for *p*-(dimethylamino)nitrobenzene indicates the through-resonance effect to increase the electron density at the nitro group by 0.2 e (or 0.1 e per oxygen atom). The resulting increase of ~30 ppm in ^{17}O shielding (X = NEt_2 vs. H) suggests the effect to be ~300 ppm per electron. This is significantly larger than the generally accepted values for ^{13}C and ^{1}H, which are 160[14] and 10 ppm/electron, respectively.

In conclusion, ^{17}O shieldings in nitrobenzenes have been found to be sensitive to the electronic character of para substituents precisely in the manner anticipated from consideration of valence bond structure **1a**. Furthermore, the large sensitivity to electron density changes indicates ^{17}O to be an attractive probe of electron distributions.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

Registry No. 4-NEt_2-$C_6H_4NO_2$, 2216-15-1; 4-NH_2-$C_6H_4NO_2$, 100-01-6; 4-OMe-$C_6H_4NO_2$, 100-17-4; 4-Me-$C_6H_4NO_2$, 99-99-0; $C_6H_5NO_2$, 98-95-3; 4-Cl-$C_6H_4NO_2$, 100-00-5; 4-COMe-$C_6H_4NO_2$, 100-19-6; 4-COOMe-$C_6H_4NO_2$, 619-50-1; 4-CHO-$C_6H_4NO_2$, 555-16-8; 4-CN-C_6H_4-NO_2, 619-72-7.

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(13) Reference 3, p 508.

(14) Lammertsma, K.; Cerfontain, H. *J. Am. Chem. Soc.* **1979**, *101*, 3618.

Intramolecular Type II "Metallo-Ene" Reactions of (2-Alkenylallyl)magnesium Chlorides: Regio- and Stereochemical Studies

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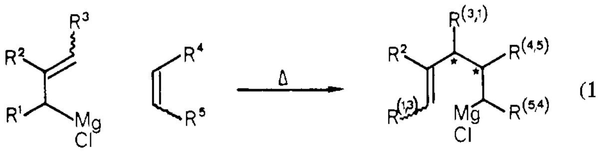
Despite the extensive pioneering work of Lehmkuhl[1], the formal ene addition of allylic Grignard reagents to olefins (eq 1) has not



(1)

yet been applied to strategically devised organic synthesis. Also the more selective intramolecular type-I reaction[2] of 2,7-octadienylmagnesium halide[3] (eq 1, $R^3 = R^4 = (CH_2)_3$, $R^1 = R^2 = R^5 = H$) is virtually unexploited.[4]

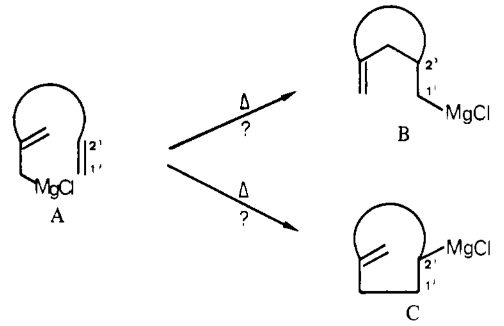
In conjunction with our interest in intramolecular ene reactions[2,5] we have examined the unprecedented "type-II metallo-ene" reaction (eq 1, $R^2 = R^4 = (CH_2)_n$). Our results showing the highly regio- and stereocontrolled formation of seven-, six-, and even five-membered methylene-substituted carbocycles are summarized in eq 2 and Table I.

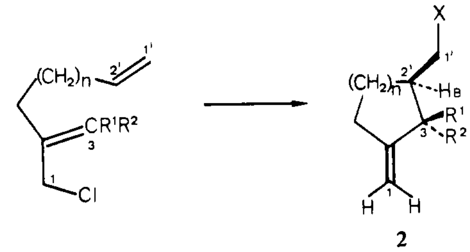
Table I. Thermal Cyclization of (2-Alkenylallyl)magnesium Chlorides Prepared from 1 and Subsequent Trapping

entry	*n*	R^1	R^2	Δ, temp, °C (time, h)	yield of *2*,[a,b] %	X
a	3	H	H	80 (17)	71	$CONHC_6H_5$[c]
b	2	H	H	80 (17)	72	$CONHC_6H_5$[c]
c	1	H	H	130 (23)	71	$CONHC_6H_5$[c]
d	3	CH_3	H	90 (60)	40[d]	$CONHC_6H_5$[c]
e	2	CH_3	H	80 (17)	86	$CONHC_6H_5$[c]
f	2	*n*-C_6H_{13}	H	80 (17)	81	H[e,f]
g	2	CH_3	CH_3	80 (17)	80	$CONHC_6H_5$[c]
h	2	CH_3	CH_3	80 (17)	*g*	H[e]

[a] Overall yield based on **1**. [b] The products **2** were also characterized by ^{13}C NMR (90.561 MHz) and by melting point (ether-pentane, °C): **2a**, 89–90; **2b**, 131–132; **2c**, 98–100.5; **2d**, 115–116; **2e**, 123–125; **2g**, 121–123; **2f** and **2h** are oils. [c] Crude **2**, X = MgCl was trapped with $C_6H_5N{=}C{=}O$ (1.2 equiv), –10 °C → room temperature 1 h, and the resulting mixture was heated in boiling bromobenzene for 12 min. [d] Noncyclized allylmagnesium chloride was trapped in 20% yield. [e] Crude **2**, X = MgCl, was trapped with aqueous NH_4Cl, 0 °C. [f] The configuration of the single product **2f** has not yet been determined. [g] Yield not determined.

Scheme I

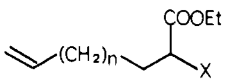




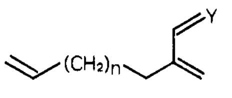
2

(2)

The allyl chlorides **1**[6] were readily prepared either from the malonates **3**[6] (**1a** to **1f**) or from the phosphonate **6**, *n* = 2[6] (**1g**).[7]



3, X = COOEt
6, X = $PO(OEt)_2$



4, Y = H, OH
1a–c, Y = H, Cl
5, Y = O

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(1) (a) For a recent review on additions of allylmagnesium halides and bis(2-alkenyl)zinc to olefins see: Lehmkuhl, H. *Bull. Soc. Chim. Fr.* **1981**, *part II*, 87. (b) See also: Shepherd, L. H., Jr. U.S. Patent 3 597 488, 1971; *Chem. Abstr.* **1971**, *75*, 88751c. Barbot, F.; Miginiac, P. *J. Organomet. Chem.* **1978**, *145*, 269.

(2) For a review on intramolecular ene reactions and their classification according to the mode by which the enophilic chain is attached at the olefinic terminal (type I), at the central atom (type II), or at the allylic terminal (type III) of the ene unit see: Oppolzer, W.; Snieckus, V. *Angew. Chem.* **1978**, *90*, 506; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.

(3) Felkin, H.; Kwart, L. D.; Swierczewski, G.; Umpleby, J. D. *J. Chem. Soc., Chem. Commun.* **1975**, 242. Felkin, H.; Umpleby, J. D.; Hagaman, E.; Wenkert, E. *Tetrahedron Lett.* **1972**, 2285. Fukutani, H.; Takizawa, M.; Okada, H. *Japan Patent* 7 239 034 1972; *Chem. Abstr.* **1973**, *78*, 111498y.

(4) For a few isolated examples see ref 1 and the following: Courtois, G.; Masson, A.; Miginiac, L. *C. R. Hebd. Seances Acad. Sci. Paris, Ser. C*, **1978**, *286*, 265.

(5) Oppolzer, W.; Andres, H. *Tetrahedron Lett.* **1978**, 3397; *Helv. Chim. Acta* **1979**, *62*, 2282. Oppolzer, W.; Robbiani, C. *Ibid.* **1980**, *63*, 2010. Oppolzer, W.; Robbiani, C.; Bättig, K. *Ibid.* **1980**, *63*, 2015; Oppolzer, W.; Marazza, F. *Ibid.* **1981**, *64*, 1575. Oppolzer, W.; Bättig, K. *Ibid.* **1981**, *64*, 2489. Oppolzer, W.; Bättig, K.; Hudlicky, T. *Tetrahedron* **1981**, *37*, 4359.

(6) All new compounds were characterized by IR, ^{1}H NMR (360 MHz), and mass spectroscopy.

(7) **3** and **6** are easily accessible by alkylation of diethyl malonate (2 equiv, NaOEt (1.1 equiv), EtOH, reflux, 2 h) or of triethyl phosphonoacetate, respectively, with alkenyl bromides. Treatment of **3** with (i) NaH, DME; (ii) $LiAlH_4$;[8] (iii) $SOCl_2$, Et_2O gave **1a**[6] (51%) and **1b**[6] (45%). **1c**[6] (32%) was prepared by reaction of **4**, *n* = 1,[6] with NCS and DMS.[9] The 3-alkylallyl chlorides **1d–f**[6] were obtained (41–68%) from **4**[6] by treatment with (i) $COCl_2$, Me_2SO;[10] (ii) RMgBr, Et_2O; (iii) $SOCl_2$, Et_2O, 0 °C. For preparation of **1g**[6] (39%), **6**, *n* = 2,[6] was treated successively with (i) NaH, DME; (ii) acetone, 80 °C, 3 h;[11] (iii) $LiAlH_4$, Et_2O; (iv) MsCl, pyridine, -10 → 0 °C; (v) 1 N aqueous HCl, 0 °C, 5 min.[12]

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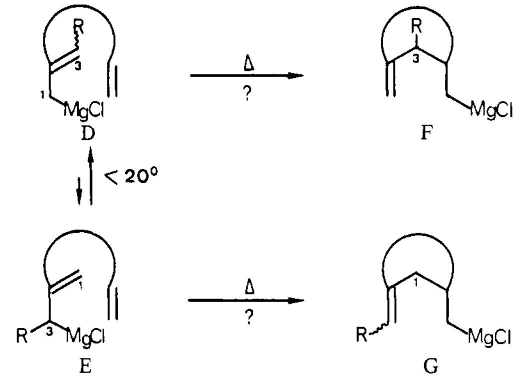
Scheme II

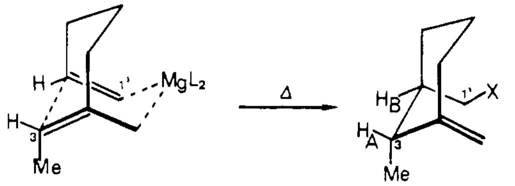


Conversion of the chlorides **1** to the corresponding allylic Grignard reagents was accomplished by a technique that minimizes the formation of 1,5-hexadienes.[13] The following general procedure is representative. Slow addition of **1** to a slurry of precondensed magnesium in THF at −65 °C[14] furnished a 1% solution of allylmagnesium chloride, which was heated in a sealed Pyrex tube under argon. Quenching of the cyclized Grignard product **2**, X = MgCl, with phenyl isocyanate gave the anilide **2**, X = $CONHC_6H_5$, together with some 1:2 adduct **2**, X = $CON(C_6H_5)CONHC_6H_5$; the latter adduct was readily thermolyzed to give the former one.

We first focused our efforts on the regiochemical options outlined in Scheme I. The initial question was whether on variation of the distance between ene and enophile, A would cyclize to give B or C implying Mg transfer either to the terminal enophilic site C(1′) or, alternatively, to the closer site C(2′).

In fact, following the general procedure **1a** and **1b** gave in each case a single product **2a** and **2b**, respectively (GC, ^1H NMR), which arise from exclusive metal-transfer to C(1′) (A → B). Surprisingly also the lower homologue prepared from **1c** was efficiently cyclized at a higher reaction temperature to give the cyclopentane **2c**; again the same regiochemistry was observed irrespective of the presumed angle strain in the transition state. The mass spectra of **2a–c** show a prominent peak at *m/e* 135 (84–100%, $(CH_2{=}C(OH)NHC_6H_5)^{+\cdot}$[15]). This peak at *m/e* 135, which militates against the hypothetical reaction A → C is also exhibited by the anilides **2d**, **2e** and **2g**, whose structures were independently based on ^1H NMR data.

Scheme II outlines another regiochemical uncertainty of type II metallo-ene reactions that remains to be clarified. On thermal cyclization of unsymmetrically substituted allylmagnesium halides, rapid 1,3-metal migration[16] D $\rightleftharpoons$ E leaves two possibilities: either C–C bond formation with the more or less substituted ene terminal C(3) (D → F) or C(1) (E → G), respectively. Accordingly, (3-alkyl-2-alkenylallyl)magnesium chlorides were prepared from **1d**, **1e**, and **1f** by using the above mentioned technique; subsequent heating and quenching gave in either case a single product, **2**. Remarkably, this holds also for the (3,3-dimethyl-2-pentenylallyl)magnesium chloride derived from **1g**, which cyclized solely by joining a quaternary with a tertiary carbon to yield **2g**, X = MgCl.[17] The presence of an exo-methylene group in the products **2d–h** (^1H NMR, ^{13}C NMR, and IR) proves clearly that in all cases C–C bonding occurs with the more substituted C(3) of the ene unit (D → F). Quenching of the cyclized Grignard products obtained from **1f** and **1g** with aqueous NH_4Cl furnished exclusively **2f** and **2h**. ^1H NMR of **2f** and **2h** exhibits a CH_3–CH doublet at δ 0.86, which confirms Mg transfer to C(1′) in the cyclization process. Partial cyclization (6–10%) of the Grignard reagents derived from **1c**, **1d**, and **1f** at lower reaction temperature furnished no isomeric cyclization products (GC), consistent with a kinetic regio- and stereoselection. Moreover, the ^1H NMR spectra of **2d** and **2e** exhibit the vicinal coupling constants $J_{AB} \simeq 2$ Hz (**2d**) and $J_{AB} = 4$ Hz (**2e**), indicating the cis disposition of $R^1 = CH_3$ and the CH_2X group in **2d** and **2e**.[18,19] This striking stereoselectivity agrees with a concerted reaction involving a (*Z*)-ene unit[20] as depicted in eq 3. We assume that the observed closure of a five-membered ring (entry c) and the clear preference of a sterically more crowded C–C bonding process (entries g, h) may be explained by a dominating coordination of the migrating magnesium with the least substituted enophile site in the transition state.[21]



(3)

Z

X = MgCl

2g, X = CONHPh (J_{AB} = 4 Hz)

Work is in progress to establish and to extend the scope of this reaction type, including variations of the migrating metal. Applications to the synthesis of natural products are presently being explored in this laboratory, as illustrated in the following communication by the synthesis of (±)-khusimone.[22]

Acknowledgment. Financial support of this work by the Swiss National Science Foundation, Sandoz Ltd., Basle, and Givaudan SA, Vernier, is gratefully acknowledged.

Registry No. 1a, 83312-89-4; **1b**, 83312-90-7; **1c**, 83312-91-8; **1d**, 83312-92-9; **1e**, 83312-93-0; **1f**, 83312-94-1; **1g**, 83312-95-2; **2a**, 83312-96-3; **2b**, 83312-97-4; **2c**, 83312-98-5; **2d**, 83312-99-6; **2e**, 83313-00-2; **2f**, 83313-01-3; **2g**, 83313-02-4; **2h**, 83313-03-5; **3a**, 69298-59-5; **3b**, 1906-96-3; **4c**, 83313-04-6; **4d**, 83313-05-7; **4e**, 83313-06-8; **6g**, 83313-07-9; diethyl malonate, 105-53-3; triethyl phosphonoacetate, 867-13-0; phenyl isocyanate, 103-71-9.

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(9) Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339.

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(13) Oppolzer, W.; Kündig, E. P.; Bishop, P. M.; Perret, C. *Tetrahedron Lett.* **1982**, 3901.

(14) For a description of the Mg evaporation–condensation procedure see: Kündig, E. P.; Perret, C. *Helv. Chim. Acta* **1981**, *64*, 2606.

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(16) Nordlander, J. E.; Young, W. G.; Roberts, J. D. *J. Am. Chem. Soc.* **1961**, *83*, 494.

(17) Despite this steric congestion the formation of the six-membered ring **2g**, X = MgCl, proceeded significantly faster than that of the cycloheptane **2d**, which even on extended exposure to higher temperature was less efficient.

(18) ^1H NMR spectra in $CDCl_3$, standard Me_4Si (δ 0), abbreviations: s = singlet, d = doublet, m = multiplet, *J* = spin–spin coupling constant (Hz). **2d**: 1.07 (d, *J* = 7 Hz, irradiation at 2.62 → s, 3 H), 1.3–1.8 (6 H), 2.0–2.5 (5 H), 2.62 (m, irradiation at 1.07 → d, $J \simeq 2$ Hz, 1 H), 4.76 (s, 1 H), 4.80 (s, 1 H), 7.0–7.6 (5 H). **2e**: 1.05 (d, *J* = 7 Hz, irradiation at 2.49 → s, 3 H), 1.4–2.4 (10 H), 2.49 (m, irradiation at 1.05 → d, *J* = 4 Hz, 1 H), 4.63 (s, 1 H), 4.68 (s, 1 H), 7.0–7.6 (5 H).

(19) For the conformation and ^1H NMR spectra of 2,3-disubstituted cycloheptanones see: Pfeffer, P. E.; Osman, S. F. *J. Org. Chem.* **1972**, *37*, 2425. Dunkelblum, E.; Hart, H. *Ibid.* **1977**, *42*, 3958. Hart, H.; Chen. B. L.; Jeffares, M. *Ibid.* **1979**, *44*, 2722.

(20) In crotylmagnesium halides the *Z* configuration is already favored over the *E* configuration: Hutchison, D. A.; Beck, K. R.; Benkeser, R. A. Grutzner, J. B. *J. Am. Chem. Soc.* **1973**, *95*, 7075. This preference should be even more pronounced in (2,3-dialkylallyl)magnesium halides.

(21) This assumption agrees with our observation that *trans*-3,3-dimethyl-(4-hexen-2-yl)magnesium chloride could not be cyclized; it thus appears that alkyl substituents in position C(1′) prevent this type of reaction.

(22) Oppolzer, W.; Pitteloud, R. *J. Am. Chem. Soc.*, following article in this issue. See also the recent application of the type-I magnesium-ene reaction for the synthesis of $\Delta^{9,12}$-capnellene: Oppolzer, W.; Bättig, K. *Tetrahedron Lett.*, in press. For the synthesis of sinularene: Oppolzer, W.; Strauss, H. F.; Simmons, D. P. *Ibid.*, in press.