however, was not successful, because their oxidation products might be unstable[6] under the conditions of anodic oxidation, whereas *N*-(methoxymethyl)tetrahydroquinoline (**20**) was obtainable by the alkylation of tetrahydroquinoline with chloromethyl methyl ether, but in low yield (43%). On the other hand, the anodic oxidation of *N*,*N*-diethylaniline gave α-methoxylated product **21** in 60% yield.

Synthesis of Tetrahydroquinoline Derivatives. Treatment of the α-methoxylated compound **11** with acid is supposed to yield the iminium ion **2**, which reacts with nucleophiles. In fact, a tetrahydroquinoline derivative (**22**)[7] was obtained in 84% yield by adding styrene to the solution of **11** and $TiCl_4$ in CH_2Cl_2 (eq 6).

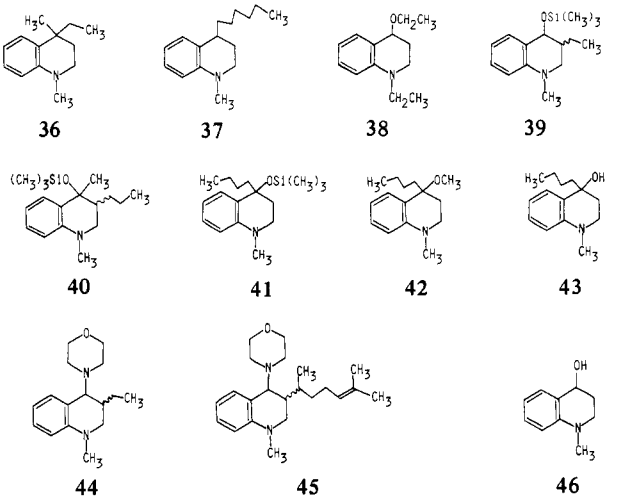


11 22 (6)

A variety of electron-rich olefins (**23**) other than styrene are also usable as nucleophiles, and results together with reaction conditions are summarized in Table I. This new cyclization is initiated by electrophilic addition of the initially formed iminium ion (**24**) to **23** to yield new cationic species (**25**)[9] that attack intramolecularly the aromatic nucleus (path i in Scheme III).

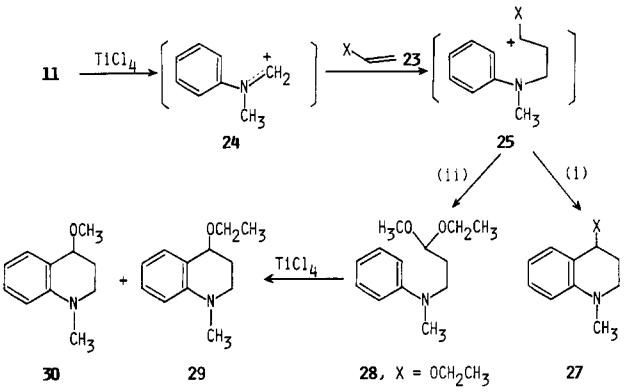
The fact that γ-methoxylated product **30** was formed together with the expected γ-ethoxylated product **29** in the reaction of **11** with ethyl vinyl ether (run 5 in Table I) might suggest an alternative reaction pathway involving an acetal (**28**) as an intermediate (path ii in Scheme III). However, the result that the γ-ethoxyl compound **29** was the sole product when the reaction

Chart I



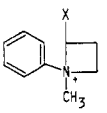
36 37 38 39 40 41 42 43 44 45 46

Scheme III



11 → 24 → 25 → 30 + 29 ← 28, X = OCH2CH3; 27

(4) Weinberg, N. L.; Brown, E. A. *J. Org. Chem.* **1966**, *31*, 4058.
(5) (a) McLeod, G. M.; Robinson, G. M. *J. Chem. Soc.* **1921**, *119*, 1472. (b) Stewort, T. D.; Bradley, W. E. *J. Am. Chem. Soc.* **1932**, *54*, 4172.
(6) The oxidation of **18** seems to take place at the α-methylene site.
(7) Some examples of the formation of tetrahydroquinoline skeleton using *N*,*N*′-diphenylmethylenediamine[8a] or aromatic Shiff bases[8b,c] as starting compounds have been reported.
(8) (a) Swan, G. A. *J. Chem. Soc., Chem. Commun.* **1969**, 20. (b) Grigos, V. I.; Povarov, L. S.; Mikhailov, B. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1965**, *12*, 2163. (c) Povarov, L. S. *Usp. Khim.* **1967**, *36*, 1533.
(9) The cationic intermediate **25** may be in equilibrium with an *N*-arylazetidinium salt **26**, which may facilitate the reaction of **24** with **23**.



26

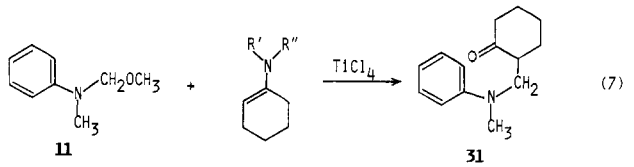
Table I. Synthesis of Tetrahydroquinoline Derivatives

run	*N*-(methoxymethyl)-*N*-alkylaniline (1 equiv)	electron-rich olefin (equiv)	Lewis acid (equiv)	reaction time, h	reaction temp, °C	product (yield, %)
1	**11**	$PhCH{=}CH_2$ (1.4)	$TiCl_4$ (1.3)	0.5	−78	**22** (84)
2	**11**	(1.4)	$TiCl_4$ (1.3)	1.5	−78 to −50	**36**[b] (89)
3	**11**	(2.0)	$TiCl_4$ (1.3)	4.0	−78 to −20	**37** (58)
4	**11**	 (1.3)	$TiCl_4$ (1.3)	1.5	−78 to −40	**29** (64)[a]
5	**11**		(1.3)	$TiCl_4$ (1.3)	1.0	−78 to rt	**29** (26) + **30** (26)
6	**15**		(1.4)	$TiCl_4$ (1.3)	0.5	−78	**38** (78)
7	**11**	(1.2)	$TiCl_4$ (1.3)	1.0	−78	**39** (61)
8	**11**	(1.6)	$TiCl_4$ (1.3)	1.0	−78	**40** (42)
9	**11**	(1.6)	$TiCl_4$ (1.3)	0.5	−78	**41** (29), **42** (11), **43** (21)
10	**11**	 (1.4)	$TiCl_4$ (1.3)	1.0	−78	**44** (81)
11	**11**	(1.4)	$TiCl_4$ (1.3)	0.6	−78	**45** (63)
12	**11**	 (1.2)	$TiCl_4$ (1.3)	5.0	−78 to 0	**28** (11), **46** (69)

[a] The use of $SnCl_4$ or BF_3OEt_2 also gave **29** in 13 or 57% yield, respectively. [b] See Chart I for structures of **36–46**.

was carried out at −78 °C (run 4 in Table I) suggests that **30** was formed from **29** as the secondary product. The conversion of **29** to **30** was also confirmed under similar conditions.

The ring closing of **25** to give **27** was highly influenced by the structure of **23**. Thus, when **23** was reacted with enamines of cyclohexanone, no cyclized product was obtained, as shown in eq 7, whereas enamines of aldehydes gave cyclized products in good yields (runs 10 and 11 in Table I).

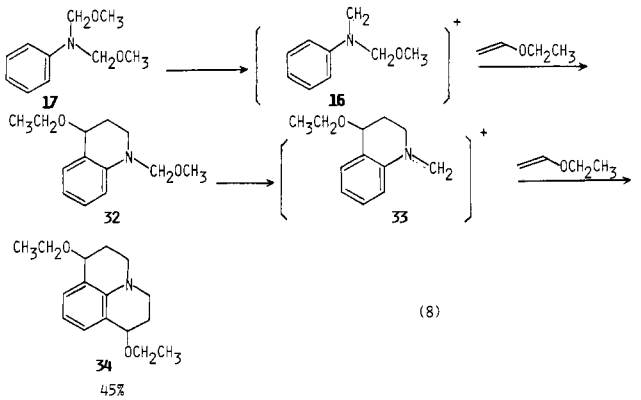


11 **31** (7)

R′,R″= $-CH_2CH_2OCH_2CH_2-$ 69%

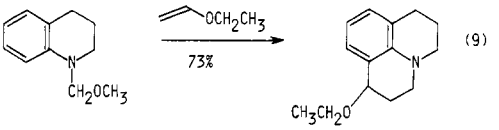
R′,R″= $-CH_2CH_2CH_2CH_2-$ 73%

Furthermore, two consecutive ring closings took place in the reaction of a dimethoxylated compound (**17**) with ethyl vinyl ether, yielding a julolidine skeleton.[10] This reaction involves two successive generations of the iminium ion as shown in eq 8.



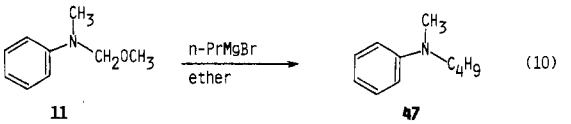
17 **16** **32** **33** **34** 45% (8)

Starting from a similar comopund (**20**) to the intermediate **32**, the reaction with ethyl vinyl ether also gave a julolidine derivative in a reasonable yield (eq 9).



20 **35** (9)

Reaction with Grignard Reagents. The iminium ions **7** are supposed to react easily with Grignard reagents, since Grignard reagents are usually more reactive as nucleophiles than electron-rich olefins like alkyl vinyl ethers. Although the reaction of *N,O*-acetals with Grignard reagents has already been studied,[11] the generatin of iminium ions from the acetals by using Lewis acid as a catalyst gave better results than the reaction without using Lewis acid (eq 10). The reaction may be useful in the



11 **47** (10)

without BF_3OEt_2 62%

with BF_3OEt_2 ~100%

synthesis of *N,N*-dialkylanilines having two different alkyl groups. Other examples are indicated in Table II.

Experimental Section

IR spectra were taken with a Hitachi 215 spectrometer. ^1H NMR spectra were recorded on a Varian Associates EM-390 spectrometer with tetramethylsilane as internal standard, except for the measurements of **39–43**, which were measured with CH_2Cl_2 as internal standard. Mass spectra were recorded on a JEOL IMS-DX300 mass spectrometer. Elemental analyses were determined by the Center for Instrumental Analysis of Kyoto University. Boiling points are uncorrected. Electrochemical oxidation was carried out by using DC Power Supply (GP050-2) of Takasago Seisakusho, Ltd.

Anodic Synthesis of α-Methoxylated Compounds (11, 15, 17, and 21). The synthesis of **11** has already been reported.[4] α-Methoxylated com-

(10) Stevens, R. V. "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley: New York, 1977; Vol. III, p 494.

(11) Glacet, C.; Couturier, J. C. *Bull. Chim. Soc. Fr.* **1962**, 2097.

Table II. Reaction of α-Methoxy-*N*,*N*-dialkylaniline with Grignard Reagents

run	α-methoxy-*N*,*N*-dialkylaniline	R^1	R^2	Grignard reagent (RMgX) R	X	Lewis acid (equiv)	solvent	reaction temp, °C	reaction time, h	product (%)
1	**11**	Me	H	Ph	Br	BF_3OEt_2 (1.1)	THF	−78	1.3	**48** (99)
2	**11**	Me	H	Ph	Br	no	THF	−78–rt	2.0	**48** (55)
3	**11**	Me	H	Me	I	BF_3OEt_2 (1.1)	3:1 ether–CH_2Cl_2	−78	2.0	**49** (70)
4	**21**	Et	Me	Ph	Br	BF_3OEt_2 (0.2)	ether	0–rt	2.0	**50** (50)

pounds **15**, **17**, and **21** were also prepared by the anodic oxidation of the corresponding *N*,*N*-dialkylanilines as follows.

***N*-Ethyl-*N*-(methoxymethyl)aniline (15)** was prepared from *N*-ethyl-*N*-methylaniline by a procedure similar to the synthesis[4] of **11**. The yield of **15** was 85% by the time 2.0 F/mol had been consumed: bp 110–112 °C (5 mm); IR (film) 3020, 2960, 1595, 1495, 1060, 740 cm^{-1}; NMR (CCl_4) δ 1.20 (t, 3 H, *J* = 7 Hz), 3.21 (s, 3 H), 3.47 (q, 2 H, *J* = 7 Hz), 4.60 (s, 2 H), 6.52–7.43 (m, 5 H); mass spectrum, *m/e* 165 (M^+), 149 ($M^+ - CH_4$), 134 ($M^+ - OCH_3$).

***N*,*N*-Bis(methoxymethyl)aniline (17).** Although **17** has been described in the literature[4] to be a byproduct of the synthesis of **11**, the preparation of **17** with a satisfactory yield was accomplished by using enough current in the dimethoxylation of *N*,*N*-dimethylaniline: 69% yield (6 F/mol).

***N*-Ethyl-*N*-(1-methoxyethyl)aniline (21).** Although the anodic oxidation of *N*,*N*-diethylaniline was achieved by a similar method to that of *N*,*N*-dimethylaniline,[4] the isolation of **21** must be carried out as follows because of the unstability of **21**. After 3.3 F/mol of current was used, the reaction mixture was charged into the distillation flask. Methanol was removed under reduced pressure, and then **21** was isolated by distillation: bp 125–128 °C (5 mm); 60% yield; IR (film) 3060, 2970, 1590, 1495, 1075, 746 cm^{-1}; NMR (CCl_4) δ 1.03 (t, 3 H, *J* = 4 Hz), 1.3 (d, 3 H, *J* = 4 Hz), 3.15 (s, 3 H), 3.3 (q, 2 H, *J* = 4 Hz), 4.83 (q, 1 H, *J* = 4 Hz), 6.45–7.32 (m, 5 H); mass spectrum, *m/e* 147 ($M^+ - CH_3OH$).

Synthesis of α-Methoxylated Compounds 11 and 20 was also achieved as follows without the use of anodic oxidation, but their yields were not satisfactory.

The Mannich Reaction of *N*-Methylaniline. To a solution of *N*-methylaniline (55 g, 0.51 mol) in methanol (40 mL) was added a solution of paraformaldehyde (16 g, 0.53 mol) in methanol (20 mL) at room temperature. The reaction mixture was refluxed for 2 h with vigorous stirring and then allowed to stand until it was cooled to room temperature. After being treated with potassium carbonate (20 g, 0.144 mol), the solution was filtered.

The filtrate was poured onto water (100 mL), and the organic portion was extracted with ether (3 × 100 mL). The combined organic layer was dried over anhydrous magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated and the residue was distilled to afford a mixture of **11** (32% yield) and **13**[12] (31% yield).

Synthesis of 1-(Methoxymethyl)-1,2,3,4-tetrahydroquinoline (20). To a stirred solution of tetrahydroquinoline (6.89 g, 0.052 mol) and sodium hydride (3.47 g, 0.078 mol) in DMF (20 mL) was added slowly chloromethyl methyl ether (5.0 g, 0.062 mol) at room temperature. The resulting reaction mixture was stirred for 1 h and then poured onto saturated brine (50 mL). The organic portion was extracted with ether (3 × 100 mL). The combined organic layer was dried over magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated and the residue was distilled under reduced pressure to yield **20** (43%): bp 110–112 °C (10 mm); IR (film) 3020, 1600, 1595, 1300, 1060, 740 cm^{-1}; NMR (CCl_4) δ 1.68–2.20 (m, 2 H), 2.72 (t, 2 H, *J* = 6 Hz), 3.22 (s, 3 H), 3.22–3.58 (m, 2 H), 4.55 (s, 2 H), 6.37–7.23 (m, 4 H); mass spectrum, *m/e* 177 (M^+), 161 ($M^+ - CH_4$).

Alkylation of *N*-methylaniline with chloromethyl methyl ether did not give **11** but yielded *N*,*N*′-dimethyl-*N*,*N*′-diphenylmethylenediamine (**13**). That is, chloromethyl methyl ether (5.0 g, 0.062 mol) was added dropwise to a stirred solution of *N*-methylaniline (4.848 g, 0.052 mol) and sodium hydride (3.74 g, 0.078 mol) in DMF (20 mL) at room temperature. The resulting reaction mixture was stirred for 1 h and then worked up in a manner similar to the synthesis of **20** to yield **13**[12] (5.1 g, 0.023 mol, 87%).

Synthesis of Tetrahydroquinoline Derivatives 22, 29, 30, and 36–46. Yields and reaction conditions are summarized in Table I. The stereochemistry of **39**, **40**, **44**, and **45** was not determined. Silyl enol ethers[13] and enamines[14] used as nucleophiles were prepared by ordinary methods. Styrene, simple olefins, ethyl vinyl ether, and vinyl acetate were commercially available and used without further purification.

A general procedure for the preparation of tetrahydroquinoline derivatives is exemplified by the preparation of **22**.

Preparation of 1-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline (22). To a stirred solution of **11** (5 mmol) in CH_2Cl_2 (5 mL) was added dropwise titanium tetrachloride (6.5 mmol) under an atmosphere of nitrogen at −78 °C. After the solution was stirred at that temperature for 5 min, a solution of styrene (7 mmol) in CH_2Cl_2 (3 mL) was added dropwise over a period of 3–5 min. The resulting reaction mixture was stirred for 30 min at −78 °C and treated with cold saturated aqueous potassium carbonate (20 mL). After being stirred for 5 min, the solution was filtered, and the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried over anhydrous magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated under reduced pressure, and the residue was chromatographed on a column of alumina (1:20 AcOEt/hexane) to yield **22** (84%): IR (film) 3060, 3020, 1600, 1500, 1320, 740, 700 cm^{-1}; NMR (CCl_4) δ 1.93–2.40 (m, 2 H), 2.78 (s, 3 H), 3.00 (t, 2 H, *J* = 5 Hz), 3.95 (t, 1 H, *J* = 6 Hz), 6.17–7.45 (m, 9 H). Anal. Calcd for $C_{16}H_{17}N$: C, 86.06; H, 7.67; N, 6.27. Found: C, 86.05; H, 7.72; N, 6.22.

1,4-Dimethyl-4-ethyl-1,2,3,4-tetrahydroquinoline (36): IR (film) 3060, 3020, 1600, 1500, 1320, 1205, 740 cm^{-1}; NMR (CCl_4) δ 0.77 (t, 3 H, *J* = 6.5 Hz), 1.20 (s, 3 H), 1.40–2.17 (m, 4 H), 2.90 (s, 3 H), 3.22 (t, 2 H, *J* = 5 Hz), 6.27–6.80 (m, 2 H), 6.80–7.23 (m, 2 H). Anal. Calcd for $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.55; H, 10.37; N, 7.41.

1-Methyl-4-hexyl-1,2,3,4-tetrahydroquinoline (37): IR (film) 3060, 3020, 1600, 1500, 1320, 740 cm^{-1}; NMR (CCl_4) δ 0.85 (t, 3 H, *J* = 4 Hz), 1.08–2.10 (m, 12 H), 2.43–2.97 (m, 1 H), 2.83 (s, 3 H), 2.97–3.63 (m, 2 H), 6.23–6.60 (m, 2 H), 6.60–7.07 (m, 2 H). Anal. Calcd for $C_{16}H_{25}N$: C, 83.06; H, 10.89; N, 6.05. Found: C, 83.08; H, 11.18; N, 5.92.

1-Methyl-4-ethoxy-1,2,3,4-tetrahydroquinoline (29): IR (film) 3060, 3020, 1600, 1500, 1325, 1220, 1080, 740 cm^{-1}; NMR (CCl_4) δ 1.16 (t, 3 H, *J* = 7 Hz), 1.73–2.10 (m, 2 H), 2.87 (s, 3 H), 2.93–3.36 (m, 2 H), 3.6 (q, 2 H, *J* = 7 Hz), 4.16 (t, 1 H, *J* = 3.5 Hz), 6.30–6.73 (m, 2 H), 6.73–7.24 (m, 2 H). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.06; H, 9.10; N, 7.24.

1-Methyl-4-methoxy-1,2,3,4-tetrahydroquinoline (30): IR (film) 3060, 3020, 1600, 1500, 1200, 1090, 740 cm^{-1}; NMR (CCl_4) δ 1.73–2.20 (m, 2 H), 2.90 (s, 3 H), 3.23 (s, 3 H), 3.06–3.57 (m, 2 H), 4.03 (t, 1 H, *J* = 3 Hz), 6.30–6.63 (m, 2 H), 6.80–7.23 (m, 2 H). Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90; O, 9.03. Found: C, 74.54; H, 8.63; N, 7.76; O, 8.76.

1-Ethyl-4-ethoxy-1,2,3,4-tetrahydroquinoline (38): IR (film) 3060, 3020, 1600, 1340, 1080, 740 cm^{-1}; NMR (CCl_4) δ 1.12 (t, 6 H, *J* = 6 Hz), 1.65–2.37 (m, 2 H), 3.47 (q, 4 H, *J* = 6 Hz), 2.84–3.87 (m, 2 H), 4.20 (t, 1 H, *J* = 3 Hz), 6.32–6.70 (m, 2 H), 7.13–7.38 (m, 2 H). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82; O, 7.79. Found: C, 76.34; H, 9.40; N, 7.03; O, 7.53.

1-Methyl-3-ethyl-4-((trimethylsilyl)oxy)-1,2,3,4-tetrahydroquinoline (39): IR (film) 3060, 3020, 1603, 1500, 1338, 1250, 1042, 740 cm^{-1}; NMR (CCl_4) δ 0.12 and 0.18 (2 s, 9 H), 0.78–1.99 (m, 6 H), 3.01 (s, 3 H), 2.85–3.49 (m, 2 H), 4.48 and 4.65 (2 br s, 1 H), 6.39–6.75 (m, 2 H), 6.95–7.29 (m, 2 H). Anal. Calcd for $C_{15}H_{25}NOSi$: C, 68.39; H, 9.56; N, 5.31. Found: C, 68.27; H, 9.78; N, 5.38.

1,4-Dimethyl-3-propyl-4-((trimethylsilyl)oxy)-1,2,3,4-tetrahydroquinoline (40): IR (film) 3050, 2950, 1600, 1500, 1340, 1250, 1005, 835, 740 cm^{-1}; NMR (CCl_4) δ 0.00 and 0.02 (2 s, 9 H), 0.83–2.17 (m, 8 H),

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1.77 (s, 3 H), 3.01 (s, 3 H), 3.18 (d, 2 H, J = 6 Hz), 6.38–6.77 (m, 2 H), 6.93–7.56 (m, 2 H). Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.05; H, 10.03; N, 4.80. Found: C, 70.20; H, 10.13; N, 4.93.

Reaction of 11 with 2-((trimethylsilyl)oxy)-1-hexene gave a mixture of **41–43**.

1-Methyl-4-butyl-4-((trimethylsilyl)oxy)-1,2,3,4-tetrahydroquinoline (41): IR (film) 3060, 3020, 1600, 1500, 1330, 1250, 1055, 835, 740 cm^{-1}; NMR (CCl_4) δ 0.00 (s, 9 H), 1.06 (t, 3 H, J = 4 Hz), 1.23–1.76 and 1.76–2.27 (m, 8 H), 3.00 (s, 3 H), 3.10–3.70 (m, 2 H), 6.43–6.83 (m, 2 H), 7.00–7.50 (m, 2 H). Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.05; H, 10.03; N, 4.80. Found: C, 70.01; H, 10.31; N, 4.61.

1-Methyl-4-butyl-4-methoxy-1,2,3,4-tetrahydroquinoline (42): IR (film) 3060, 3020, 1600, 1450, 1325, 1070, 740 cm^{-1}; NMR (CCl_4) δ 1.00 (t, 3 H, J = 4 Hz), 1.20–2.62 (m, 8 H), 2.97 (s, 3 H), 3.06 (s, 3 H), 3.32 (t, 2 H, J = 5 Hz), 6.40–6.80 (m, 2 H), 6.90–7.40 (m, 2 H). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.71; H, 10.26; N, 5.60.

1-Methyl-4-butyl-4-hydroxyl-1,2,3,4-tetrahydroquinoline (43): IR (film) 3400, 3060, 3020, 1600, 1320, 1100, 740 cm^{-1}; NMR (CCl_4) δ 1.02 (t, 3 H, J = 4 Hz), 1.18–1.65 and 1.65–2.18 (m, 8 H), 2.95 (s, 3 H), 3.18 (t, 3 H, J = 5 Hz), 6.42–6.85 (m, 2 H), 6.95–7.52 (m, 2 H). Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.41; H, 9.77; N, 6.22.

1-Methyl-3-ethyl-4-morpholino-1,2,3,4-tetrahydroquinoline (44). Isolation of **44** was achieved by silica gel column chromatography (1:20 AcOEt/hexane): IR (film) 3030, 2950, 1600, 1505, 1120, 745 cm^{-1}; NMR (CCl_4) δ 1.13 (t, 3 H, J = 3 Hz), 1.17–1.53 (m, 2 H), 1.93–2.22 (m, 1 H), 2.30–2.70 (m, 4 H), 2.95 and 3.13 (2 d, 2 H, J = 1.5 Hz), 3.05 (s, 3 H), 3.50–3.87 (m, 1 H), 3.70 (t, 4 H, J = 2 Hz), 6.55–6.78 (m, 2 H), 7.05–7.35 (m, 2 H); mass spectrum, m/e 261 ($M^+ + 1$), 260 (M^+). Anal. Calcd for $C_{16}H_{24}N_2O$: C, 73.81; H, 9.29; N, 10.76. Found: C, 73.88; H, 9.33; N, 10.90.

1-Methyl-3-(1,5-dimethyl-4-hexenyl)-4-morpholino-1,2,3,4-tetrahydroquinoline (45) was isolated by silica gel column chromatography (1:30 AcOEt/hexane): IR (film) 3030, 2950, 1600, 1505, 1120, 750 cm^{-1}; NMR (CCl_4) δ 0.73–1.00 (m, 3 H), 1.00–2.13 (m, 4 H), 1.57 (s, 3 H), 1.67 (s, 3 H), 2.17–2.70 (m, 4 H), 2.92 (s, 3 H), 2.83–3.27 (m, 2 H), 3.33–3.47 (m, 1 H), 3.53 (t, 4 H, J = 2 Hz), 4.86–5.17 (m, 1 H), 6.33–6.67 (m, 2 H), 6.87–7.30 (m, 2 H); mass spectrum, m/e 343 ($M^+ + 1$), 342 (M^+). Anal. Calcd for $C_{22}H_{34}N_2O$: C, 77.15; H, 10.01; N, 8.18. Found: C, 77.32; H, 10.09; N, 8.03.

1-Methyl-4-hydroxy-1,2,3,4-tetrahydroquinoline (46): IR (film) 3350, 3060, 3020, 1600, 1495, 1315, 740 cm^{-1}; NMR (CCl_4) δ 1.67–2.17 (m, 3 H), 2.85 (s, 3 H), 2.71–3.62 (m, 2 H), 4.50 (t, 1 H, J = 4 Hz), 6.28–6.67 (m, 2 H), 6.76–7.17 (m, 2 H). Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58; O, 9.80. Found: C, 73.66; H, 8.33; N, 8.17; O, 9.74.

Synthesis of Julolidine Derivatives. Reaction of *N*,*N*-Bis(methoxymethyl)aniline (17) with Ethyl Vinyl Ether. To a stirred solution of **17** (0.906 g, 5 mmol) in CH_2Cl_2 (5 mL) was added dropwise ethyl vinyl ether (1.082 g, 15 mmol) under an atmosphere of nitrogen at −78 °C. After the solution was stirred for 1 min at that temperature, titanium tetrachloride (2.275 g, 12 mmol) was added dropwise over a period of 3–5 min. The resulting reaction mixture was stirred for 40 min at −78 °C and then treatd with cold saturated aqueous potassium carbonate (20 mL). After being stirred for 5 min, the solution was filtered, and the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried over anhydrous magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated under reduced pressure, and the residue was chromatographed on a column of alumina (1:20 AcOEt/hexane) to afford 3,3′-diethoxyjulolidine (**34**) in 45% yield: IR (film) 3020, 1600, 1500, 1310, 1080, 740 cm^{-1}; NMR (CCl_4) δ 1.16 (t, 6 H, J = 6 Hz), 1.47–2.27 (m, 4 H), 2.77–3.78 (m, 4 H), 3.47 (q, 4 H, J = 6 Hz), 4.03–4.37 (m, 2 H), 6.20–6.73 (m, 1 H), 6.73–7.12 (m, 2 H). Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 72.96; H, 9.04; N, 5.09.

Reaction of *N*-(Methoxymethyl)-1,2,3,4-tetrahydroquinoline (20) with Ethyl Vinyl Ether. A solution of **20** (0.886 g, 5 mmol) in CH_2Cl_2 (5 mL) was treated with titanium tetrachloride (1.233 g, 6.5 mmol) and ethyl viny ether (0.505 g, 7 mmol) successively in a similar manner to the preparation of **22**. After the reaction mixture was stirred for 1 h at −78 °C, usual workup afforded 3-ethoxyjulolidine (**35**) (73% yield): IR (film) 3020, 1600, 1595, 1310, 1080, 740 cm^{-1}; NMR (CCl_4) δ 1.17 (t, 3 H, J = 6 Hz), 1.72–2.26 (m, 4 H), 2.54–2.92 (t, 2 H, J = 7 Hz), 3.48 (q, 2 H, J = 6 Hz), 4.17 (t, 1 H, J = 3 Hz), 6.17–6.53 (m, 1 H), 6.53–6.87 (m, 2 H). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.11; H, 8.90; N, 6.54.

Reaction of 11 with Enamines of Cyclohexanone. Titanium tetrachloride (1.423 g, 6.5 mmol) and 1-morpholinocyclohexene (1.003 g, 6 mmol) or 1-pyrrolidinocyclohexene (1.218 g, 8 mmol) were successively added to a solution of **11** (0.756 g, 5 mmol) in CH_2Cl_2 (5 mL) at −78 °C. Usual workup and isolation by column chromatography (alumina) afforded uncyclized product **31**. The yield was 69% for 1-morpholinocyclohexene or 73% for 1-pyrrolidinocyclohexene: IR (film) 3050, 1690, 1595, 1340, 740 cm^{-1}; NMR (CCl_4) δ 1.16–2.73 (m, 9 H), 2.87–3.97 (dd, 2 H, J = 15 Hz and 6 Hz), 2.97 (s, 3 H), 6.30–7.16 (m, 4 H). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.14; H, 9.08; N, 6.40.

Reaction of α-Methoxylated Compounds with Grignard Reagents. A general procedure for the reaction of α-methoxylated compounds with Grignard reagents is described in the reaction of **11** with *n*-PrMgBr. Yields of **48–50** and the reaction conditions are summarized in Table II.

General Procedure. To a solution of *n*-PrMgBr (7.5 mmol) in dry ether (3 mL) was added dropwise a solution of **11** (0.756 g, 5 mmol) in dry ether (2 mL) under an atmosphere of nitrogen at −78 °C. After the solution was stirred for 5 min at that temperature, BF_3OEt_2 (0.781 g, 5.5 mmol) was added dropwise over a period of 3–5 min. After the resulting reaction mixture was stirred for 1.7 h at −78 °C and treated with water (20 mL), the organic portion was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried over anhydrous magnesium sulfate, and then the drying agent was removed by filtration. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a column of silica gel (1:10 AcOEt/hexane) to afford **47**: IR (film) 3050, 2960, 1600, 1505, 742, 690 cm^{-1}; NMR (CCl_4) δ 0.67–1.87 (m, 7 H), 2.93 (s, 3 H), 3.29 (t, 2 H, J = 6 Hz), 6.3–7.38 (m, 5 H). Anal. Calcd for $C_{11}H_{17}N$: C, 80.93; H, 10.50; N, 8.58. Found: C, 80.66; H, 10.72; N, 8.58.

***N*-Methyl-*N*-benzylaniline (48)**[15] **and *N*-ethyl-*N*-methylaniline (49)**[16] were identified by comparison of their spectroscopic data with those of authentic samples.

***N*-Ethyl-*N*-(1-phenylethyl)aniline (50)**: IR (film) 3050, 2960, 1600, 740, 690 cm^{-1}; NMR (CCl_4) δ 1.00 (t, 3 H, J = 6 Hz), 1.50 (d, 3 H, J = 6 Hz), 3.13 (q, 2 H, J = 6 Hz), 4.97 (q, 1 H, J = 6 Hz), 6.25–7.75 (m, 10 H). Anal. Calcd for $C_{16}H_{19}N$: C, 85.29; H, 8.50; N, 6.22. Found: C, 85.29; H, 8.50; N, 6.04.

Registry No. 11, 13657-45-9; **13**, 1145-27-3; **15**, 82769-47-9; **17**, 13657-44-8; **20**, 82769-63-9; **21**, 82769-48-0; **22**, 27623-83-2; **29**, 22456-81-1; **30**, 82769-51-5; **31**, 82769-62-8; **34**, 82769-60-6; **35**, 82769-61-7; **36**, 82769-49-1; **37**, 82769-50-4; **38**, 82769-52-6; **39**, 82769-53-7; **40**, 82769-54-8; **41**, 82769-55-9; **42**, 82769-56-0; **43**, 24206-56-2; **44**, 82769-57-1; **45**, 82769-58-2; **46**, 24206-53-9; **48**, 614-30-2; **49**, 613-97-8; **50**, 30432-65-6; $TiCl_4$, 7550-45-0; *N*-ethyl-*N*-methylaniline, 613-97-8; *N*,*N*-dimethylaniline, 121-69-7; *N*,*N*-diethylaniline, 91-66-7; 1-morpholinocyclohexene, 670-80-4; 1-pyrrolidinocyclohexene, 1125-99-1; tetrahydroquinoline, 635-46-1; julolidine, 479-59-4; styrene, 100-42-5; 2-methyl-1-butene, 563-46-2; 1-octene, 111-66-0; ethyl vinyl ether, 109-92-2; 1-trimethylsiloxy-1-butene, 6651-33-8; 2-trimethylsiloxy-2-hexene, 82769-59-3; 2-trimethylsiloxy-1-hexene, 60585-82-2; 1-(morpholino)-1-butene, 15431-03-5; 3,7-dimethyl-1-(morpholino)-1,6-octadiene, 42822-94-6; vinyl acetate, 108-05-4; phenylmagnesium bromide, 100-58-3; methylmagnesium iodide, 917-64-6; boron trifluoride diethyl etherate, 109-63-7.

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