Reaction of 2,4,6-Tri-*t*-butylnitrobenzene with Alkyl Grignard Reagents

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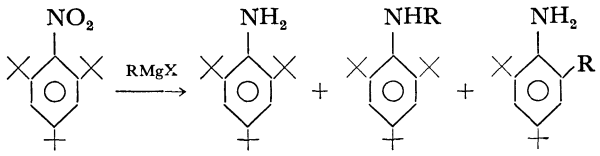
Reactions of 2,4,6-tri-*t*-butylnitrobenzene (**1**) with alkylmagnesium halides afforded 2,4,6-tri-*t*-butylaniline (**2**), *N*-alkyl-2,4,6-tri-*t*-butylanilines (**3**), 6-alkyl-2,4-di-*t*-butylanilines (**4**), 4-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,5-cyclohexadienes (**5**), and 6-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,4-cyclohexadienes (**6**) depending on the Grignard reagents used. Reduction of the oxime **6** proved to be responsible for the formation of the aniline **4**. Comparison of the present reactions with those of 2,4,6-tri-*t*-butylnitrosobenzene (**7**) with Grignard reagent, *syn-anti*-isomers of the oxime **6**, and the formation mechanisms of the products have been discussed.

Only a few studies have been reported on the reaction between Grignard reagents and nitroarenes.[1-3] Grignard reagents have been reported to attack nitroarenes usually on the nitro group resulting in its reduction; for example, reactions of ethylmagnesium bromide with nitrobenzene and nitrotoluenes merely afforded the corresponding *N*-ethylanilines and azobenzenes.[3] The only one exception is an abnormal addition of a Grignard reagent to 1,3,5-trinitrobenzene leading to 1,3,5-trinitro-2,4,6-trialkylcyclohexanes.[2]

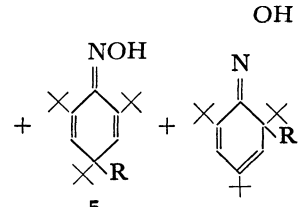
We describe here the reaction of 2,4,6-tri-*t*-butylnitrobenzene (**1**) with Grignard reagents giving some abnormal products,[4] and discuss the mechanism of their formation. This reaction was carried out with the intention of obtaining cyclohexadienone oximes (6-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,5-cyclohexadienes and 4-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,4-cyclohexadienes) whose properties we are interested in:[5] the only one route to the oximes is the reaction of 2,4,6-tri-*t*-butylnitrosobenzene (**7**) with Grignard reagents.[6] However, considering reducing ability of Grignard reagents, it seemed to be possible to prepare the oximes using the nitrobenzene **1** instead of the nitrosobenzene **7**, and such reaction is more convenient because **1** is the starting material in the preparation of **7**.[7]

Results and Discussion

Reaction Products. Reactions of **1** with a large excess of alkylmagnesium halides in ether at 0 °C afforded some of the following compounds: 2,4,6-tri-*t*-butylanilines(**2**), *N*-alkyl-2,4,6-tri-*t*-butylanilines (**3**), 6-alkyl-2,4-di-*t*-butylanilines (**4**), 4-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,5-cyclohexadienes (**5**), and 6-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,4-cyclohexadienes (**6**).



R	
a	Me
b	Et
c	*i*-Pr
d	*t*-Bu
e	$PhCH_2$
f	1-Ad*



* Ad represents adamantyl group.

The yields of the products and the reaction conditions are summarized in Table 1. The structures of the products were confirmed by the analytical and spectral data. Compound **6α** which was obtained also in the reactions of Grignard reagents with 2,4,6-tri-*t*-butylnitrosobenzene (**7**)[6] is one of the *syn*- and *anti*-isomers, and **6β** is the other. These two isomers could easily be distinguished from each other by the NMR spectra and separated by chromatography: R_f value of **6α** was smaller than that of **6β**. The NMR spectra of **6αa** showed two olefinic protons at δ 5.42 and 6.15, whereas **6βa** at 5.17 and 6.10, similarly **6αb** at 5.33 and 6.22, but **6βb**

Table 1. Reaction conditions and yields (%) of the products

No.[a]		RMgX	Reaction time (hr)	Yields (%)					
				2	**3**	**4**	**5**	**6α**	**6β**
1		MeMgI	3.7	40	2	17	—	—	—
2[b,c]	**a**	MeMgI	5	5	—	—	5	19	2
3[b]		MeMgI	20	5	—	—	15	43	7
4	**b**	EtMgBr	1.5	41	4	7	14	—	8
5	**c**	*i*-PrMgBr	4.8	40	16	6	21	—	—
6	**d**	*t*-BuMgCl	5.9	49	28	—	—	—	—
7	**e**	$PhCH_2MgCl$	3.4	12	—	—	25	38	—
8[d]	**f**	1-AdMgBr	5	12	—	—	4	—	—

a) Excess amount of magnesium was used in preparation of Grignard reagents except for Nos. 2 and 3. b) Excess amount of methyl iodide was used in preparation of Grignard reagent. c) 51% of **1** was recovered. d) A considerable amount of **1** was recovered.

at 5.13 and 6.12. The difference in the chemical shifts of the two olefinic protons of **6β** is larger than that of **6α**. There are other features on the NMR spectra: the signals due to the methyl group on the 6-position of **6αa** appeared at δ 1.32, but that of **6βa** at 1.61, similarly the methylene protons of the 6-ethyl group of **6αb** appeared at δ 1.4—2.3, but that of **6βb** at 3.00. Thus the signals of 6-alkyl group on **6β** appeared at a lower field than those of **6α**. This difference makes it possible to evaluate the isomer ratio.

Absorption maxima of **6αa**, **6αb**, **6βa**, and **6βb** are listed in Table 2. The isomers **6β** are characterized by the absorption maxima at longer wavelength by a few nm than those of **6α**.

Table 2. Absorption maxima of **6α** and **6β** in hexane

6	λ_{max} (nm)	ε
6αa	304	4400
6βa	308.5	4370
6αb	308	4400
6βb	310.5	3690

Although these data are insufficient to establish their configuration, we tentatively assign **6α** to structure (A) and **6β** to (B) on the following basis: (1) the protons *syn* to the hydroxyl group of the oximes have lower chemical shifts (δ) than those of the other isomer,[8] (2) the slight hypsochromic shift in the UV absorption of α-isomer is consistent with the larger twisting of the hydroxyimino group from the molecular plane, because the 2-*t*-butyl group is in the molecular plane but the 6-*t*-butyl and the 6-alkyl groups are out of the molecular plane, and (3) the larger R_f value of **6β** than that of **6α** in thin layer chromatography (tlc) is consistent with structure (B), in which the hydroxyl group is more thickly covered with two alkyl groups than that of (A).

(A)≡**6α** (B)≡**6β**

The formation of **5**, **6α**, and **6β**, which seemingly shows that the Grignard reagents attacked to *ortho*- and the *para*-positions of the nitro group, is unprecedented in the reactions of the Grignard reagents with nitro arenes,[1-3] though a similar compound, 1-hydroxyimino-2,4,6-tri-*t*-butyl-2,4-cyclohexadiene (**6**, R=H), could be obtained by the reduction of **1** with sodium-bis(2-methoxyethoxy)aluminum hydride (Vitride).[9] The direct formation of **3c** and **3d** from the readily available nitrobenzene **1** is of synthetic significance, considering the difficulties reported for alkylation of **2**.[10] The only alternative route to these compounds is the reaction of 2,4,6-tri-*t*-butylnitrosobenzene (**7**) with Grignard reagents,[6] but the present reaction seems to provide a more convenient method for preparation of these compounds.

Reaction Mechanism. Although a possibility of direct addition of Grignard reagents to **1** cannot be ruled out, reducing ability of Grignard reagents suggests that oximes **5** and **6**, and secondary amines **3** are probably produced by addition of Grignard reagents to the nitrosobenzene **7** formed by reduction of **1**, for the reaction rate depends on the amount of magnesium metal which was found to play an important role in the reduction process as discussed below: in the reaction with methylmagnesium iodide prepared by use of excess magnesium, **1** was consumed completely in 3.5 hr, but the reaction with methylmagnesium iodide prepared by use of an excess of methyl iodide resulted in 51% recovery of **1** even after 5 hr.

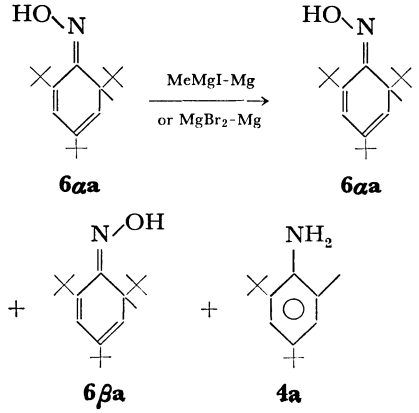
However, in Nos. 1, 4, and 5 in Table 1, the reaction products were different from those of the reaction with **7**; the reactions of **7** afforded the cyclohexadienone oximes (R=Me, Et, *i*-Pr, $PhCH_2$, 1-Ad) or **3a** (R=*t*-Bu) mainly but reduction products **2** and **4** only in small amounts.[6] This difference is ascribed to some secondary reactions discussed below.

The yields of **4** were decreased in the following order:

Me>Et>*i*-Pr

The yields of **6α** obtained in the reactions of **7** with Grignard reagents were also in the same order.[6] These facts suggest that **4** was formed *via* **6α**. Since a longer reaction time is required in the reaction with **1**, it is considered that further reaction of **6α** into **4** is effected in the case of **1**. In order to prove this pathway, reaction of **6αa** with methylmagnesium iodide in the absence of magnesium was carried out, and **6αa** was recovered quantitatively. However, reaction of **6αa** with methylmagnesium iodide in the presence of excess magnesium at room temperature for 3 hr afforded 32% of **4a** and 30% of **6βa** besides 38% recovery of **6αa** based on the NMR spectrum, and they were isolated by tlc in 18, 13, and 12% yields, respectively. This result suggests that magnesium metal in combination with magnesium halide is responsible for the reduction of **6α** into **4**.

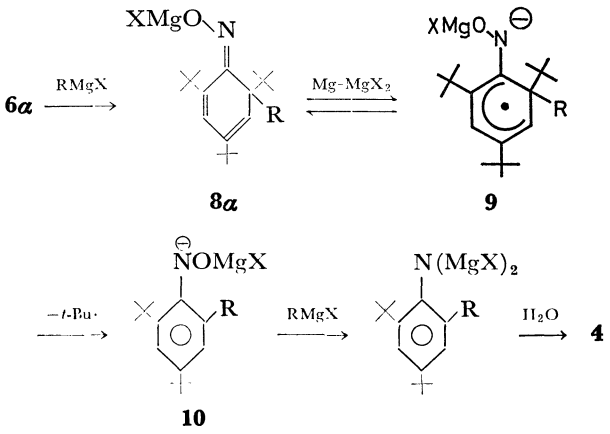
In fact, the reaction mixture of **6αa**, magnesium, and magnesium bromide (at room temperature for 2.8 hr) showed NMR signals due to **4a** and **6αa**. The molar ratio was found to be 8 : 3 (73 and 27% respectively) from the NMR spectrum, and the chromatographic separation afforded 27% of **4a** and 9% of **6αa**, which seemed to be contaminated by a trace of **6βa** according to the NMR spectrum.



6αa **6αa**

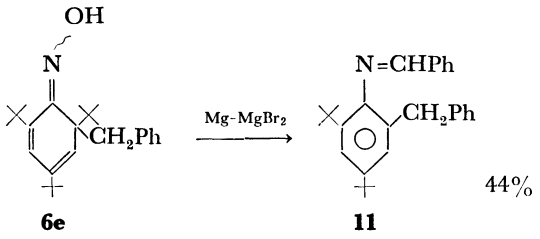
6βa **4a**

Therefore, the formation of **4** is interpreted as follows:



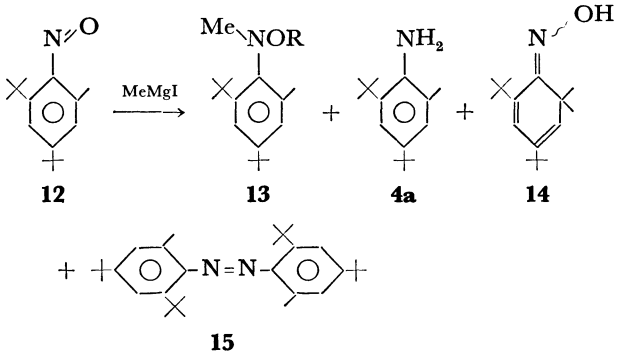
The isomerization of the oxime **6** may be ascribed to the reversibility between **8** and **9**.

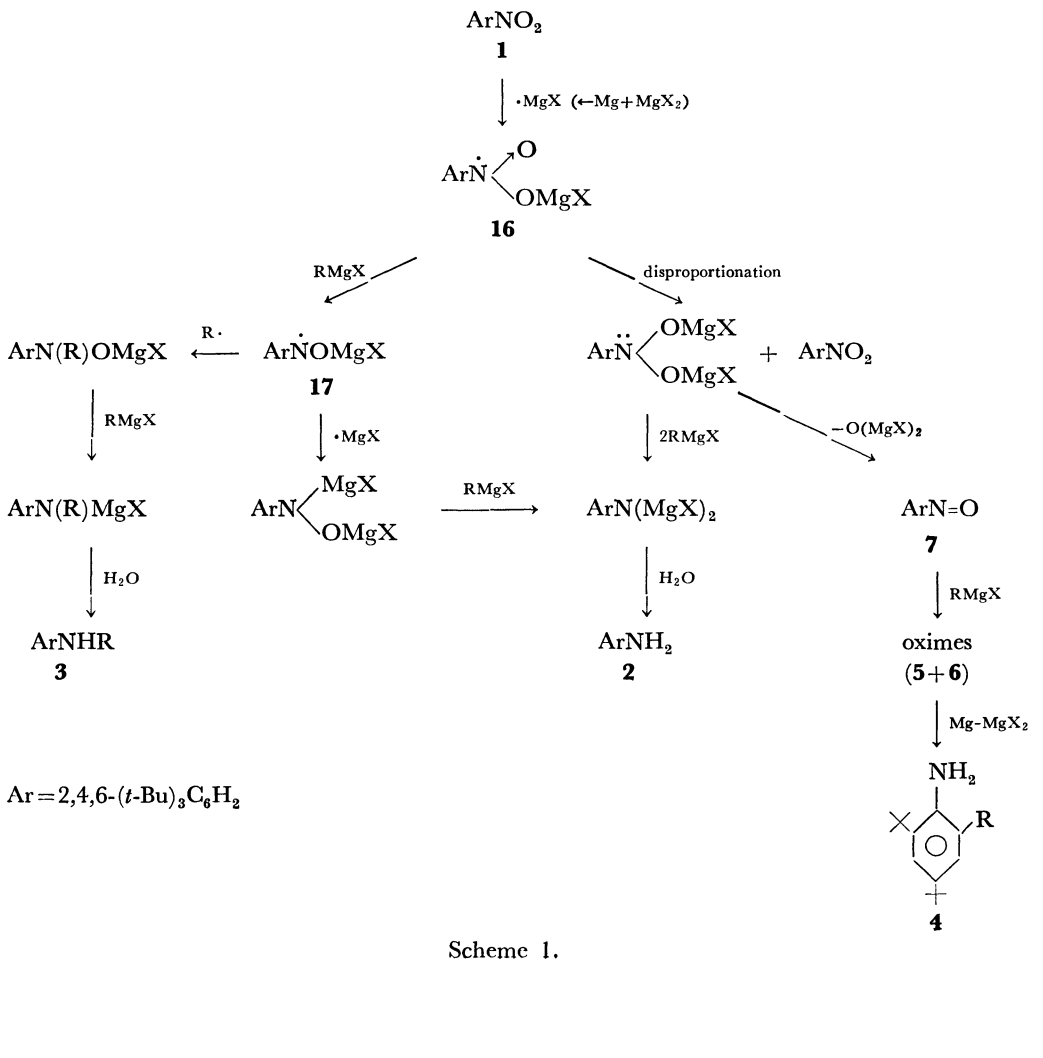
This interpretation may explain a reason why **4** was not produced in the case of benzylmagnesium chloride despite of the presence of excess magnesium,



because the reducing ability of Mg–$MgCl_2$ system may be weaker than that of Mg–$MgBr_2$ system. However, **6e** afforded an unusual product, 2-benzyl-4,6-di-*t*-butyl-*N*-benzylideneaniline (**11**) by reaction with Mg–$MgBr_2$. The formation mechanism is obscure.

In contrast to these lines of evidence suggesting that **4** was formed *via* **6**, any proof for reduction of the oxime **5** into 4-alkyl-2,6-di-*t*-butylaniline was not obtained. Actually, the reaction of **5c** with isopropylmagnesium bromide in the presence of magnesium metal resulted in complete recovery of **5c**. This selectivity in reduction is probably because an electron affinity of **5** is less than that of **6** as a simple HMO calculation demonstrates that the orbital energy (-0.445β)for the LUMO of 1,3,5-hexatriene has a lower value than that (-0.581β) of 2-vinyl-1,3-butadiene.[11] Namely, the single electron transfer into the





Scheme 1.

LUMO of **6** leading to the radical anion **9** is energetically more advantageous than that of **5**.

A route to **4** *via* 2,4-di-*t*-butyl-6-methylnitrosobenzene (**12**) can be ruled out: reaction of **12** with methylmagnesium iodide afforded **4a** only in a 22% yield besides 44% of *N*-(2,4-di-*t*-butyl-6-methylphenyl)-*N*-methylhydroxylamine (**13**), 17% of 1-hydroxyimino-2,4-di-*t*-butyl-6,6-dimethyl-2,4-cyclohexadiene (**14**), and 0.6% of 2,4,2′,4′-tetra-*t*-butyl-6,6′-dimethylazobenzene (**15**). The formation of considerable amounts of **13** and **14** was inconsistent with the result of the reaction of **1** with methylmagnesium iodide.

The formation of a large amount of **2** remains unresolved. The reduction of intermediary nitrosobenzene **7** might be possible but not be predominant, because the addition of Grignard reagents to **7** is faster than the reduction of **7** as suggested by the fact that only a small amount of **2** was obtained in the reaction of **7** with Grignard reagents.[6] Two processes may be possible: the one is a process involving a disproportionation of the radical anion **16**.[12] The other pathway involves reduction of **1** into an anion radical **17** which is considered to be the common intermediate for **2** and **3** as described in a previous paper,[6] and this route might explain the increased yield of the secondary amine **3** in the present reaction compared with the reaction of **7**.[6]

The probable reaction mechanism is summarized in Scheme 1.

It is concluded that the higher yields of oximes (**5** and **6**) can be obtained by the reaction of **1** with Grignard reagents in the absence of magnesium. Actually, the oxime **6αa** was obtained as a main product in No. 3 in Table 1 where an excess amount of methyl iodide was used in preparation of the Grignard reagent.

Experimental

All melting points were not corrected. The IR and UV spectra were recorded with Hitachi EPI-G2 and EPS-3 spectrophotometers respectively. The NMR spectra were measured with a Hitachi R-24 spectrometer using tetramethylsilane as an internal standard. The mass spectra were recorded with a Hitachi RMU-6L mass spectrometer. All reactions were carried out under nitrogen.

Materials. 2,4,6-Tri-*t*-butylnitrobenzene[10] (**1**) (mp 202.5—203.5 °C), 2,4-di-*t*-butyl-6-methylnitrosobenzene[7] (**12**) (mp 31.5—33.5 °C), 2,4-di-*t*-butyl-6-methylaniline[13] (**4a**) (mp 31.5—32.5 °C), 2,4,6-tri-*t*-butyl-*N*-methylaniline[10] (**3a**) (mp 109.5—111.0 °C), and 2,4,6-tri-*t*-butyl-*N*-ethylaniline[10] (**3b**) (mp 79.5—81.0 °C) were prepared by the reported methods. 2,4,6-Tri-*t*-butyl-*N*-isopropylaniline (**3c**), 2,4,6,*N*-tetra-*t*-butylaniline (**3d**), 6-alkyl-1-hydroxyimino-2,4,6-tri-*t*-butyl-2,4-cyclohexadienes (**6α**), and 4-alkyl-2,4,6-tri-*t*-butyl-2,5-cyclohexadienes (**5**) were prepared as described previously.[6]

Reaction of 2,4,6-Tri-t-butylnitrobenzene (1) with Methylmagnesium Iodide. To an ice-cold Grignard solution prepared from 2.02 g (83.1 mmol) of magnesium and 9.77 g (68.8 mmol) of methyl iodide in 25 ml of ether, a solution of 2.00 g (6.87 mmol) of **1** in 30 ml of ether was added dropwise with stirring over 1.7 hr. After additional stirring at 0 °C for 2 hr, the reaction mixture was poured into aqueous ammonium chloride and extracted with ether. The extract was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was chromatographed on a silica gel dry column with carbon tetrachloride to be devided into nine fractions, each of which was eluted with ether. The first fraction gave 12 mg of orange crystals, which could not be purified. The third fraction afforded 45 mg of pale yellow crystals. The fourth fraction gave 111 mg of colorless crystals, which recrystallized from methanol to give the same material as that obtained from the third fraction by the spectral data, mp 143—145 °C; IR (KBr): 3000, 2950, 1625, 1600, 1455, 1420, 1390, 1360, 1240, and 1210 cm^{-1}; NMR (CCl_4): δ 0.78 (s, 9H), 1.18 (s, 9H), 1.27 (s, 27H), 1.54 (s, 9H), 6.50 (broad s, 1H), 6.60 (broad s, 1H), and 7.05 (s, 2H); λ_{max}(hexane): 241 and 260 nm (the absorbances of a solution (28.5 mg/l) were 1.09 and 0.61 respectively); Mass: *m/e* 260 (22%), 245 (100), and 231 (64). These data were insufficient to elucidate the structure. From the mother liquor 40 mg (2%) of 2,4,6-tri-*t*-butyl-*N*-methylaniline (**3a**) was isolated, and identified by the IR and NMR spectra. The sixth fraction afforded 720 mg (40%) of 2,4,6-tri-*t*-butylaniline (**2**) (by NMR and IR). The eighth fraction afforded 330 mg of tarry material, which was rechromatographed on alumina with carbon tetrachloride as eluent to give 262 mg (17%) of 2,4-di-*t*-butyl-6-methylaniline (**4a**) (by NMR and IR) and 60 mg of unidentified crystalline material. The other fractions afforded small amounts of unidentified materials.

Reaction of 1 with Methylmagnesium Iodide Prepared Using Excess of Methyl Iodide. Reaction of a Grignard solution prepared from 5.25 g (37 mmol) of methyl iodide and 816 mg (33.6 mmol) of magnesium in 15 ml of ether with 1.00 g (3.44 mmol) of **1** in 19 ml of ether for 5 hr at 0 °C afforded 507 mg (50.7%) of recovered **1**, 102 mg of a mixture of **2** and the oxime **6βa** (molar ratio 7 : 4 based on the NMR signal intensity), 54 mg (5%) of **5a**, and 190 mg (19%) of **6αa**, after a similar treatment. The mixture of **2** and **6βa** was rechromatographed on an alumina dry column with hexane to give 43 mg (5%) of **2** and 21 mg (2%) of **6βa**·**6βa**: mp 103—105 °C; IR (KBr): 3300, 3180 (νOH), 980, and 960 cm^{-1} (νNO); NMR (CCl_4): δ 0.89 (s, 9H), 1.09 (s, 9H), 1.24 (s, 9H), 1.61 (s, 3H), 5.17 (d, J=2 Hz, 1H), 6.10 (d, J=2 Hz, 1H), and 7.10 (broad s, 1H), λ_{max} (hexane): 305 nm (ε 4520); Mass: *m/e* 291 (M^+, trace) and 57 (100%).

Reaction of 1 with Ethylmagnesium Bromide. Reaction of a Grignard solution prepared from 2.03 g (83.5 mmol) of magnesium and 7.94 g (68.7 mmol) of ethyl bromide in 26 ml of ether with 2.00 g (6.87 mmol) of **1** in 30 ml of ether for 1.5 hr at 0 °C gave 80 mg (4%) of 2,4,6-tri-*t*-butyl-*N*-ethylaniline (**3b**) (by IR and NMR), 35 mg of white crystals, which failed to be purified (NMR (CCl_4): δ 0.91 (s, 9H), 1.11 (s, 9H), 1.28 (s, 9H), 5.15 (d, J=2 Hz, 1H), 6.15 (d, J=2 Hz, 1H), and the signals of the ethyl group were not resolved clearly), 169 mg of **2** (by IR and NMR), 871 mg of a mixture of **2** (570 mg) and 1-hydroxyimino-2,4,6-tri-*t*-butyl-4-ethyl-2,5-cyclohexadiene (**5b**, 301 mg, 14%) (by NMR), and 428 mg of tarry material. The mixture of **2** and **5b** was rechromatographed on an alumina dry column with hexane to give 508 mg of **2** and 228 mg (11%) of **5b**. Therefore, the total amount of **2** was 677 mg (38%, isolated), and 739 mg (41%) from NMR. The last tarry material was again chromatographed on a silica gel dry column with carbon tetrachloride to divide into A and B fractions. Fraction A gave 160 mg (8%) of an isomer of 1-hydroxyimino-2,4,6-tri-*t*-butyl-6-ethyl-2,4-cyclohexadiene (**6βb**) as white crystals, which were recrystallized three times from aqueous methanol, mp 122—123.5 °C; IR (KBr): 3300, 3170 (νOH), and 975 cm^{-1} (νNO); NMR (CCl_4): δ 0.74 (t,J=

7 Hz, 3H), 0.91 (s, 9H), 1.10 (s, 9H), 1.26 (s, 9H), 3.00 (q, J=7 Hz, 2H), 5.13 (d, J=2 Hz, 1H), 6.12 (d, J=2 Hz, 1H), and 6.95 (broad s, 1H); λ_{max} (hexane): 310.5 nm (ε 3690); Mass: *m/e* 305 (M^+, 0.8%) and 57 (100).

Found: C, 78.58, H. 11.25; N, 4.45%. Calcd for $C_{20}H_{35}NO$: C, 78.63; H, 11.55; N, 4.58%.

Fraction B afforded 113 mg (7%) of 2,4-di-*t*-butyl-6-ethylaniline (**4b**) as tarry material, which was treated twice with tlc (silica gel, benzene) and distilled twice molecularly to give white crystals, mp 34.5—37 °C; IR (neat): 3490 and 3405 cm^{-1} (νNH_2); NMR (CCl_4): δ 1.23 (t, J=7 Hz, 3H), 1.26 (s, 9H), 1.42 (s, 9H), 2.50 (q, J=7 Hz, 2H), 3.57 (broad s, 2H), and 6.95 (ABq, $\Delta\delta$=0.16, J=2 Hz, 2H), λ_{max} (hexane): 240 (ε 8620) and 289 nm (2490); Mass: *m/e* 233 (M^+, 21%) and 218 (100).

Found: C, 82.29; H, 11.74; N, 6.06%. Calcd for $C_{16}H_{27}N$: C, 82.35; H, 11.66; N, 6.00%.

Reaction of ***1*** *with Isopropylmagnesium Bromide.* Reaction of a Grignard solution prepared from 2.02 g (83.1 mmol) of magnesium and 9.30 g (75.6 mmol) of isopropyl bromide in 25 ml of ether with 2.00 g (6.87 mmol) of **1** in 29 ml of ether for 4.8 hr at 0 °C produced 330 mg (16%) of 2,4,6-tri-*t*-butyl-*N*-isopropylaniline (**3c**) (by NMR and IR), 1.23 g of white crystals, and 100 mg (6%) of 2,4-di-*t*-butyl-6-isopropylaniline (**4c**), which was recrystallized eight times from methanol, mp 86.0—87.5 °C; IR (KBr): 3485 and 3405 cm^{-1} (νNH_2); NMR (CCl_4): δ 1.20 (d, J=7 Hz, 6H), 1.26 (s, 9H), 1.43 (s, 9H), 2.89 (sep, J=7 Hz, 1H), 3.54 (broad s, 2H), and 7.00 (ABq, J=2 Hz, $\Delta\delta$=0.08, 2H); Mass: *m/e* 247 (M^+, 23%) and 232 (100).

Found: C, 82.77; H, 11.81; N, 5.87%. Calcd for $C_{17}H_{29}N$: C, 82.52; H, 11.82; N, 5.66%.

The white crystals were rechromatographed on an alumina dry column with hexane to give 449 mg (21%) of 1-hydroxyimino-2,4,6-tri-*t*-butyl-4-isopropyl-2,5-cyclohexadiene (**5c**) and 710 mg (40%) of **2**, which were identified by the spectral data.

Reaction of ***1*** *with* t-*Butylmagnesium Chloride.* Reaction of a Grignard solution prepared from 2.02 g (83.1 mmol) of magnesium and 6.34 g (68.5 mmol) of *t*-butyl chloride in 20 ml of ether with 2.00 g (6.87 mmol) of **1** in 27 ml of ether for 5.9 hr at 0 °C afforded 646 mg (28% based on consumed **1**) of 2,4,6,*N*-tetra-*t*-butylaniline (**3d**) (by NMR), 113 mg (5.7%) of recovered **1**, and 833 mg (49%) of **2** (by IR and NMR).

Reaction of ***1*** *with Benzylmagnesium Chloride.* Reaction of a Grignard solution prepared from 3.47 g (151 mmol) of magnesium and 9.59 g (75.5 mmol) of benzyl chloride in 25 ml of ether with 2.00 g (6.87 mmol) of **1** in 22 ml of ether for 3.5 hr at 0 °C gave 1.86 g of bibenzyl contaminated with a small amount of impurities, 535 mg of white crystals, 460 mg 1-hydroxyimino-4-benzyl-2,4,6-tri-*t*-butyl-2,5-cyclohexadiene (**5e**), 961 mg (38%) of 1-hydroxyimino-6-benzyl-2,4,6-tri-*t*-butyl-2,4-cyclohexadiene (**6e**) (by IR and NMR), and 594 mg of brown oil, which seemed to be mainly benzyl alcohol according to the IR and NMR spectra. The white crystals were treated with hexane. The insoluble part (100 mg) was identified as **5e** by IR and NMR. The soluble part was chromatographed on an alumina dry column with hexane to give 222 mg (12%) of **2** and 78 mg of **5e**, the total amount of which was 638 mg (25%).

Reaction of ***1*** *with* 1-*Adamantylmagnesium Bromide.* The Grignard reagent was prepared from 586 mg (24.2 mmol) of magnesium and 4.34 g (20.2 mmol) of 1-adamantyl bromide in 24 ml of ether over 2 hr. An ethereal solution (14 ml) of **1** (1.00 g, 3.44 mmol) was added to the Grignard reagent dropwise with stirring at 0 °C over 1 hr. After additional stirring for 4 hr, the reaction mixture was treated with aqueous ammonium chloride, extracted with ether and filtered to give 943 mg of light gray crystals, mp>220 °C (lit,[14] 288—290 °C); Mass: *m/e* 270 (M^+, 11%) and 135 (100). This compound was considered to be biadamantane. The filtrate was dried over anhydrous magnesium sulfate. After the solvent was removed, the residue was chromatographed on a silica gel dry column with carbon tetrachloride.

The first fraction (R_f=1.0—0.4) gave 2.153 g of pale yellow crystalline material, which seemed to contain **1** according to the NMR spectrum but the accurate amount could not be determined, NMR (CCl_4): δ 1.33 (s), 1.38 (s), 7.46 (s) [these three signals are due to **1**], and broad signals at 1.62, 1.79, and 1.81. The second fraction (R_f=0.4—0.2) afforded 352 mg of tarry material, which was rechromatographed on an alumina dry column with hexane to give 110 mg (12.2%) of **2** and 59 mg (4.2%) of 1-hydroxyimino-4-(1-adamantyl)-2,4,6-tri-*t*-butyl-2,5-cyclohexadiene (**5f**) as colorless tar, which showed the identical IR and NMR spectra with those of an authentic sample.[6] The other fractions gave unidentified materials.

*Reaction of 1-Hydroxyimino-2,4,6-tri-*t*-butyl-6-methyl-2,4-cyclohexadiene (**6αa**) with Methylmagnesium Iodide in the Presence of Excess Magnesium.* The Grignard reagent was prepared from 2.4 g (16.9 mmol) of methyl iodide and 530 mg (21.8 mmol) of magnesium in 9 ml of ether. Into a reaction tube containing an ethereal solution (0.5 ml) of **6αa** (50.0 mg, 0.171 mmol), 2 ml of the Grignard reagent with excess of magnesium metal was pipetted. After being stirred for 3 hr at room temperature, the reaction mixture was worked up as usual to give 36.1 mg of tarry material, which was a mixture of **6αa**, **6βa**, and 2,4-di-*t*-butyl-6-methylaniline (**4a**) (molar ratio: 19 : 15 : 16 ; 38, 30, and 32%, respectively, according to the signal intensity on the NMR spectrum). The separation of the products was carried out by tlc (silica gel, benzene) to afford 8.8 mg (17.6%) of an isomer of 1-hydroxyimino-2,4,6-tri-*t*-butyl-6-methyl-2,4-cyclohexadiene (**6βa**), 6.1 mg (12%) of **6αa**, and 5.0 mg (13%) of **4a**.

Reaction of ***6αa*** *with Magnesium and Magnesium Dibromide.* Anhydrous magnesium dibromide was prepared by the reaction of 1,2-dibromoethane (3.88 g, 20.7 mmol) with magnesium (624 mg, 26.4 mmol) in ether (14 ml).[15] The mixture separated into colorless upper layer and gray lower layer. The lower layer was pipetted with excess magnesium remaining therein into a reaction tube containing an ethereal solution (1 ml) of **6αa** (50.5 mg, 0.174 mmol). The mixture was stirred for 2.8 hr at room temperature and worked up as usual to give 46.5 mg of tarry material, whose NMR spectrum exhibited two sets of the signals due to **6αa** and **4a** in a molar ratio of 3 : 8 (27 and 73% respectively). The residue was subjected to preparative tlc (silica gel, benzene). The first fraction (R_f=0.68) gave 4.6 mg (9%) of **6αa**, which was identified by the NMR and IR spectra but contamination of a small amount of **6βa** was suggested by the following weak signals, NMR (CCl_4): δ 0.91 (s), 1.28 (s), 1.63 (s), and 5.25 (weak). The second fraction (R_f=0.24) afforded 18.9 mg of tarry material, whose NMR spectrum was nearly identical with that of **4a** but some other peaks were observed in the aromatic region. The purification by further tlc (silica gel, dichloromethane) gave 10.3 mg (27%) of **4a** (by IR and NMR).

Reaction of ***6e*** *with Magnesium and Magnesium Dibromide.* An ethereal solution (5 ml) of **6e** (203 mg, 0.55 mmol) and magnesium-containing 3 ml portion of an ethereal solution of magnesium dibromide prepared from magnesium (1 g, 41.2 mmol), 1,2-dibromoethane (5 g, 26.6 mmol), and ether (20 ml) were stirred for 3.5 hr at 0 °C. After hydrolysis, the

reaction mixture was chromatographed on an alumina dry column to give 29.4 mg (14.5%) of **6e** and 90 mg of tarry material, which was again chromatographed on a silica gel dry column with hexane–benzene (4 : 1) as eluent to give 46 mg (44%) of 2-benzyl-4,6-di-*t*-butyl-*N*-benzylideneaniline (**11**) as a yellow tar, which crystallized on standing and was recrystallized three times from aqueous ethanol to give pale yellow crystals, mp 92—93 °C; IR (KBr): 1625 (νC=N), 875 (1,2,4,6-substituted phenyl), 728, 695, and 685 cm^{-1} (two phenyls); NMR (CCl_4): δ 1.35 (s, 18H), 3.76 (s, 2H), and 7.0—7.7 (m, 13H); λ_{max} (hexane): 253 (ε 14300) and 349 nm (1730); Mass: *m/e* 383 (M^+, 38%), 368 (M^+-15, 100), 292 (M^+-PhCH_2, 11), 91 (33), and 57 (26).

Found: C, 87.60; H, 8.81; N, 3.64%. Calcd for $C_{28}N_{33}N$: C, 87.68; H, 8.67; N, 3.65%.

Reaction of 2,4-Di-t-butyl-6-methylnitrosobenzene (12) with Methylmagnesium Iodide. 1) To an ice-cold Grignard solution prepared from 9.47 g (71.8 mmol) of methyl iodide and 1.78 g 73.2 mmol) of magnesium in 30 ml of ether, an ethereal solution (20 ml) of 1.55 g (6.65 mmol) of **12** was added dropwise with stirring over 20 min. After additional stirring for 50 min at 0 °C and usual work-up, the residue was chromatographed on a silica gel dry column with carbon tetrachloride. The first fraction (R_f=1—0.81) gave 18 mg (0.6%) of 2,4,2′,4′-tetra-*t*-butyl-6,6′-dimethylazobenzene (**15**) as orange crystals, mp 156—158 °C; NMR (CCl_4): δ 1.37 (s, 36H), 2.24 (s, 6H), 7.04 (d, J=2 Hz, 2H), and 7.32 (d, J=2 Hz, 2H); λ_{max} (hexane): 238 (ε 9040), 247 (sh) (8750), 311.5 (15650), and 486 nm (1750); Mass: *m/e* 434 (M^+, 5.4%), 217 (35), and 57 (100).

The second fraction (R_f=0.81—0.48) gave 281 mg (17%) of 1-hydroxyimino-2,4-di-*t*-butyl-6,6-dimethyl-2,4-cyclohexadiene (**14**) as white crystals, which were recrystallized four times from methanol, mp 144.5—146 °C; IR (KBr): 3295, 3170 (νOH), and 965 cm^{-1} (νNO); NMR (CCl_4): δ 1.06 (s, 9H), 1.22 (s, 9H), 1.46 (s, 6H), 5.10 (d, J=2 Hz, 1H), 6.12 (d, J=2 Hz, 1H), and 6.96 (s, 1H); λ_{max} (hexane): 300 (sh) (ε 6510), 308.5 (7250), and 319 (sh) nm (4700); Mass: *m/e* 249 (M^+, 14%), 176 (100), and 57 (80).

Found: C, 77.34; H, 11.14; N, 5.33%. Calcd for $C_{16}H_{27}NO$: C, 77.06; H, 10.92; N, 5.62%.

The third fraction (R_f=0.48—0.36) gave 975 mg of pale yellow tarry material, which was a mixture of **13** (44%) and **4a** (22%) (molar ratio by NMR; 2 : 1). When 50 mg portion of the mixture was treated with tlc (silica gel, benzene), **13** and **4a** were isolated. The IR and NMR spectra of **4a** were identical with those of an authentic sample.[13] The compound **13** was tentatively identified as *N*-(2,4-di-*t*-butyl-6-methylphenyl)-*N*-methylhydroxylamine by the spectral data. **13**; pale yellow oil; IR (neat): 3560 and 3400 cm^{-1} (broad, νOH); NMR (CCl_4): δ 1.27 (s, 9H), 1.39 (s, 9H), 2.55 (s, 3H), 3.09 (s, 3H), 4.95 (broad s, 1H), and 6.98 (ABq, $\Delta\delta$=0.15, J=2 Hz, 2H). This compound changed into a crystalline material on standing, which seemed to be a mixture of many components because of the complexity of the NMR and mass spectra.

2) Reaction of a Grignard solution prepared from 1.16 g (47.7 mmol) of magnesium and 6.09 g (42.9 mmol) of methyl iodide in 15 ml of ether with 998 mg (4.28 mmol) of **12** in 12 ml of ether for 3.7 hr at 0 °C gave a small amount of **15**, 224 mg (21%) of **14**, and 620 mg of a mixture of **13** and **4a** (molar ratio: 1.7 : 1, which was calculated on the base of the intensity of the NMR signals due to the methyl group; a singlet at δ 3.09 of **13** and a singlet at 2.12 of **4a**).

References

1) M. S. Kharasch and O. Reinmuth, "Grignard Reagents with Nonmetallic Substances," Prentice-Hall, Engelwood Chliffs, N. J. (1954).
2) T. Severin and R. Schmitz, *Chem. Ber.*, **96**, 3081 (1963).
3) H. Hepworth, *J. Chem. Soc.*, **117**, 1004 (1920).
4) Preliminary report: R. Okazaki, Y. Inagaki, and N. Inamoto, *Chem. Lett.*, **1974**, 1503.
5) R. Okazaki, Y. Inagaki, and N. Inamoto, *Chem. Lett.*, **1974**, 1543.
6) Y. Inagaki, R. Okazaki, and N. Inamoto, This Bulletin, **48**, 621 (1975).
7) R. Okazaki, T. Hosogai, E. Iwadare, M. Hashimoto, and N. Inamoto, This Bulletin, **42**, 3611 (1969).
8) C. G. McCarty, in "The Chemistry of the Carbon-Nitrogen Double Bond," ed. by S. Patai, Interscience Publishers, New York, p. 363 (1970).
9) L. R. C. Barclay, I. T. McMaster, and J. K. Burgess, *Tetrahedron Lett.*, **1973**, 3947.
10) J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser, and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, **77**, 491 (1958).
11) E. Heilbronner and H. Bock, "Das HMO-Modell und seine Anwendung; Tabellen berechneter und experimenteller Größen," Verlag Chemie, GmbH, Weinheim/Bergstr. (1970).
12) G. A. Russell, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, **86**, 1807 (1964); G. A. Russell, E. J. Geels, F. J. Smentowski, K. -Y. Chang, J. Reynolds, and Gerd Kaupp, *ibid.*, **89**, 3821 (1967).
13) J. Geuze, C. Ruinard, J. Soeterbroek, P. E. Verkade, and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, **77**, 491 (1958).
14) H. F. Reinhardt, *J. Org. Chem.*, **27**, 3258 (1962).
15) E. C. Ashby and R. C. Arnott, *J. Organometal. Chem.*, **14**, 1 (1968).