

g of mechanically separable, large chunks. Sublimation of the powder (100° *in vacuo*) followed by hot benzene extraction of the sublimate residue gave a total of 2.5 g (8.5%) of  $\alpha$ -naphthol (melting point, mixture melting point, ir); only purple-brown tarry material remained, from which no other compounds in workable amounts could be separated by sublimation, extraction, or column chromatography. Hot benzene digestion of the large chunks yielded 6.1 g of gray-white powder, mp 285–295°, which was suspected to be **3a** (yield 10%). Heating for 30 min with excess Ac<sub>2</sub>O and a few drops of pyridine gave an oil which solidified. Recrystallization from benzene-petroleum ether (30–60°) gave white solid **3b**: mp 217–218° (lit.<sup>11</sup> mp 217°); ir (KBr) 1760 (s), 1370 (m), 1200 (s), 1150 (m), 760 (m); mass spectrum *m/e* 370 (parent). *Anal.* Calcd for C<sub>24</sub>H<sub>18</sub>O<sub>4</sub>: C, 77.82; H, 4.90; O, 17.28. Found: C, 78.10; H, 4.93. Evaporation of the benzene supernatant (from the chunks) gave a dark, tarry residue (19 g); chromatography on alumina, using various benzene, petroleum ether (30–60°), chloroform eluent mixtures gave several fractions, all of which were fluffy, high melting (dec), dark powders, whose ir spectra (Nujol) exhibited broad OH (3400), carbonyl (1650), and other strong peaks at 1580 and 760 (*inter alia*). These powders are probably condensation products of the quinone and quinol type.

**Dehydration of 1,8-Dihydroxynaphthalene.**—The solid diol [K and K, recrystallized from H<sub>2</sub>O, mp 140.5–141.0° (lit.<sup>10</sup> mp 140°)] (5 g) was heated at 300° in a CO<sub>2</sub> atmosphere; some evolution of H<sub>2</sub>O was observed. After 15 min, the dark, glassy residue was cooled and subjected to standard work-up (extraction, sublimation, chromatography, etc.). Only starting material (~100 mg) could be identified from the otherwise intractable mixture.

**Acknowledgment.**—The generous support of the National Science Foundation (NSF GP-7325) is greatly appreciated.

(11) Z. Rappaport, Ed., "Handbook of Tables for Organic Compound Identification," 3rd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1967, p 127.

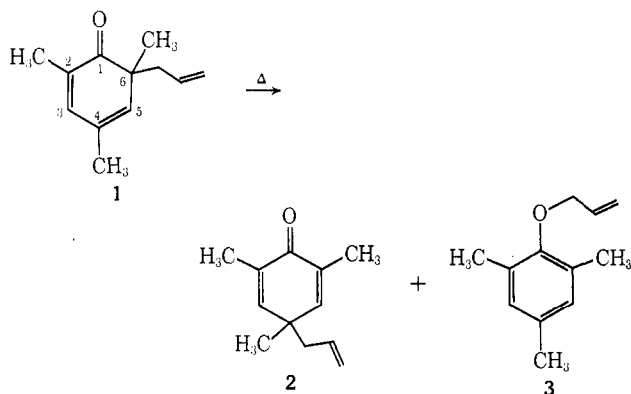
## Thermal Migrations of Allyl Groups in Linearly Conjugated Cyclohexadienones<sup>1</sup>

BERNARD MILLER

Department of Chemistry, University of Massachusetts,  
Amherst, Massachusetts 01002

Received May 19, 1970

Allyl groups at the quaternary carbons of linearly conjugated cyclohexadienones undergo facile thermal [3,3] sigmatropic shifts to C-4 (Cope migrations) or to the carbonyl oxygen (reverse-Claisen migrations).<sup>2</sup>

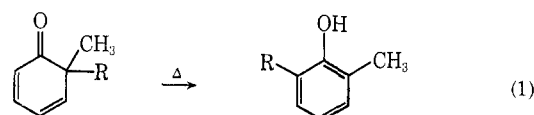


(1) Reactions of Cyclohexadienones, XXVI. Part XXV: *J. Amer. Chem. Soc.*, **92**, 6252 (1970).

(2) B. Miller in "Mechanisms of Molecular Migrations," Vol. I, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., 1968.

Migration of allyl or 2-butenyl groups to C-4 is the major reaction when C-4 is unsubstituted,<sup>3</sup> or when C-4 bears a methyl group and an unsubstituted allyl group migrates.<sup>4</sup> Thus, rearrangement of **1** gives **2** as the major product, presumably accompanied by smaller amounts of **3**.<sup>4</sup> This process is a useful synthetic method for the preparation of cross-conjugated cyclohexadienones, which are often difficult to prepare in other ways.

Other work in this laboratory has shown that migrating groups which cannot undergo [3,3] shifts (*e.g.*, benzyl and cyclopropylmethyl groups) will undergo [1,5] sigmatropic shifts from C-6 to C-2 of the dienone (eq 1).<sup>5</sup> We have also shown that substituted allyl

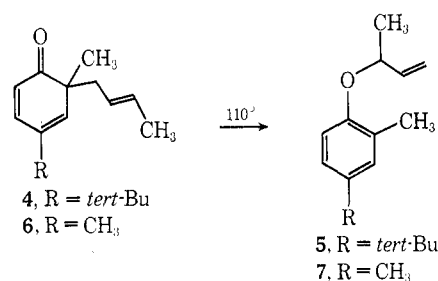


groups undergo acid-catalyzed [1,5] shifts to C-2 when the "normal" acid-catalyzed Cope migrations to C-4 are inhibited by the presence of bulky substituents at C-4 or at the terminus of the migrating allyl chain.<sup>6</sup>

No previous work reports whether allyl groups can similarly undergo thermal [1,5] shifts in addition to, or in preference to, the normal [3,3] shifts. It seemed of interest to determine whether such shifts can occur.

In order to maximize the possibility of observing [1,5] shifts, it was desirable to inhibit, insofar as possible, the competing [3,3] shifts. It seemed difficult to design a molecule in which the possibility of reverse-Claisen migration to oxygen would be severely inhibited. It was found, however, that the normally more important Cope migration to C-4 could be inhibited quite easily by steric interference between appropriate substituents at C-4 and at the end of the migrating allyl chain.

Dienone **4** was chosen as a molecule in which migration to C-4 should be quite difficult. Thermal rear-



rangement of **4** at 110° was found to give a quantitative yield of the reverse-Claisen rearrangement product, **5**. Vpc analysis showed that less than 0.5% of any [1,5] migration to give 2-butenyl-4-*tert*-butyl-6-methylphenol could have occurred.

Thermal rearrangement of dienone **6** similarly gave a quantitative yield of ether **7**. This not only demonstrates that [1,5] migration cannot compete with the reverse-Claisen migration, but shows that the normal

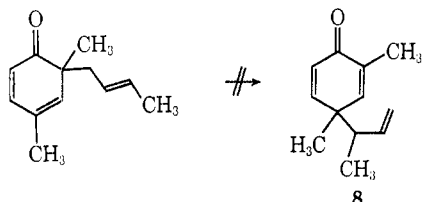
(3) (a) F. Kalberer, K. Schmid, and H. Schmid, *Helv. Chim. Acta*, **39**, 555 (1956); (b) D. Y. Curtin and R. J. Crawford, *J. Amer. Chem. Soc.*, **79**, 3156 (1957).

(4) B. Miller, *ibid.*, **87**, 5115 (1965).

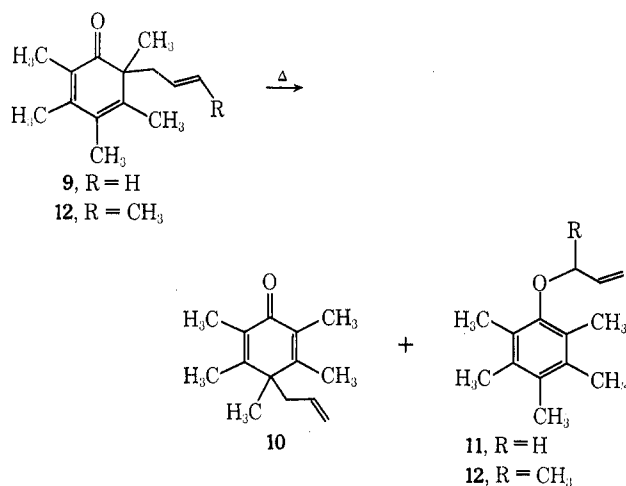
(5) B. Miller and K.-H. Lai, unpublished work.

(6) (a) B. Miller, *Chem. Commun.*, 1435 (1968); (b) B. Miller, *J. Amer. Chem. Soc.*, **91**, 2170 (1969).

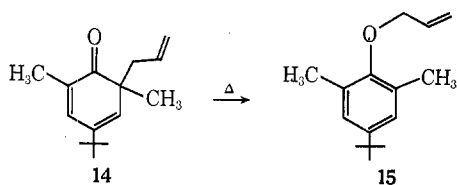
Cope migration to C-4 is completely inhibited in this molecule, presumably by interaction between the methyl group at C-4 and the methyl group on the migrating butenyl chain. Any migration to C-4 to form the cross-conjugated dienone **8** should have resulted in further migration of the 1-methylallyl group to the unoccupied ortho position of **8**, giving 2-butenyl-4,6-dimethylphenol, which was not obtained.



In view of the differences between the products obtained from **1** and from **6**, we investigated the thermal rearrangements of several other cyclohexadienones with substituents at C-4, in order to obtain a better idea of the degree to which steric interactions will inhibit migration to that position. Thermal rearrangement of dienone **9** gave the cross-conjugated dienone **10** and the allyl ether **11** in the ratio 2:1. Migrations of allyl groups in dienones lacking any substituents at C-4 have been reported<sup>1,2</sup> to give Cope–reverse–Claisen migration ratios of from 2.7 to 3.0.<sup>3</sup> Thus, steric interferences be-



tween a migrating allyl group and a methyl group at C-4 have relatively little effect upon the nature of the rearrangement products. In contrast, rearrangement of dienone **12** gives only the ether **13**, in agreement with the conclusion arrived at from the rearrangement of dienone **6** that interaction between a methyl group on a migrating butenyl chain and a methyl at C-4 is sufficient to completely prevent any migration to C-4. Finally, rearrangement of dienone **14** was found to give



only ether **15**. Thus a methyl group at C-4 gives little interference with migration of an allyl group to that position, while a *tert*-butyl group at C-4 completely prevents migration.

### Experimental Section

Unless otherwise noted, all uv spectra were recorded in methanol solution and nmr spectra in CCl<sub>4</sub>. Vpc analyses were carried out on a Varian 202 gas chromatographic unit with thermal conductivity detector, using a 5-ft, 3% SE-30 on Chromosorb W column. Microanalyses were carried out by Charles Meade, University of Massachusetts Microanalytics Laboratory or by Galbraith Laboratories, Knoxville, Tenn.

**Rearrangement of 6-(*trans*-2-Butenyl)-4-*tert*-butyl-6-methylcyclohexa-2,4-dien-1-one (4).**—Dienone **4**<sup>7</sup> (0.23 g) was heated at 110° until the uv peak at 323 m $\mu$  had disappeared (*ca.* 2.5 hr). The nmr and ir spectra of the product were identical with those of 4-*tert*-butyl-2-methylphenyl 1-methylallyl ether (**5**).<sup>7</sup> Vpc analysis at 150° showed that less than 0.5% of 2-(*trans*-2-butenyl)-4,6-dimethylphenol<sup>7</sup> could have been present. Similarly, solutions of **1** in cyclohexane and pyridine were heated at 110° in sealed tubes for 3 hr. Vpc analyses of the products showed only the presence of **5**.

**Rearrangement of 6-(*trans*-2-Butenyl)-4,6-dimethylcyclohexa-2,4-dien-1-one (6).**—Dienone **6**<sup>7</sup> (0.8 g, 0.0045 mol) was heated at 120° for 3 hr. Vpc analysis of the product at 125° showed it to consist essentially of one compound, contaminated with *ca.* 3% of 2,4-dimethylphenol. Chromatography of the product on alumina (eluting with pentane) gave 0.6 g (0.0034 mol, 75%) of 1-methylallyl 2,4-dimethylphenyl ether (**7**). The ir and nmr spectra of **7** were essentially identical with those of the reaction product before chromatography.

*Anal.* Calcd for C<sub>12</sub>H<sub>16</sub>O: C, 81.8; H, 9.10. Found: C, 81.7; H, 9.30.

Its nmr spectrum showed a three-proton doublet ( $J = 6.3$  Hz) at  $\tau$  8.76, singlets totalling six protons at  $\tau$  7.93 and 7.97, a four-proton multiplet from  $\tau$  4.7 to 6.0, and a complex three-proton aromatic signal from  $\tau$  3.2 to 3.7.

**Thermal Rearrangement of 6-Allyl-2,3,4,5,6-pentamethylcyclohexa-2,4-dien-1-one (9).**—Dienone **9** (0.81 g, 0.0039 mol) was heated at 110° until the peak at 333 m $\mu$  disappeared (2.5 hr). Nmr analysis showed the product to consist of allyl pentamethylphenyl ether (**11**) and 4-allyl-2,3,4,5,6-pentamethylcyclohexa-2,5-dien-1-one (**10**).<sup>7</sup> Comparison of the areas of the doublet at  $\tau$  6.0 with that at  $\tau$  7.5 showed the ratio of **10**:**11** to be 2:0. Isolation of the products by column chromatography gave a similar but less precise value.<sup>7</sup>

**Preparation of Allyl Pentamethylphenyl Ether (11).**—Pentamethylphenol (8.4 g, 0.050 mol) was dissolved in 100 ml of dimethyl sulfoxide. Sodium methoxide (2.7 g, 0.050 mol) was added and the mixture shaken for 10 min. Allyl bromide (6.05 g, 0.050 mol) was added. After 20 min, the mixture was poured into water and extracted with methylene chloride. The methylene chloride layer was washed with water several times, dried, and evaporated to give 9.9 g of yellow oil. The product was distilled under vacuum to give 6.9 g (0.034 mol, 68%) of allyl pentamethylphenyl ether as a colorless liquid, bp 137–139° (15 mm).

*Anal.* Calcd for C<sub>14</sub>H<sub>20</sub>O: C, 82.4; H, 9.80. Found: C, 82.6; H, 9.81.

Its nmr spectrum showed a broad doublet ( $J = 6.0$  Hz) (2 H) at  $\tau$  6.0, a complex multiplet (3 H) from  $\tau$  3.8 to 5.2, and a broad singlet (15 H) at  $\tau$  8.0.

**Rearrangement of 6-(*trans*-2-Butenyl)-2,3,4,5,6-pentamethylcyclohexa-2,4-dien-1-one (12).**—Dienone **12** (1.0 g, 4.9 mmol) was heated at 110° for 4 hr. The uv maximum at 333 m $\mu$  and the peak at 6.0  $\mu$  were monitored during the course of the reaction and were found to decrease at approximately the same rate, indicating that little cross-conjugated ketone could be produced as an intermediate in the reaction. Vpc analysis at 150° at the end of the reaction showed the product to consist largely of a single compound, contaminated with *ca.* 4% of pentamethylphenol. Chromatography of the crude product on activity I alumina (eluting with petroleum ether, bp 30–60°) gave 0.75 g (3.4 mmol, 70%) of 1-methylallyl pentamethylphenyl ether as a pale yellow fluid.

*Anal.* Calcd for C<sub>15</sub>H<sub>22</sub>O: C, 82.5; H, 10.2. Found: C, 82.7; H, 10.0.

Its nmr spectrum had a singlet (*ca.* 15 H) at  $\tau$  8.00, a doublet (3 H,  $J = 6.5$  Hz) at  $\tau$  8.82, a multiplet (1 H) at  $\tau$  5.7–6.2, and a multiplet (3 H) at  $\tau$  3.8–5.3.

**Preparation of 6-Allyl-4-*tert*-butyl-2,6-dimethylcyclohexa-2,4-dien-1-one (14).**—4-*tert*-Butyl-2,6-dimethylphenol (18.0 g, 0.101

(7) B. Miller, *J. Amer. Chem. Soc.*, **92**, 6246 (1970).

mol) was dissolved in 500 ml of benzene and sodium methoxide (5.4 g, 0.10 mol) was added. The mixture was stirred and solvent distilled out until all water and methanol had been removed. The mixture was then cooled to 35°, and allyl bromide (12.8 g, 0.106 mol) was added. After being stirred at room temperature for 3 days, the mixture was washed with water, diluted with twice its volume of petroleum ether, extracted with Claisen alkali, washed with water, dried over magnesium sulfate, and evaporated under vacuum to give 18.3 g of brown oil. Chromatography on Florisil (eluting with 20% methylene chloride in petroleum ether) gave 6.7 g (0.031 mol, 31%) of dienone 14,  $\lambda_{\max}$  320 m $\mu$  (log  $\epsilon$  3.67).

*Anal.* Calcd for C<sub>15</sub>H<sub>20</sub>O: C, 82.5; H, 10.2. Found: C, 82.9; H, 10.4.

Its nmr spectrum had singlets (combined total 12 H) at  $\tau$  9.07 and 9.11, a doublet (3 H,  $J = 0.5$  Hz) at  $\tau$  8.36, complex peaks (2 H and 3 H, respectively) at  $\tau$  7.5 to 8.0 and from  $\tau$  4.4 to 5.65, a doublet (1 H,  $J = 2.0$  Hz) at  $\tau$  4.32, and a multiplet (1 H) at  $\tau$  3.23.

**Rearrangement of Dienone 14.**—Dienone 14 (0.75 g, 0.0034 mol) was heated at 120° for 3 hr. The carbonyl peak was then completely gone. Vpc analysis at 150° showed the presence of only one compound in the product. An analytical sample was isolated by vpc on a 20%, 5-ft SE-30 column at 200°.

*Anal.* Calcd for C<sub>15</sub>H<sub>20</sub>O: C, 82.5; H, 10.2. Found: C, 82.5; H, 9.98.

The product was identified as allyl 4-*tert*-butyl-2,6-dimethylphenyl ether (15) by its nmr spectrum: singlets (9 H and 6 H, respectively) at  $\tau$  8.75 and 7.80, a jagged doublet (2 H,  $J = ca.$  6 Hz) at  $\tau$  5.77, a complex group of peaks (3 H) at  $\tau$  4.2–5.3, and a singlet (2 H) at  $\tau$  3.10.

**Registry No.**—4, 26319-90-4; 6, 26332-98-9; 7, 26319-92-6; 9, 20966-24-9; 11, 26319-93-7; 12, 26347-47-7; 13, 26347-39-7; 14, 26319-94-8; 15, 26319-95-9.

**Acknowledgment.**—I wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a grant in support of this work.

### Chihuahuin, a New Germacranolide from *Ambrosia confertiflora* DC. (*Compositae*)<sup>1</sup>

WALTER RENOLD, HIROSUKE YOSHIOKA, AND TOM J. MABRY\*

The Cell Research Institute and Department of Botany,  
The University of Texas at Austin, Austin, Texas 78712

Received April 16, 1970

A continuation of our investigation<sup>2</sup> of the infra-specific variation of sesquiterpene lactones in *Ambrosia confertiflora* DC. led to the isolation and structure determination of a new germacranolide. Chloroform extraction of plant material collected north of

\* Author to whom correspondence should be addressed.

(1) The senior author was a National Institutes of Health Predoctoral Trainee, 1967–1969, Grant 5-T01-GM-00789. The work was supported by grants from the Robert A. Welch Foundation (F-130) and the National Science Foundation (GB-5548X). This study represents a portion of a dissertation presented by the senior author to the Graduate School of The University of Texas at Austin in partial fulfillment of the requirements for the Degree of Doctor of Philosophy.

(2) For recent investigations on the sesquiterpene lactones in this species, see (a) T. J. Mabry in "Phytochemical Phylogeny," J. B. Harborne, Ed., Academic Press, London, 1970, Chapter 13; (b) N. H. Fischer, and T. J. Mabry, *Tetrahedron*, **23**, 2529 (1967); (c) N. H. Fischer, and T. J. Mabry, *Chem. Commun.*, 1235 (1967); (d) N. H. Fischer, T. J. Mabry, and H. B. Kagan, *Tetrahedron*, **24**, 4091 (1968); (e) J. Romo, A. Romo de Vivar, A. Velez, and E. Urbina, *Can. J. Chem.*, **46**, 1535 (1968); (f) N. S. Bhacca and N. H. Fischer, *Chem. Commun.*, 68 (1969); (g) W. Herz, G. Anderson, S. Gibaja, and D. Raulais, *Phytochemistry*, **8**, 877 (1969); (h) H. Yoshioka, W. Renold, N. H. Fischer, A. Higo, and T. J. Mabry, *ibid.*, **9**, 823 (1970).

Chihuahua, Mexico, yielded artemisiifolin<sup>3</sup> (2), a germacranolide of known structure, and a new substance which we named chihuahuin (1), C<sub>17</sub>H<sub>22</sub>O<sub>5</sub>. The spectral data suggested that the new sesquiterpene lactone was a germacranolide:  $\lambda_{\max}$  (EtOH) 209 nm ( $\epsilon$  17,200); ir bands (CHCl<sub>3</sub>) at 3550 (hydroxyl), 1760 ( $\gamma$ -lactone), 1740 and 1210 (acetate), 1650 cm<sup>-1</sup> (double bonds). The 60-Mc nmr spectrum exhibited seven isolated and well-resolved signals which are characteristic for the germacranolides: two vinylic methyl doublets at 1.59<sup>4</sup> ( $J = 1$  Hz) and 1.63 ( $J = 1.5$  Hz), a pair of double doublets for the C-11 methylene protons of the  $\alpha,\beta$ -unsaturated  $\gamma$ -lactone at 5.79 ( $J = 3$  and 1 Hz) and 6.30 ( $J = 3.5$  and 1 Hz), a one-proton triplet at 4.42 ( $J = 3$  Hz), a complex one-proton signal at 3.1, and an acetate methyl singlet at 2.07. The region between 4.6 and 5.5, integrating for 4 protons, was a complex set of signals that could only be resolved with a 100-Mc spectrum and extensive spin-decoupling experiments. Irradiation at the center of the complex one-proton signal at 3.1 altered the signals for the two C-11 methylene protons at 5.79 and 6.30 into a pair of broadened singlets; hence the C-7 proton could be ascribed to the 3.1 signal. Furthermore, the region around the C-6 and C-8 proton signals (4.9–5.0) was also affected. Indeed, irradiation at 4.98 changed the C-7 proton signal into a broad doublet and also changed the C-5 proton doublet at 5.37 ( $J = 10$  Hz) into a broadened singlet, thus suggesting that the C-7 proton had only 2 adjacent protons. In reverse, irradiation at 5.37 altered the two vinyl methyl doublets into two singlets and also changed the C-6 proton double doublet at 4.95 ( $J = 8$  and 10 Hz) into a doublet ( $J = 8$  Hz) thus confirming the assignment for the C-6 proton. The position of the second vinyl proton became evident when irradiation was carried out at either 1.66 or 1.59, the resonance of the vinylic methyl groups: (a) a clearly resolved double doublet became evident for the first time at 5.18 ( $J = 8$  and 10.5 Hz), hence establishing the position of the C-1 proton with respect to certain other groups to be as shown in 1; (b) the broad doublet at 5.37 for the C-5 proton became a sharp doublet ( $J = 10$  Hz).

The data presented above left only the positions of the hydroxyl and acetate groups to be determined. That the one-proton triplet at 4.42 ( $J = 3$  Hz) indeed belonged to a proton located on a carbon atom bearing a hydroxyl group became apparent when (a) acetylation of 1 yielded 3 and the triplet shifted, as expected, downfield to 5.27, and (b) irradiation of either 2.47 or 2.36 (the region of CH<sub>2</sub> resonance) changed the triplet at 4.42 into a singlet and irradiation at 4.44 had a marked effect upon the CH<sub>2</sub> region between 2.28 and 2.65. Thus, the hydroxyl group could either be placed at C-3 or C-9. The latter position was excluded when dihydrochihuahuin (4) was heated for 5 min at 205° to yield a compound which appeared from nmr data to be the expected Cope product 5; it was characterized

(3) The structure assigned to artemisiifolin was previously ascribed to salonenolide, a germacranolide from *Centaurea salonitana* Vis.: cf. (a) T. H. Porter, T. J. Mabry, H. Yoshioka, and N. H. Fischer, *Phytochemistry*, **9**, 199 (1970); (b) H. Yoshioka, W. Renold, and T. J. Mabry, *Chem. Commun.*, 147 (1970).

(4) All chemical shift values are reported in ppm ( $\delta$  scale) relative to TMS as an internal standard. Numbers in parentheses denote coupling constants in hertz.