Reaction of a Stable Free Nitrogen-centered Radical, 3,4-Dihydro-2,4,6-triphenyl-2*H*-1,2,4,5-tetrazin-1-yl, with Grignard Reagents[1)]

Yozo MIURA, Yuzo MORIMOTO, and Masayoshi KINOSHITA

Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sumiyoshi-ku, Osaka 558

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The reactions of 3,4-dihydro-2,4,6-triphenyl-2*H*-1,2,4,5-tetrazin-1-yl (**1**) with Grignard reagents such as ethyl-, isopropyl-, butyl-, isobutyl-, *s*-butyl-, *t*-butyl-, cyclohexyl-, phenethyl-, phenyl-, and 2-naphthylmagnesium bromides and benzylmagnesium chloride were examined. In the reactions with the alkylmagnesium halides, coupling compounds (**2**) of **1** with alkyl radicals derived from the alkylmagnesium halides were isolated in 41—50% yields. On the other hand, in the reactions with arylmagnesium bromides the corresponding coupling compounds were not isolated, but biphenyl and 2,2′-binaphthyl were isolated in 87 and 86% yields, respectively. From these results, the reactions of **1** with Grignard reagents are concluded to proceed through a homolytic process.

Recently, many reactions of oxygen-centered radicals with organometallic compounds have been investigated,[2)] and these reactions have been demonstrated to proceed through a homolytic process at metal centers, by stereochemical, kinetic, and ESR studies. However, only a few examples of homolytic reactions with nitrogen-centered radicals have been so far reported.[3)]

In the course of preparation of polymers containing stable free radicals,[4)] the reactions of 3,4-dihydro-2,4,6-triphenyl-2*H*-1,2,4,5-tetrazin-1-yl (**1**, 1,3,5-triphenylverdazyl),[5)] which is a typical stable free nitrogen-centered radical, with alkylmagnesium halides or alkyllithiums used as an initiator, were examined. It was found that coupling compounds of **1**, 1-alkyl-2,4,6-triphenyl-1,2,3,4-tetrahydro-1,2,4,5-tetrazines (**2**), with radicals derived from these organometallic compounds were formed.[6)] The formation of **2** suggests that the reactions proceed through a homolytic process.

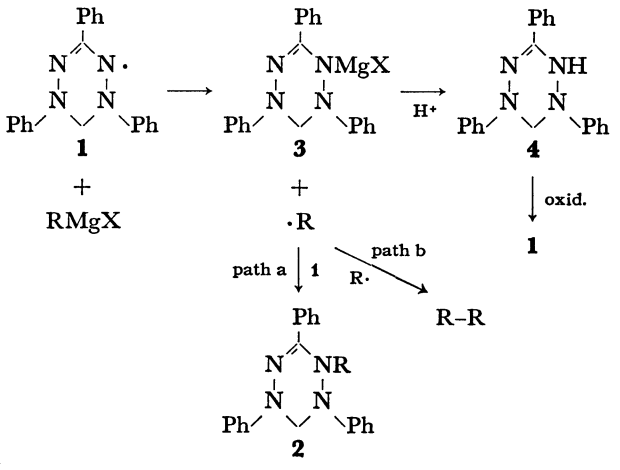
In this paper, the results of the reactions of **1** with various Grignard reagents are described, and the reaction mechanisms will be discussed.

Results and Discussion

Reaction of 1 with Alkylmagnesium Halides. As a Grignard reagent was added gradually to a tetrahydrofuran (THF) solution of **1**, the characteristic dark green color of **1** slowly faded, and turned finally to light yellow within *ca.* 10 min after the Grignard reagent had been added. This yellow solution maintained its color in the absence of moisture. However, when the solution was poured into water, its color retured immediately to green, the coloration indicating that **1** was regenerated. The solution was extracted with benzene, and thin layer chromatography (tlc) revealed the presence of three components in the benzene solution. One of them was easily identified to be **1** on the basis of the green color and the R_f value. One of the other spots disappeared when the benzene solution was allowed to stand for two days under ambient conditions, and the amount of **1** recovered was found to increase gradually from the measurement of absorbance at 720 nm. The spot also disappeared immediatelly upon the addition of catalytic amounts of lead dioxide. A leuco compound (**4**) of **1** is known to be easily oxidized to **1** even by atmospheric oxygen,[5)] and thus, the component was identified to be **4**. This was also ascertained by the R_f value. From these results it is clear that **1** is formed by the oxidation of **4**. The amount of **1** recovered was determined by measuring the absorbance at 720 nm after **4** was oxidized thoroughly to **1**. The results are summarised in Table 1.

Next, the benzene solution was concentrated and subjected to column chromatography. The results indicate the formation of a coupling compound (**2**) of **1** with an alkyl radical derived from the Grignard reagent in 41—50% yields (based on the amount of **1** used).

Reaction of 1 with Arylmagnesium Bromides. The reactions of **1** with arylmagnesium bromides such as phenyl- and 2-naphthylmagnesium bromides were examined. In these cases, the green solution turned to light yellow within *ca.* 2 hr after the addition of the Grignard reagent, and the reaction proceeded much more slowly than that with alkylmagnesium halides. In the extracted benzene solution three components were found. Two of them were identified to be **1** and **4**, respectively. However, the corresponding coupling compound (**2**) was not detected. The amounts of **1** recovered were determined by the same procedure as described above to be 79 and 81% yields (Table 1).



2a : R = C_2H_5 **2f** : R = *t*-C_4H_9
2b : R = *i*-C_3H_7 **2g** : R = ⬡
2c : R = *n*-C_4H_9 **2h** : R = CH_2Ph
2d : R = *i*-C_4H_9 **2i** : R = CH_2CH_2Ph
2e : R = *s*-C_4H_9

Scheme 1.

These values are much larger than those for alkylmagnesium halides. The benzene solution was then concentrated and subjected to column chromatography to give biphenyl and 2,2′-binaphthyl in almost quantitative yields (Table 1).

Reaction Mechanism. From these results a reasonable reaction mechanism may be illustrated as shown in Scheme. In the reactions of **1** with alkylmagnesium halides, **1** and a Grignard reagent are converted into the corresponding magnesium salt (**3**) and an alkyl radical. The alkyl radical formed is captured exclusively by another **1** to give a coupling compound (**2**, path a). This is also supported by the fact that **1** has been found to be an efficient inhibitor in radical polymerization,[7] and that the amount of octane detected in the reaction of **1** with butylmagnesium bromide was almost the same as found in the course of the preparation of the Grignard reagent. Although **3** is stable under anhydrous conditions, it decomposes immediately in contact with water to give a lueco compound (**4**), which is oxidized gradually by atmospheric oxygen to **1**.

In the reactions with arylmagnesium bromides, aryl radicals formed are not captured by **1**, but are coupled with each other to give the biarlys (path b), and therefore, the amounts of **1** recovered were much larger than those for the alkylmagnesium halides.

In order to confirm whether **1** reacts with a phenyl radical, an attempted reaction of **1** with phenylazotriphenylmethane[8] was examined. A benzene solution containing **1** and two equivalents of the azo-compound was refluxed for a few hours. The resulting reaction mixture was examined by tlc, but the corresponding coupling compoung was not detected.

Experimental

All melting points were uncorrected. Thin layer chromatography was performed on Kieselgel GF_{254} according to Stahl Type 60 (E. Merck, Darmstadt, West Germany), using benzene, and detection was effected by UV irradiation. The NMR spectra were recorded using a Hitachi-Perkin Elmer R-20 Spectrometer in $CDCl_3$, using TMS as an internal standard. The visible spectra were measured with a Hitachi Recording Spectrometer Model EPS-3T.

THF was distilled from KOH, sodium wire, and from $LiAlH_4$ before use. All Grignard reagents were prepared by treating alkyl and aryl halides [2.0 ml except for 2-bromonaphthalene (2.0 g)] with a slight excess of magnesium in THF (50 ml), and the conversions were determined by the method of Gilman *et al.*[9]

3,4-Dihydro-2,4,6-triphenyl-2*H*-1,2,4,5-tetrazin-1-yl (**1**) was prepared by treating 1,3,5-triphenylformazan with 37% formalin in the presence of potassium hydrogensulfate according to the procedure of Kuhn and Trischmann,[5] and was recrystallized from methanol, mp 141—142 °C (lit,[5] 139—140 °C).

General Procedure for the Reactions of 1 with Grignard Reagents. **1** (0.50 g, 1.6 mmol) and THF (15 ml) were put in a vessel with a rubber-capped neck. After the dark green THF solution was degassed by freeze-and-thaw cycles, the vessel was sealed. A Grignard reagent was then added gradually to the THF solution at 0 °C through the rubber-cap with a syringe. The green reaction mixture was allowed to stand for *ca.* 10 min (in the reactions with alkylmagnesium halides) and *ca.* 2 hr (for arylmagnesium bromides) at the same temperature, after which, turned to light yellow. After 2 hr, the solution was poured into water, and extracted with benzene. The benzene solution was washed with dilute hydrochloric acid (*ca.* 1 M), and with water, and dried over sodium sulfate. The amount of **1** recovered was determined by the measurement of absorbance at 720 nm (ε 4330 in benzene) in the benzene solution (total volume 3000 ml). Next benzene was evaporated under reduced pressure and the residue obtained was subjected to chromatography on a silica-gel column (Mallinckrodt 100 mesh, 25×400 cm) with benzene, giving a coupling compound (**2**) in the case of reactions with alkylmagnesium halides, and biaryls with arylmagnesium bromides. All results of the reactions are summarized in Tables 1 and 2.

The biphenyl isolated by this method was in the form of pure crystals, 0.12 g (0.78 mmol), mp 70—71 °C (lit,[10] 71 °C). The isolated 2,2′-binaphthyl contained small amounts of naphthalene, which was removed by recrystallization from ethanol, 0.19 g (0.75 mmol), mp 184—185 °C (lit,[11] 185—186 °C). The amounts of biaryls which arise from the preparation procedure of arylmagnesium bromides were determined as follows; the same amounts of arylmagnesium bromides used in the reactions were hydrolyzed, and extracted with benzene. The benzene solution was concentrated, and the residue was analyzed by column chromatography. The amounts of biphenyl and 2,2′-binaphthyl isolated were 0.013 g (0.084 mmol) and 0.015 g (0.059 mmol), respectively.[12] The yields of the

Table 1. The results of the reactions of 3,4-dihydro-2,4,6-triphenyl-2*H*-1,2,4,5-tetrazin-1-yl (**1**) with Grignard reagents[a]

Grignard reagent	mmol[b]	Recovered **1** (%)	Isolated coupling compound	(%)[c]
Ethylmagnesium bromide	1.6	36	**2a**	47
Isopropylmagnesium bromide	1.5	39	**2b**	41
Butylmagnesium bromide	1.0	40	**2c**	43
Isobutylmagnesium bromide	1.5	39	**2d**	50
s-Butylmagnesium bromide	1.3	38	**2e**	46
t-Butylmagnesium bromide	1.5	37	**2f**	46
Cyclohexylmagnesium bromide	1.6	34	**2g**	43
Benzylmagnesium chloride	1.4	42	**2h**	50
Phenethylmagnesium bromide	1.5	33	**2i**	48
Phenylmagnesium bromide	1.9	81	Biphenyl	87
2-Naphthylmagnesium bromide	2.2	78	2,2′-Binaphthyl	86

a) Reaction condition: **1**, 0.50 g (1.6 mmol); tetrahydrofuran, 15 ml, at 0 °C. b) Molar amount required for the completion of the reaction. c) Based on the amount of **1** used.

TABLE 2. PHYSICAL AND ANALYTICAL DATA OF 1-ALKYL-2,4,6-TRIPHENYL-1,2,3,4-TETRAHYDRO-1,2,4,5-TETRAZINE (**2**)

2	Mp (°C) (lit)	Formula	Anal (%) Found / Calcd C	H	N	NMR ($CDCl_3$) δ (ppm)
2a	133—134	$C_{22}H_{22}N_4$	77.12	6.54	16.43	1.28(t, J=8 Hz, 3H), 2.50—3.60(b, 2H), 4.20—4.70
			77.16	6.48	16.36	(b, 1H), 5.35—5.90(b, 1H), 6.70—8.00(m, 15H)
2b	124—125	$C_{23}H_{24}N_4$	77.25	6.73	15.57	1.10(d, J=7 Hz, 3H), 1.17(d, J=7 Hz, 3H), 3.95
			77.49	6.97	15.72	(q, J=7 Hz, 1H), 4.86(q, J=12 Hz, 2H), 6.63—7.93 (m, 15H)
2c	109—111	$C_{24}H_{26}N_4$	77.67	6.88	15.08	0.65—2.10(m, 7H), 2.50—3.65(b, 2H), 4.13—4.70
			77.80	7.07	15.12	(b,1H), 4.35—5.90(b, 1H), 6.70—8.00(m, 15H)
2d	158—160	$C_{24}H_{26}N_4$	78.16	7.18	15.25	0.65—1.30 (b, 6H), 1.80—2.63(m, 1H), 2.65—3.20
			77.80	7.07	15.12	(b, 2H), 4.98(q, J=12 Hz, 2H), 6.70—8.13(m, 15H)
2e[a]	104—105	$C_{24}H_{26}N_4$	78.02	7.04	14.93	0.75 and 0.80(t, J=7 Hz, 3H), 1.06 and 1.14(d, J=
			77.80	7.07	15.12	7 Hz, 3H), 1.20—1.92(m, 2H), 3.68(q, J=7 Hz, 1H), 4.90 and 4.98(q, J=12 Hz, 2H), 6.60—7.90(m, 15H)
2f	189—190	$C_{24}H_{26}N_4$	77.82	6.97	15.10	1.26(s, 9H), 5.25(q, J=13 Hz, 2H), 6.70—7.79(m,
			77.80	7.07	15.12	15 H)
2g	142—144	$C_{26}H_{28}N_4$	78.93	7.10	13.97	0.65—2.15(b, 10H), 3.25—3.80(b, 1H), 4.98(q, J=
			78.75	7.12	14.13	12 Hz, 2H), 6.55—7.96(m, 15H)
2h	168—169 (172)[13]					
2i	116—118	$C_{28}H_{26}N_4$	80.30	6.19	13.59	2.80—3.70(b, 4H), 4.20—4.80(b, 1H), 5.40—6.00
			80.36	6.26	13.39	(b, 1H), 6.55—7.85(m, 20H)

a) A mixture of diastereoisomers.

biaryls in Table 1 were determined on the basis of these reductions.

References

1) A preliminary report: Y. Miura, Y. Morimoto, and M. Kinoshita, *Chem. Lett.*, **1975**, 19.

2) a) K. U. Ingold and B. P. Roberts, "Free Radical Substitution Reaction," Interscience, New York, N. Y. (1970), p. 10. b) A. G. Davies and B. P. Roberts, *Accounts Chem.. Res.*, **5**, 387 (1972). c) A. G. Davies and B. P. Roberts, "Free Radicals," Vol. 1, ed. by J. K. Kochi, Interscience, New York, N. Y. (1973), p. 547.

3) a) A. G. Davies, S. C. W. Hook, and B. P. Roberts, *J. Organometal. Chem.*, **22**, C 11 (1970). b) A. G. Davies, S. C. W. Hook, B. P. Roberts, and J. M. Smith, *J. Chem. Soc., Perkin II*, **1972**, 993.

4) For a recent report, see, Y. Miura and M. Kinoshita, *Makromol. Chem.*, **175**, 33 (1974).

5) R. Kuhn and H. Trischmann, *Monatsh. Chem.*, **95**, 457 (1964).

6) Y. Miura, Y. Morimoto, and M. Kinoshita, *Makromol. Chem.*, **175**, 3487 (1974).

7) M. Kinoshita and Y. Miura, *ibid.*, **124**, 211 (1969).

8) R. F. Bridger and G. A. Russell, *J. Amer. Chem. Soc.*, **85**, 3754 (1963).

9) H. Gilman, E. A. Zoellner, and J. B. Dickey, *ibid.*, **51**, 1576 (1929).

10) R. Fittig, *Ann.*, **121**, 361 (1862).

11) S. Chooker and L. K. Fieser, *J. Amer. Chem. Soc.*, **63**, 2316 (1936).

12) M. S. Kharasch and E. K. Fields, *ibid.*, **63**, 2316 (1941).

13) M. Kinoshita, N. Yoshizumi, and M. Imoto, *Makromol. Chem.*, **127**, 185 (1969).