Synthesis of 2,4,6-Triaryl-1,3,5-triazabicyclo[3.1.0]hexane using *N,N'*-Diarylmethylenearylmethanediamine

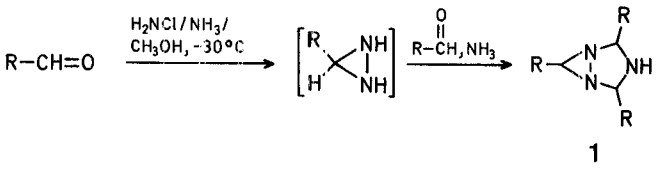
Tokiharu TAKAJO*, Satoshi KAMBE

Oyama National College of Technology, Oyama-shi, Tochigi, 323, Japan

Wataru ANDO

Department of Chemistry, University of Tsukuba, Sakura-mura, Niiharigun, Ibaraki, 305, Japan

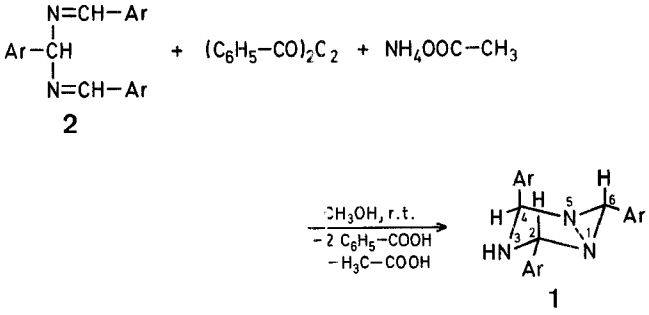
2,4,6-Trisubstituted 1,3,5-triazabicyclo[3.1.0]hexanes **1** are obtained in 32–80% yield by the Schmitz reaction[1]: addition of aldehydes to chloroamine in methanolic ammonia (Scheme **A**), and the stereochemistry and the reaction mechanism have been reported[2,3,4].



R = CH_3, C_2H_5, n-C_3H_7, C_6H_5

Scheme **A**

We report here on the synthesis of 2,4,6-triaryl-1,3,5-triazabicyclo[3.1.0]hexanes using *N,N'*-diarylmethylenearylmethanediamine[5]. When a mixture of *N,N'*-dibenzylidenephenylmethanediamine (**2a**; Ar = C_6H_5), benzoyl peroxide, and ammonium acetate in methanol was stirred at ambient temperature, 2,4,6-triphenyl-1,3,5-triazabicyclo[3.1.0]hexane (**1a**; Ar = C_6H_5) was formed in 40% yield. 1,3,5-Triazabicyclo[3.1.0]hexanes **1b–e** are similarly prepared (Scheme **B**).

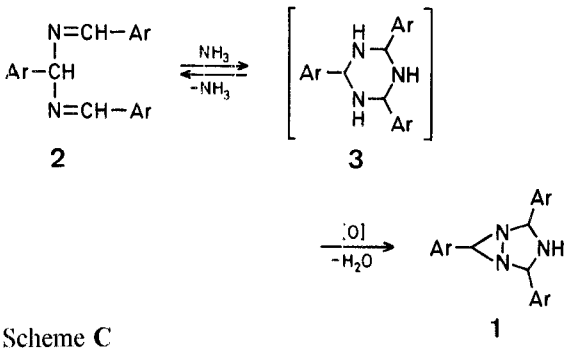


1,2	Ar	1,2	Ar
a		d	
b		e	
c			

Scheme **B**.

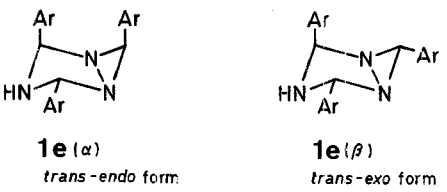
It is believed that the reaction proceeds via 2,4,6-triphenyl-1,3,5-hexahydrotriazine[6] (**3a**; Ar = C_6H_5), a very unstable substance said to form from benzaldehyde in methanolic ammonia at −10 °C (Scheme **C**).

All of the structures show the conformations of substituent-2 and substituent-4 to be in the *trans*-form, since the chemical shifts of H-2 are observed to be different from those of H-4. As a result of long range shielding from the diaziridine ring



Scheme **C**

and the shielding from the n-σ^* interaction of the axial lone-pair of N-1, the axial protons, H-2, are at higher field than the equatorial protons, H-4. Furthermore, when the signals of H-2 and H-4 show, respectively, singlets, decoupling of H-3 leads to a decrease of the H-2 peak heights and an increase of the H-4 peak heights. The ^{13}C-N.M.R. signals for C-2, C-4, and C-6, which show, respectively, couplings of 147–150 Hz, 155–159 Hz, and 166–173 Hz for $^1J_{CH}$, are observed at 79–82 ppm, 77–81 ppm, and 50–59 ppm, respectively.



Scheme **D**

Two isomers, **1e(α)** (m.p. 177–178 °C) and **1e(β)** (m.p. 199–200 °C), are isolated from **1e**. The spectra of the minor product **1e(α)** suggest the *trans-endo* form, and the major product **1e(β)** *trans-exo* form (Scheme **D**). As a result of the anisotropic effect of the 1,2,4-triazolidine ring and the shielding from the n-σ^* interaction of the axial lone-pairs of N-1 and N-5, the ^{1}H-N.M.R. signal of H-6 of the *exo*-form, **1e(β)**, is at higher field than that of the *endo*-form, **1e(α)**.

2,4,6-Triphenyl-1,3,5-triazabicyclo[3.1.0]-hexane[1,2,4] (1a):
A mixture of *N,N'*-dibenzylidenephenylmethanediamine (**2a**; 5.96 g, 20 mmol), benzoyl peroxide (4.84 g, 20 mmol), ammonium acetate (4.62 g, 60 mmol), and methanol (15 ml) in Erlenmeyer flask stoppered with a ground-glass stopper is magnetically stirred at ambient temperature for 5 h. The deposited precipitate is collected, washed with methanol, and then recrystallized from acetonitrile to give colorless needles of **1a**; yield: 2.7 g (43%); m.p. 169–170 °C (Ref.[1], m.p. 160–162 °C; Refs.[2,4], m.p. 162–164 °C).

I.R. (Nujol): ν = 3280 (NH), 895, 730, 700 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 7.7, 7.35 (2m, 2 and 13 H_{arom}); 5.59 (d, 1 H, H-4, $J_{3,4}$ = 6.5 Hz); 5.21 (d, 1 H, H-2, $J_{2,3}$ = 12.5 Hz); 3.17 (s, 1 H, H-6); 2.97 ppm (br. t, 1 H, H-3).

^{13}C-N.M.R. ($CDCl_3$): δ = 140.4 (s, C-1' at C-6); 136.2 (s, C-1' at C-2 and C-4); 128.7, 128.4, 128.0, 127.2, 126.8 (5d, 3, 5, 3, 2 and 2 C_{arom} each); 81.4 (d, C-4, $^1J_{CH}$ = 149 Hz); 80.50 (d, C-2, $^1J_{CH}$ = 155 Hz); 5.86 ppm (d, C-6, $^1J_{CH}$ = 169 Hz).

2,4,6-Tris[2-methylphenyl]-1,3,5-triazabicyclo[3.1.0]hexane (1b):
Similar treatment of a mixture of *N,N'*-bis[2-methylbenzylidene]-2-methylphenylmethanediamine (**2b**; 1.70 g, 5 mmol), benzoyl peroxide (1.21 g, 5 mmol), and ammonium acetate (1.16 g, 15 mmol) in methanol (5 ml) for 2.5 h forms colorless crystals; yield: 0.95 g (53%); m.p. 177–178 °C (from CH_3CN).

$C_{24}H_{25}N_3$	calc.	C 81.09	H 7.07	N 11.82
(355.5)	found	81.07	7.12	11.87

I.R. (Nujol): ν = 3330 (NH), m 885, 735, 725 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 7.95–7.35 (m, 3H$_{arom}$); 7.25 (m, 9H$_{arom}$); 5.78 (s, 1H, H-4); 5.42 (s, 1H, H-2); 3.57 (s, 1H, H-6); 2.93 (br, 1H, H-3); 2.53, 2.22 ppm (2s, 6 and 3H, CH_3).

^{13}C-N.M.R. ($CDCl_3$): δ = 138.4, 138.1, 136.8, 136.5, 134.6, 133.8 (6s, 1C$_{arom}$ each); 131.0, 130.8, 129.9, 128.6, 128.2, 126.2, 124.2 (7d, 1C$_{arom}$ each); 127.9 (d, 2C$_{arom}$); 125.9 (d, 3C$_{arom}$); 79.4 (d, C-4, $^1J_{CH}$ = 147 Hz); 7.81 (d, C-2, $^1J_{CH}$ = 157 Hz); 50.6 (d, C-6, $^1J_{CH}$ = 166 Hz); 19.9 (q, CH_3 at C-2′ of C-2 and 4, $^1J_{CH}$ = 127 Hz); 18.7 ppm (q, CH_3 at C-2′ of C-6, $^1J_{CH}$ = 126 Hz).

2,4,6-Tris[4-methylphenyl]-1,3,5-triazabicyclo[3.1.0]hexane[7] (1c): Similar treatment of the mixture of *N,N′*-bis[4-methylbenzylidene]-4-methylphenylmethanediamine (**2c**; 1.70 g, 5 mmol), benzoyl peroxide (1.21 g, 5 mmol), and ammonium acetate (1.16 g, 15 mmol) in methanol (5 ml) for 4 h affords white crystals; yield: 1.2 g (67%); m.p. 168–169 °C (from ethanol/hexane) (Ref.[7], m.p. 175 °C).

I.R. (Nujol): ν = 3270 (NH), 1515, 1090, 900, 810 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 7.58, 7.31 (2d, 2 and 4H$_{arom}$); 7.1 (m, 6H$_{arom}$); 5.50 (s, 1H, H-4); 5.16 (s, 1H, H-2); 3.12 (s, 1H, H-6); 2.87 (br, 1H, H-3); 2.32, 2.29 ppm (2s, 6 and 3H, CH_3).

^{13}C-N.M.R. ($CDCl_3$): δ = 138.5, 138.1, 137.8, 137.4, 133.5 (5s, 6C$_{arom}$); 129.3 (d, 2C$_{arom}$); 129.1 (d, 4C$_{arom}$); 127.9, 127.1, 126.7 (3d, 2C$_{arom}$ each), 81.4 (d, C-4, $^1J_{CH}$ = 147 Hz); 80.3 (d, C-2, $^1J_{CH}$ = 155 Hz), 51.9 (d, C-6, $^1J_{CH}$ = 167 Hz), 21.1 ppm (q, 3C, CH_3, $^1J_{CH}$ = 127 Hz).

2,4,6-Tris[2-chlorophenyl]-1,3,5-triazabicyclo[3.1.0]hexane (1d): Similar treatment of mixture of *N,N′*-bis[2-chlorobenzylidene]-2-chlorophenylmethanediamine (**2d**; 2.0 g, 5 mmol), benzoyl peroxide (5 mmol), and ammonium acetate (15 mmol) in methanol (5 ml) for 5 h gives colorless crystals; yield: 1.02 g (49%); m.p. 174–175 °C (from CH_3CN).

$C_{21}H_{16}ClN_3$	calc.	C 60.53	H 3.87	N 10.08
(416.7)	found	60.58	3.88	9.96

I.R. (Nujol): ν = 3330 (NH), 1035, 875, 740, 730 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 7.9, 7.55, 7.35 (3 m, 1,2 and 9H$_{arom}$); 5.97 (s, 1H, H-4); 5.50 (d, 1H, H-2, J = 8.5 Hz, s, on addition of D_2O); 4.21 (s, 1H, H-6); 2.95 ppm (br. 1H, H-3).

^{13}C-N.M.R. ($CDCl_3$/DMSO-d_6, 4/1): δ = 138.0, 134.8, 133.5, 132.7 (4s, 1C$_{arom}$ each); 134.2 (s, 2C$_{arom}$); 130.0, 129.5, 129.1, 128.9, 128.1, 127.6 (6d, 1C$_{arom}$ each); 129.9, 129.8, 126.9 (3d, 1C$_{arom}$ each); 79.0 (d, C-4, $^1J_{CH}$ = 150 Hz); 77.2 (d, C-2, $^1J_{CH}$ = 159 Hz); 50.0 ppm (d, C-6, $^1J_{CH}$ = 173 Hz).

2,4,6-Tris[4-chlorophenyl]-1,3,5-triazabicyclo[3.1.0]hexane (1e): A mixture of *N,N′*-bis[4-chlorobenzylidene]-4-chlorphenylmethanediamine (**2e**; 2.0 g, 5 mmol), benzoyl peroxide (5 mmol), and ammonium acetate (5 mmol) in methanol is magnetically stirred for 5 h. The deposited precipitate is collected, washed with aqueous methanol, and dried; yield: 2.0 g; m.p. 175–177 °C. When the white crude product (2.0 g) is treated with refluxing acetonitrile (50 ml), and filtered, evaporation of the filtrate gives white substance **1e**(α); yield: 0.25 g (12%); m.p. 177–178 °C, and the substance insoluble in acetonitrile is purified by recrystallization from benzene to afford **1e**(β); yield: 0.58 g (28%), m.p. 198–199 °C.

1e(α): I.R. (Nujol): ν = 3280 (NH), 1592, 1491, 1090, 1015, 905, 805, 718, 518 cm^{-1}.

^{1}H-N.M.R. (DMSO-d_6): δ = 7.85, 7.4 (2 m, 2 and 10H$_{arom}$); 5.99 (d, H-4, $J_{3,4}$ = 7.1 Hz); 5.50 (d, H-2, $J_{2,3}$ = 11.6 Hz); 4.79 (q, H-3, J = 7.4, 11.6 Hz); 4.17 ppm (s, H-6).

^{13}C-N.M.R. (DMSO-d_6/$CDCl_3$, 5/1); δ = 139.8, 135.7, 134.6, 133.3, 133.2, 132.4 (6s, 1C$_{arom}$ each); 130.9, 139.4, 129.2, 128.8, 128.7, 128.4, 128.2, 128.0, 127.6 (9d, 12C$_{arom}$); 80.1 (d, C-4); 79.0 (d, C-2); 49.7 ppm (d, C-6)

1e(β): I.R. (Nujol): ν = 3280 (NH), 1600, 1495, 1094, 1020, 910, 809, 520 cm^{-1}.

^{1}H-N.M.R. (DMSO-d_6); δ = 7.76 (d, 2H$_{arom}$); 7.45 (m, 10H$_{arom}$); 5.56 (d, H-4, $J_{3,4}$ = 6.6 Hz); 4.98 (d, H-2, $J_{2,3}$ = 12.3 Hz); 4.50 (q, H-3, J = 6.6, 12.3 Hz); 3.68 ppm (s, H-6).

^{13}C-N.M.R. (DMSO-d_6/$CDCl_3$, 5:1); δ = 139.8, 135.7, 134.6, 133.3, 133.2, 132.4 (6s, 1C$_{arom}$ each); 129.5, 128.9, 128.7, 128.5, 128.2, 128.0 (6d, 2C$_{arom}$ each); 80.1 (d, 1C, C-4); 78.9 (d, 1C, C-2); 49.7 ppm (d, 1C, C-6).

Received: June 12, 1984

[1] E. Schmitz, *Chem. Ber.* **95**, 798 (1962).
[2] A.T. Nielsen et al, *Tetrahedron Lett.* **1973**, 1167.
[3] A.T. Nielsen et al., *J. Org. Chem.* **39**, 1349 (1974).
[4] A.T. Nielsen et al., *J. Org. Chem.* **41**, 3221 (1976).
[5] T. Takajo, S. Kambe, W. Ando, *Synthesis* **1983**, 564.
[6] S.V. Svetozarski, E.N. Zilberman, A.I. Finkelshtein, *Zh. Obshch. Khim.* **31**, 1717 (1961).
[7] R.A.G. Smith, J.R. Knowles, *J. Chem. Soc. Perkin Trans. 2*, **1975**, 686.