^{13}C NMR ($CDCl_3$) δ 18.34, 20.61, 23.37, 25.76, 27.87, 28.36, 33.18, 34.05, 37.08, 52.63, 56.37, 93.53, 120.62, 132.32, 165.91; HMRS, m/e calcd 220.1827, found 220.1829.

Trichoenone and Bazzanenone. The enol ether (0.110 g) was dissolved in THF (5 mL). HCl (10% aqueous) (1 mL) was added and the mixture was stirred at room temperature for 12 h. The THF was removed in vacuo and the residue was extracted 3 times with 10 mL of ether. The organic layer was washed with brine and dried. The solvent was removed in vacuo and the crude product passed through a small silica gel column with 9:1 hexanes/ethyl acetate. Trichoenone was produced in 92% yield. Bazzanenone was similarly produced in 87% yield.

Bazzanenone (6): 300-MHz NMR ($CDCl_3$) δ 0.89 (s, 3 H), 1.00 (s, 3 H), 1.30-2.42 (m, 12 H), 1.63 (br s, 3 H), 5.23-5.29 (m, 1 H); IR ($CDCl_3$) 1728, 1450, 1407, 1370, 1160, 1058 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 17.65 (2 C), 18.58, 23.23, 27.25, 28.06, 31.95, 33.24, 35.71, 40.69, 53.22, 119.73, 132.38, 223.39; HRMS, m/e calcd 191.14359, found 191.14347.

Trichoenone (8): 300-MHz NMR ($CDCl_3$) 0.90 (s, 3 H), 1.01 (s, 3 H), 1.25-2.38 (m, 12 H), 1.63 (br s, 3 H), 5.23-5.30 (m, 1 H); IR ($CDCl_3$) 1729, 1450, 1407, 1380, 1162, 1058 cm^{-1}; ^{13}C NMR ($CDCl_3$) 18.28, 18.36, 18.71, 23.28, 27.37, 27.82, 33.10, 33.67, 36.30, 40.92, 53.89, 119.67, 132.36, 223.92; HRMS, calcd 191.14359, found 191.14339.

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Regioselective Addition of Butenyl Grignard Reagent to the Unactivated Double Bond of 2-(α-Methylallyl) Aza Aromatic Compounds

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The addition of the butenyl Grignard reagent to the unactivated double bond of 2-(α-methylallylic) aza aromatic compounds is completely regioselective, giving the 2-(1,4-dimethyl-5-hexen-1-yl) aza aromatics in good yield. A preliminary coordination of magnesium atom to nitrogen atom and the formation of a six-center transition state involving the butenyl Grignard and the vinyl group has been proposed in order to explain the selectivity of the reaction.

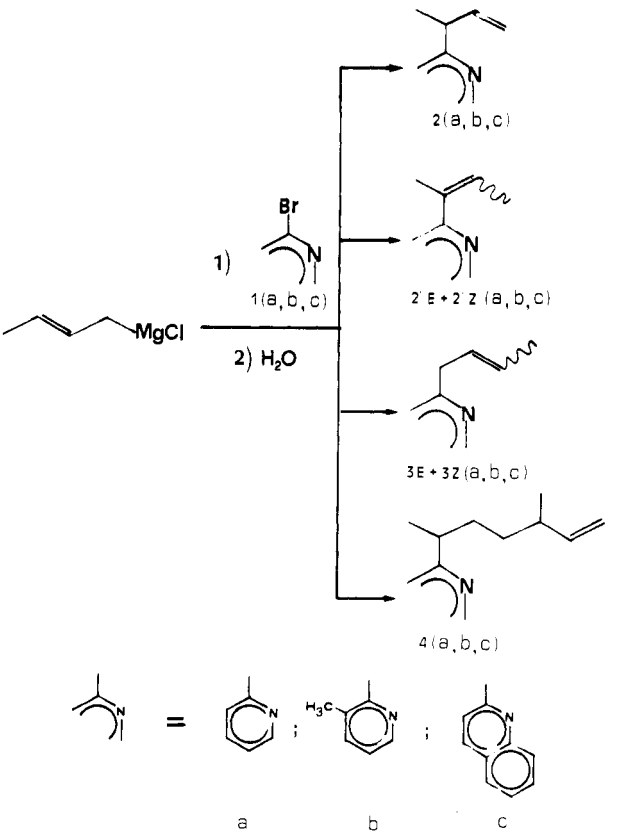
The butenyl Grignard reagent is known to react with many electrophilic substrates and to give crotyl or α-methylallyl derivatives depending on the reaction conditions and the substrates used.[1,2] Recently, we found[3] that the butenyl Grignard reagent is very reactive toward 2-bromo derivatives of aza aromatic heterocyclic compounds such as 2-bromopyridine (**1a**), 2-bromo-3-methylpyridine (**1b**), and 2-bromoquinoline (**1c**). Upon addition of Grignard reagent at 0 °C to the substrates **1a**, **1b**, and **1c** in a 1:1 molar ratio the isomerically pure α-methylallyl derivatives 2-(1-methyl-2-propen-1-yl)pyridine (**2a**), 2-(1-methyl-2-propen-1-yl)-3-methylpyridine (**2b**), and 2-(1-methyl-2-propen-1-yl)quinoline (**2c**) were obtained in good yield.

In the present paper we report the results obtained in the reaction between the aza aromatic compounds **1a**, **1b**, and **1c** and a large excess of butenyl Grignard reagent (molar ratio 1:6).

Results and Discussion

As shown in Scheme I, the most significant result is the formation of the 2-(1,4-dimethyl-5-hexen-1-yl) aza aromatic compounds **4**, arising from the addition of the α-methylallyl group to the CH_2 vinyl carbon atom of the α-methylallyl derivatives **2**. In addition to **4**, the α-methylallyl derivatives **2**, the isomers (*E*)-**2'** and (*Z*)-**2'**, and the crotyl derivatives **3** are obtained. The above compounds were separated by preparative VPC and identified by ^1H NMR and VPC-MS techniques; the results obtained are reported in Table I. The addition compound **4** is the main product in the case of **1a** and **1b**. In particular, **4b** is obtained in very good yield and high chemical purity, the other reaction products **2b**, **2'b**, and **3b** being formed in a very low amounts (<3%). In contrast, the product **4c** was obtained in a low yield (3%) from the substrate **1c**, the main

Scheme I



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0022-3263/86/1951-0505$01.50/0

Table I. Reaction[a] between the Butenyl Grignard Reagent and the Bromo Derivatives 1

substrate 1[b]	reacn time, h	yield,[c] %	composition[d] % of reacn products			
			2	2′	3	4
a	8	76	14	21	18	47
b	1	85	2	<1	<1	97
c	8	70	6	85	5	4

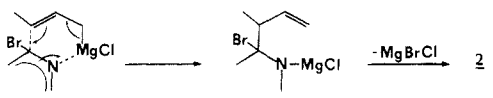
[a] Molar ratio Grignard reagent/substrate 1 = 6/1. [b] A quantitative conversion of the substrates 1 was obtained in all the cases. [c] Calculated as (moles of isolated products/mole of substrate) × 100. [d] Determined by VPC on the crude reaction product.

Table II. Reaction[a] between the Butenyl Grignard Reagent and the α-Methylallyl Derivatives 2

substrate 2	reacn time, h	conversion of 2, %	composition[b] % of reacn products			yield,[c] %	
			2	2′	4	2′	4
a	8	89	11	25	64	28	72
b	1	94	6	<1	93	<1	99
c	8	90	10	86	4	95	5

[a] Molar ratio Grignard reagent/substrate 2 = 2/1. [b] Determined by VPC on the crude reaction product. [c] Calculated as (moles of products/mole of reacted substrate) × 100.

Scheme II



product being 2′c, i.e., the derivative arising from isomerization of the first formed reaction product **2c**.

A six-center intermediate involving the coordination of butenyl Grignard reagent to the nitrogen atom of aromatic ring and the allylic rearrangement of the crotyl group explain the formation of the α-methylallyl derivative **2** (Scheme II). This product easily isomerizes to **2′** (*E* and *Z*) in the basic medium of the reaction due to the excess of Grignard used. In the presence of a large excess of butenyl Grignard reagent a direct displacement of bromine by the crotyl group affording the product **3** (*E* and *Z*) also takes place.

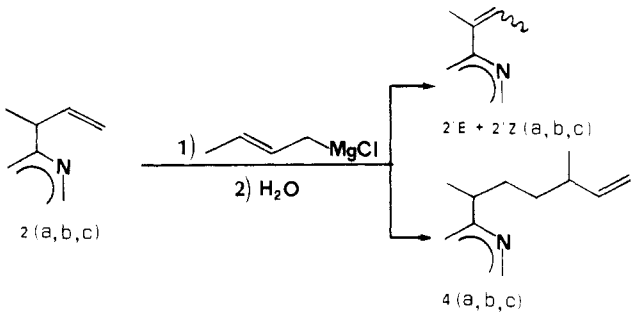
As far as the formation of the product **4** is concerned, few examples of the addition of the butenyl magnesium reagent to unactivated double bonds have been until now reported.[4-6] Thus we have investigated the formation of the addition derivatives **4**, using the α-methylallyl derivatives **2** as substrates.

Samples **2a**, **2b**, and **2c** were added, at room temperature, in a molar ratio of 1:2 to an ether solution of butenyl Grignard reagent. The reaction was monitored via VPC analysis by observing the decrease of the substrate **2** in the reaction mixture after heating at reflux for 1 h in the case of **2b** and for 8 h in the cases of **2a** and **2c**. The reaction products were separated by fractional distillation and characterized by MS, ^{1}H NMR, and determination of physical constants. The conversion of the substrates **2** was always in excess of 80% (Table II) with two products being formed. They were identified as **2′** and the addition product **4** (Scheme III). Isomers of **4** having a crotyl structure were not observed in this reaction.

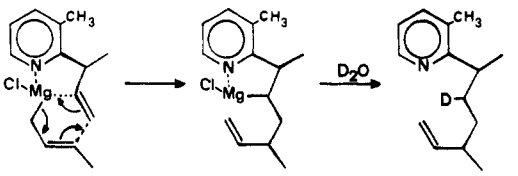
The composition of the products is strongly affected by the nature of the substrate **2** used in these reactions (Table II). The addition product **4** predominates in the case of pyridine derivatives **2a** and **2b**, while the isomerization product **2′** is the major compound for the quinoline derivative **2c** (Table II).

The reaction rate is much higher in the case of **2b** with respect to either **2a** or **2c**, as noted above for the addition

Scheme III



Scheme IV



of the butenyl Grignard reagent to the bromoderivatives **1**.

The results obtained demonstrate that the reaction of the butenyl Grignard reagent with the unactivated double bond of 2-(α-methylallyl) aza aromatic substrates is completely regioselective, the magnesium atom and the α-methylallyl group adding to the CH= and =CH_2 carbon atoms, respectively. Indeed, when the mixture arising from the reaction of **2b** with the butenyl Grignard was hydrolyzed with D_2O, the deuterated derivative 2-([2-^{2}H]-1,4-dimethyl-5-hexen-1-yl)-3-methylpyridine was obtained. Taking into account what is known about the addition of the allyl Grignard reagent to allyl or propargyl alcohols[4] and to unsaturated amines,[7] we suggest that a preliminary coordination of the magnesium atom to the basic nitrogen atom of the pyridine ring assists the addition of the butenyl Grignard to the ethylene linkage of substrate **2** as shown in Scheme IV for the compound **2b**.

A reaction pathway involving the formation of a six-center transition state between the butenyl Grignard reagent and the vinyl group explains the observed regioselectivity of the reaction.

According to this hypothesis the use of a noncomplexing solvent instead of a complexing one should favor the chelate structure and hence the selective formation of

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product **4**. Indeed by reacting 2-bromopyridine with a large excess of butenyl Grignard reagent (molar ratio 1:6) in *n*-hexane, the substrate **1a** completely reacts at room temperature in 4 h, and the derivative **4a** is formed in a good yield (82%), the other reaction products **2a**, **2'a**, and **3a** being less than 15%.

The higher reactivity and selectivity shown by 3-methylpyridine substrates **1b** and **2b** are probably connected with the steric interaction between the methyl and α-methylallyl groups. This interaction could force the α-methylallyl group into a conformation more suitable for the addition of the butenyl Grignard and also hinder the attack of the Grignard reagent at the CH proton of the α-methylallyl group. This could be responsible for the isomerization of **2** to **2'**.

Experimental Section

Vapor phase chromatographic analyses (VPC) were carried out on a Perkin-Elmer F30A instrument, equipped with 200 × 0.29 cm dual columns packed with 8% Carbowax and 2% KOH on 80–100 mesh Chromosorb W. Preparative VPC separations were performed on a Perkin-Elmer F21 instrument equipped with 300 × 0.5 cm columns of the same stationary phase. Mass spectra were measured with a Varian Mat CH-7 mass spectrometer (70 eV). Proton magnetic resonance spectra (^{1}H NMR) were recorded on Varian T-60 and Bruker AC-250 instruments. The chemical shifts are reported on the δ scale in parts per million downfield from the internal standard tetramethylsilane.

Materials. 3-Chloro-1-butene was obtained from Fluka AG (purum grade), treated with $NaHCO_3$ 10% aqueous solution, dried over anhydrous $MgSO_4$, and distilled before use. **2-Bromopyridine (1a)** was obtained from Fluka AG (purum grade) and distilled under reduced pressure. **2-Bromo-3-methylpyridine (1b)** was prepared by using the same procedure reported by Craig[8] for 2-bromopyridine and described by us in a previous paper.[3] **2-Bromoquinoline (1c)** was synthesized by using the method of Young[9] by reaction of the carbostyril with phosphorus oxybromide. **Butenylmagnesium chloride** was prepared in the usual manner as described by us in a previous paper.[3]

Preparations. Reaction of 2-Bromopyridine (1a) with the Butenyl Grignard Reagent. To an ether solution of 0.5 mol of butenylmagnesium chloride was added 0.083 mol of **1a**. The reaction mixture, after refluxing for 8 h, was hydrolyzed with cold water at 0 °C. The solvent was removed, and two fractions of 4.4 g [bp 50–60 °C (1.5 torr)] and 5.7 g [bp 85–89 °C (1.5 torr)] respectively were obtained by distillation of the organic layer. The former, analyzed by VPC, was a mixture of isomeric pyridine derivatives which were separated by preparative VPC and identified by MS and ^{1}H NMR as 2-(1-methyl-2-propen-1-yl)pyridine (**2a**), 2-(1-methyl-1-propen-1-yl)pyridine [(*E*)- + (*Z*)-**2'a**], and 2-(2-buten-1-yl)pyridine [(*E*)- + (*Z*)-**3a**]. The VPC analysis of the second fraction collected shows, in addition to a small amount (5%) of the alkenyl pyridines reported above, the presence of a product having longer retention time. The last was obtained as pure sample (4.3 g) by preparative VPC and identified as 2-(1,4-dimethyl-5-hexen-1-yl)pyridine (**4a**) by MS [*m/e* 189 (M^+)] and ^{1}H NMR ($CDCl_3$): δ 1.0 (d, 3 H), 1.3 (d, 3 H), 1.2–2.3 (m, 5 H), 3.2 (m, 1 H), 4.7–5.1 (m, 2 H), 5.4–6.0 (m, 1 H), 6.8–7.4 (m, 3 H, py H3, H4, and H5), 8.3 (m, 1 H, py H6). Anal. Calcd for $C_{13}H_{19}N$: C, 82.54; H, 10.06; N, 7.40; M_r 189. Found: C, 82.60; H, 10.11; N, 7.29.

Reaction of 2-Bromo-3-methylpyridine (1b) with the Butenyl Grignard Reagent. The reaction was carried out by using a procedure similar to that described above for the preparation of **1a**. The reaction mixture, hydrolyzed after refluxing for 1 h and then distilled, furnished 2-(1,4-dimethyl-5-hexen-1-yl)3-methylpyridine (**4b**), having high chemical purity (97%). The total of 2-(1-methyl-2-propen-1-yl)-3-methylpyridine (**2b**), 2-(1-methyl-1-propen-1-yl)-3-methylpyridine (**2'b**), and 2-(2-buten-1-yl)-3-methylpyridine (**3b**) was only 3%. Also in this case compound **4b** was purified by VPC and characterized by MS [*m/e* 203 (M^+)] and 250-MHz ^{1}H NMR ($CDCl_3$): δ 0.95 (d, 3 H, C-(CH_3)C=), 1.24 (d, 3 H, py C(CH_3)), 1.08–1.35 (m, 2 H, CH_2CC=), 1.78–1.89 (m, 2 H, py CCH_2), 2.07 (m, 1 H, CHC=), 2.29 (br s, 3 H, py CH_3), 3.04 (m, 1 H, py CH), 4.84–4.95 (m, 2 H, =CH_2), 5.59–5.71 (m, 1 H, CH=), 6.95 (dd, 1 H, py H5, J_{5-4} = 7.5 Hz, J_{5-6} = 4.7 Hz), 7.35 (m, 1 H, py H4), 8.42 (dd, 1 H, py H6, J_{6-5} = 4.7 Hz, J_{6-4} = 1.4 Hz). Anal. Calcd for $C_{14}H_{21}N$: C, 82.76; H, 10.35; N, 6.89; M_r 203. Found: C, 82.64; H, 10.41; N, 6.95.

Reaction of 2-(1-Methyl-2-propen-1-yl)pyridine (2a) with the Butenyl Grignard Reagent. To 200 mL of a 0.1 M ether solution of butenylmagnesium chloride was added, at room temperature, 1.3 g (0.01 mol) of **2a** in 20 mL of ether. After refluxing for 8 h, the reaction mixture was cooled in ice–water and the ether layer separated and dried. After removing the solvent, the residue (1.5 g) was analyzed by VPC, which gave a composition of **2a** (11%), (*E*)- + (*Z*)-**2'a** (25%), and **4a** (64%).

Reaction of 2-(1-Methyl-2-propen-1-yl)-3-methylpyridine (2b) with the Butenyl Grignard Reagent. The experimental procedure was the same as reported for the reaction of **2a** with butenylmagnesium chloride. From 0.01 mol of **2b**, reacted with 0.02 mol of Grignard reagent and refluxed for 1 h, was obtained 1.8 g containing **2b** (6%), (*E*)- + (*Z*)-**2'b** (1%), and **4b** (93%).

2-([2-^2H]-1,4-Dimethyl-5-hexen-1-yl)-3-methylpyridine. To 360 mL of 0.1 M ether solution of Grignard reagent was added 3.4 g (0.018 mol) of **2b**, and the reaction mixture was refluxed for 1 h. The hydrolysis was carried out with D_2O (isotopic purity 99 atom %D). After removing the solvent, 2.8 g (0.015 mol) of deuterated product was isolated. The 250 MHz ^{1}H NMR spectrum shows the same proton resonance as **4b** with the following differences: ($CDCl_3$) δ 1.52–1.65 (m, 1 H, py CCHD), 3.04 (quintet, 1 H, py CH, J = 6.5 Hz).

Reaction of 2-(1-Methyl-2-propen-1-yl)quinoline (2c) with the Butenyl Grignard Reagent. With using the same procedure reported for **2a** and **2b**, from 0.01 mol of **2c** and 0.02 mol of Grignard reagent a mixture (1.8 g) of three compounds was obtained. They were identified by VPC–MS analyses as **2c** (10%), **2'c** (86%) [a 1:1 mixture of *E* and *Z* isomers; *m/e* 183 (M^+)] and as the addition product **4c** (4%) [*m/e* 239 (M^+)]. A pure sample of **2'c** was obtained by preparative VPC. Anal. Calcd for $C_{13}H_{13}N$: C, 85.25; H, 7.10; N, 7.65; M_r 183. Found: C, 85.16; H, 7.16; N, 7.68.

Reaction of 2-Bromoquinoline (1c) with the Butenyl Grignard Reagent. Following the same procedure reported for **1a**, 0.01 mol of **1c**, and 0.06 mol of Grignard reagent gave a mixture (1.3 g) of four products, which was analyzed by VPC and by VPC–MS. In addition to **2c** (6%), **2'c** (*E* + *Z*) (85%), and **4c** (4%), an isomer of **2c** and **2'c** was present (5%) in the reaction products. According to what found in the case **1a**, the crotyl structure **3c** [*m/e* 183 (M^+)] is proposed for this isomer.

Registry No. **1a**, 109-04-6; **1b**, 3430-17-9; **1c**, 2005-43-8; **2a**, 53364-08-2; (*E*)-**2'a**, 71532-18-8; (*Z*)-**2'a**, 71532-25-7; **2b**, 87673-60-7; (*E*)-**2'b**, 99747-47-4; (*Z*)-**2'b**, 99747-48-5; **2c**, 87673-61-8; (*E*)-**2'c**, 99747-50-9; (*Z*)-**2'c**, 99747-51-0; (*E*)-**3a**, 71532-22-4; (*Z*)-**3a**, 71532-21-3; **3b**, 99747-46-3; **3c**, 99747-53-2; **4a**, 99747-44-1; **4b**, 99747-45-2; **4c**, 99747-52-1; CH_3CH=$CHCH_2MgCl$, 6088-88-6; carbostyril, 59-31-4; 2-([2-^{2}H]-1,4-dimethyl-5-hexen-1-yl)-3-methylpyridine, 99747-49-6.

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