of the aldehyde **21**. After crystallization from methanol–ethyl acetate, there was obtained 70 mg (65%) of the pure aldehyde: mp 241–242 °C; IR (KBr) 3430, 1675, 1475, 1435, 1300, 1215, 1142, 1085, 1055, 965, 880, 725 cm^{-1}; NMR (DMSO-d_6) δ 12.17 (1 H, s, NH), 10.42 (1 H, s, CHO), 10.28 (1 H, s, H_1), 8.66–8.64 (2 H, m), 8.17–8.11 (2 H, m), 7.84 (1 H, d, J = 9.0, H_4), 7.21 (1 H, dd, J = 8.8, 2.2, H_9), 3.99 (3 H, s, OCH_3), 3.34 (H_2O); MS, m/e 277 (M + 1).

Anal. Calcd for $C_{17}H_{12}N_2O_2 \cdot H_2O$: C, 69.39; H, 4.76. Found: C, 69.66; H, 4.49.

6-Ethyl-10-methoxy-7*H*-pyrido[4,3-*c*]carbazole (29). A solution of 44 mg of the aldehyde **27** in 6 mL of dry DMSO was added to a solution of 0.01 M methylenetriphenylphosphorane in 6 mL of DMSO. The mixture was stirred overnight and poured into H_2O. The mixture was worked up as in the case of the olefin **22**. There was obtained 30 mg (72%) of the desired olefin, mp 220–224 °C, suitable for use in the next step: NMR (DMSO-d_6) δ 12.03 (1 H, s, NH), 10.13 (1 H, s, H_1), 8.52 (1 H, d, J = 5.6, H_3), 8.14 (1 H, s, H_{11}), 8.08 (1 H, d, C*H*=CH_2), 7.95 (1 H, d, J = 5.6, H_4), 7.76–7.52 (2 H, m), 7.18 (1 H, dd, J = 8.8, 2.2, H_9), 6.28 (1 H, d, CH=CH_2), 5.72 (1 H, d, CH=CH_2), 3.98 (3 H, s, OCH_3), 3.37 (s, H_2O); MS, m/e 275 (M + 1).

A solution of 15 mg of the above olefin was hydrogenated in the presence of 10% Pd/C at 3 atm. The product was isolated as in the case of the olefin **22** to give 10 mg of the known **29**: mp 236–238 °C (lit.[11] mp 238 °C); IR (KBr) 3520–3300, 1435, 1185, 1115, 755, 725, 700 cm^{-1}; NMR (DMSO-d_6) δ 11.85 (1 H, s, NH), 10.09 (1 H, s, H_1), 8.49 (1 H, d, J = 5.8, H_3), 8.05 (1 H, d, J = 2.0, H_{11}), 7.89 (1 H, d, J = 5.8, H_4), 7.72–7.33 (2 H, m), 7.17 (1 H, dd, J = 8.8, 2.2, H_9), 3.97 (3 H, s, OCH_3), 3.34 (s, H_2O), 3.17 (2 H, q, CH_2CH_3), 1.44 (3 H, t, CH_2CH_3); MS, m/e 277 (M + 1).

Acknowledgment. This work was supported by a grant (CA-19674) from the National Cancer Institute.

Synthesis of Homoallylic Alcohols in Aqueous Media

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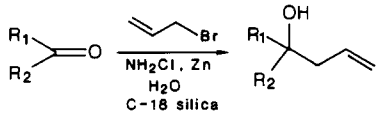
Received August 30, 1988

The reaction of aldehydes or ketones with allyl halides/Zn takes place readily in aqueous NH_4Cl solution in the presence of C-18 silica as a solid organic cosolvent. This efficient and high-yield reaction parallels the Grignard reaction in terms of stereo- and regioselectivity. There are two applications, however, where this process has special advantages. The formation of the Grignard reagent with dimethylallyl halides is plagued by coupling side products while our aqueous cases react smoothly. Another advantage is that the reaction can be carried out without the protection of additional hydroxy functional groups. A diverse selection of examples are presented, and a potential mechanism is discussed.

While the Grignard reaction is perhaps the most widely used and general C–C bond forming reaction in organic chemistry, large-scale industrial application is limited[1] by the expense of the metal, the anhydrous ether solvents required, and complications of waste solvent disposal. For these reasons we were intrigued by a unique C–C bond forming reaction, the allylation of aldehydes *in aqueous media* reported by Luche (eq 1).[2] This reaction is one of



(1)

the few carbon–carbon bond forming processes that occurs in water. We have carried out an extensive study[3] of the scope and stereochemistry of the Luche reaction and most importantly have devised a modification that involves the use of a solid organic support instead of the cosolvent THF (eq 1). Thus, the organic phase can be reused and disposal of the reaction solvent after the reaction is uniquely enviromentally safe!

A Solid Organic Cosolvent. The most efficient modification of the Luche reaction we have examined uses a solid organic phase instead of THF as the cosolvent. Our results are summarized in Table I. All the reactions were carried out on a 1-mmol scale, with 1 mL of the aqueous phase and 100–200 mg of the organic phase. The reaction times vary from 0.5 to 16 h.

The reactions proceed at about the same rate as reactions with THF as a cosolvent. Reverse-phase C-18 silica gel was used as our standard although another excellent support for the reaction was biobeads S-X8, a spherical, porous styrene divinylbenzene copolymer with 8% cross-links. The reaction also proceeded satisfactorily on GC column packing OV-101 on Chromosorb.

The simplicity of the allylation reaction and its workup makes this procedure highly recommended. A slurry of zinc, C-18 silica (reverse-phase chromatography support), allyl bromide, and the aldehyde in saturated aqueous ammonium chloride solution was stirred at room temperature in an open beaker. After the reaction was complete (as monitored by GC), filtration and washing the residue with water left the product adsorbed on the support. Elution with ether, drying, and evaporation led to high yields of pure alcohols. The organic solid remaining can be reused, although it appears gray in color.

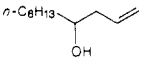
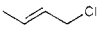
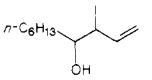
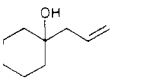
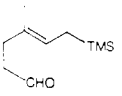
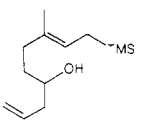
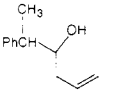
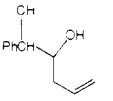
Scope and Limitations

After this work was completed,[3] a report by the Luche group[2c] appeared which largely confirmed our stereochemical conclusions. While no special selectivity was observed for this reaction, some unique features are apparent. In addition, since formation of the allyl Grignard reagents is often plagued by low yields due to competing coupling reactions,[4] this modification is a valuable alter-

(1) Waugh, T. D. The Grignard Reacton In *Kirk-Othmer Encyclopedia of Science and Technology*, 3rd ed.; J. Wiley: New York, 1980.
(2) (a) Petrier, C.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 910. (b) Petrier, C.; Einhhorn, J.; Luche, J. L. *Tetrahedron Lett.* **1985**, *26*, 1449. (c) Einhorn, C.; Luche, J.-L. *J. Organomet. Chem.* **1987**, *322*, 177.
(3) Taken, in part, from the Ph.D. Thesis of Maria Guazzaroni, New York University, October 1987.

0022-3263/89/1954-3087$01.50/0

Table I. Reaction of Carbonyl Compounds with Allyl Halides/Zinc and Solid Organic Phases

entry	carbonyl compound	allyl halide	solid phase	time, h	yield,[a] %	product
1	n-$C_6H_{13}CHO$		C-18 silica[b]	16	98	
			Bio-beads[c]	0.5	64	
			OV-101[d]	16	70	
			tenax GC[e]	0.5	35	
2	n-$C_6H_{13}CHO$		C-18 silica	16	85	
			Bio-beads	4	77	
3			C-18 silica	1.5	82	
4			C-18 silica	16	68	
5	$PhCH(CH_3)CHO$		C-18 silica	1.5	>90	
6	$PhCH(CH_3)CHO$		Merrifield Resin[f]	0.6	80	
7	$PhCH(CH_3)CHO$		Amberlite CG-400[g]	-	no reaction	-

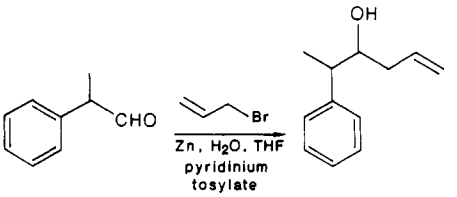
[a] Isolated yields. All reactions except 7 with saturated NH_4Cl solution. [b] Silica-C_{18} from Custom Chemical Laboratories. [c] Bio-beads S-X8 200–400 mesh from Bio-Rad Laboratories. [d] OV-101 20% on Chromosorb (60–80 mesh). [e] Tenax-GC (Alltech Associates). [f] Chloromethylated Polystyrene (Calbiochem). [g] Strong base anion exchange resin (Mallinkrodt) and distilled water.

native. We have collected examples from our study in Table II and briefly summarized our conclusions.

Three types of stereoselectivity in carbonyl addition reactions were explored and led to the conclusion that no special selectivity can be expected. Cram selectivity[5a] is observed in the reaction of 2-phenylpropionaldehyde (entry 6), as well as in the reacton with 3-(benzyloxy)-2-methylpropionaldehyde (entry 7). In contrast, the addition of allylmagnesium bromide to 3-(benzyloxy)-2-methylpropionaldehyde[5b] gives a 1:2 ratio in favor of the anti-Cram product. Lack of chelation control in water solution, however, is not surprising. The erythro–threo selectivity[6] is identical with that observed in the corresponding Grignard or alkyllithium additions (entries 3 and 4). Finally, addition to 4-*tert*-butylcyclohexanone (entry 11) gave 60% axial alcohol/40% equatorial alcohol, again a result virtually identical with that obtained by the addition of allylmagnesium chloride to 4-*tert*-butylcyclohexanone.[7]

A noteworthy feature of this reaction, however, is that it can be carried out *without protection of the hydroxyl substituents* in the molecule (entries 9, 10, and 12).[8] This undoubtedly will lead to useful applications.

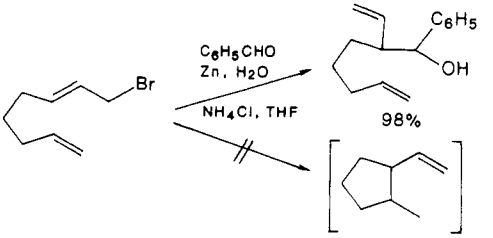
Saturated aqueous NH_4Cl solution is necessary for the reaction. No product is formed when the reaction is run in distilled water. An organic cosolvent is also required (although a solid organic polymer can also be used. The reaction medium is actually *three* phases). Excellent results are obtained when a 50% solution of pyridinium tosylate was employed (2 mL per mmol of aldehyde). The reaction went to completion in 2.5 h and an 89% isolated yield of product was obtained (78% after Kugelrohr distillation).



(2)

Mechanistic Considerations

Since organozinc compounds are known to react violently with water, a free allylzinc species seems unlikely. Luche[2a] proposed that a free radical pair process of the type proposed by Bauer[9] for the Barbier reaction could be involved and has suggested[2c] that a radical derived from the bromide attacks the carbonyl group. We have examined a free-radical probe, compound 1, and observed no apparent effect, i.e. normal products were obtained in the reaction of allyl bromide 1 with benzaldehyde. This

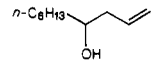
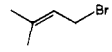
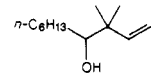
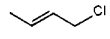
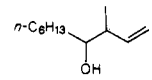
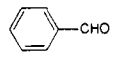
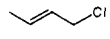
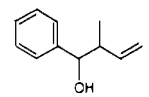
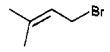
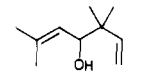
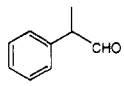
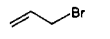
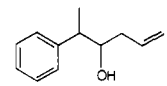
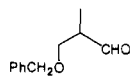
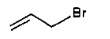
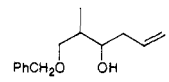
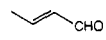
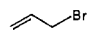
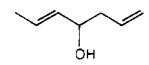
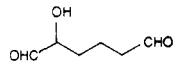
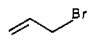
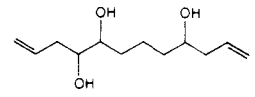
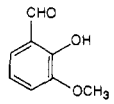
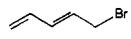
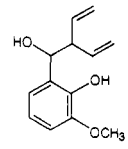
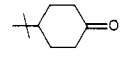
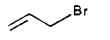
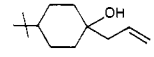
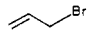
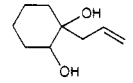
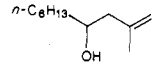
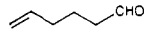
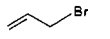
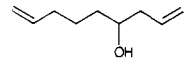
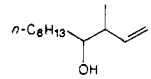


(3)

contrasts with the formation of a Grignard reagent from 1[10] which cyclizes and suggests that a radical intermediate, if formed, must either be associated with the metal surface or react faster than the known $\sim 10^5$ s^{-1} rate of cyclization of the hexenyl radical system.[11]

(4) Benkeser, R. A. *Synthesis* **1971**, 347.
(5) (a) Cram, D. J.; Elhafez, F. A. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. (b) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035.
(6) Hijama, T.; Kimura, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1037.
(7) Gaudemar, M. *Tetrahedron* **1976**, *32*, 1689.
(8) Other examples of additions to hydroxy aldehydes were reported in ref 2c.
(9) Molle, G.; Bauer, P. *J. Am. Chem. Soc.* **1982**, *104*, 3481.
(10) Fukutani, H.; Tokizawa, M.; Okada, H. Jpn. Patent 47/39034; *Chem. Abstr.* **1973**, *78*, 111498y.

Table II. Addition of Allyl Halides to Aldehydes or Ketones in Aqueous Media

entry	aldehyde/ketone	halide	product	yield, %
1	n-$C_6H_{13}CHO$			~100
2	n-$C_6H_{13}CHO$			95
3	n-$C_6H_{13}CHO$			88 (1:1 threo/erythro)
4				90 (43:57 threo/erythro)
5				76
6				90 (8:2 Cram/anti-Cram)
7				64 (56:44 Cram/anti-Cram)
8				37
9				60
10				36
11				40
12				90
13	n-$C_6H_{13}CHO$			56
14				70
15	n-$C_6H_{13}CHO$			~100 (1:1 threo/erythro)
16	PhCHO			78

Experimental Section

General Procedure for the Reaction of Aldehydes or Ketones with Zinc and an Allyl Halide. Method A. To a solution of 1 mmol of the aldehyde or ketone in 1 mL of saturated aqueous ammonium chloride and 0.2 mL of THF were added 1.2–2 mmol of the allyl halide and 1.2–2 mmol of zinc dust (Matheson Coleman and Bell). The mixture was stirred at room temperature open to the air for 1 h (unless otherwise indicated). The suspension (containing zinc salts) was then extracted with diethyl ether, and the ether layer was dried over $MgSO_4$. Evaporation of the organic solvent at reduced pressure yielded the product.

Method B. A mixture was prepared with 1 mmol of the aldehyde or ketone, 1 mL of saturated aqueous ammonium chloride solution, 100 or 200 mg of reverse phase silica gel (or other organic polymer), 1.2–2 mmol of the allyl halide, and 1.2–2 mmol of zinc dust. The mixture was stirred for 0.5–16 h at room temperature open to the air. The reacton mixture was filtered through a fritted-glass funnel with the help of a water aspirator, washing first with 5 mL of water to remove the inorganic materials. The product was washed off the polymer with diethyl ether, and the ether layer was dried ($MgSO_4$) and concentrated under vacuum to yield the product.

Synthesis of 1-Decen-4-ol. (1) Method A was used with 127.49 mg (1.1 mmol) of heptaldehyde, 0.15 mL (1.7 mmol) of allyl bromide, and 113.47 mg (1.74 mmol) of zinc dust. After workup 187.56 mg of a yellow oil was obtained (100% = 171.6 mg). GC (3 ft): 3.44 min. TLC: silica gel, 10% ethyl acetate/hexane, R_f = 0.30. NMR: δ 0.90 (br), 1.30 (br s), 1.45–1.50 (br d), total area 14 H, 2.10–2.21 (m, 1 H), 2.27–2.37 (m, 1 H), 3.65 (br m, 1 H), 5.09–5.20 (m, 2 H), 5.77–5.92 (m, 1 H). GC–MS (relative abundance): 115.1 (16.9), 97.1 (46.1), 69.1 (16.1), 55.0 (100.0), 43.1 (35.7),

(11) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317.

41.1 (33.8). ^{13}C: δ 14.18, 22.72, 25.76, 29.45, 31.94, 36.98, 42.06, 70.85, 118.05, 135.04. IR (Perkin-Elmer): 3550 (s), 3000 (s) shoulder at 2950, 1650 (w), 1470 (m), 910 (m) cm^{-1}.

(2) Method B was used on 119.5 mg (1.05 mmol) of heptaldehyde, 0.1 mL (1.2 mmol) of allyl bromide, and 78 mg (1.2 mmol) of zinc with 200 mg of C_{18} silica gel. The reaction was stirred overnight giving 98% yield of the adduct.

(3) Method B was followed with use of 200 mg of Bio-beads SX-8 (Biorad), 121.3 mg (1.06 mmol) of heptanal, 0.14 mL (1.6 mmol) of allyl bromide, and 126.92 mg (1.9 mmol) of zinc. The reaction was complete in 0.5 h, and 165.3 mg (64%) of the adduct was obtained.

(4) Method B with 200 mg of Tenax GC (Alltech Associates) as the organic phase, 120 mg (1.05 mmol) of heptanal, 0.17 mL (1.94 mmol) of allyl bromide, and 130 mg (2 mmol) of zinc was complete in 0.5 h and produced 54 mg of product (35%).

(5) Method B, employing 100 mg of 20% OV-101 on Chromosorb (60–80 mesh), 125.83 mg (1.1 mmol) of heptaldehyde, 0.17 mL (2 mmol) of allyl bromide, and 130 mg (2 mmol) of zinc for 16 h, gave after workup 120.19 mg of product (70%).

3,3-Dimethyl-1-decen-4-ol. Method A, on 0.570 g of heptaldehyde (5 mmol), 1.2 mL of 3,3-dimethylallyl bromide (10 mmol), and 0.650 g of zinc (10 mmol) in 5 mL of saturated aqueous NH_4Cl and 1 mL of THF, gave the product, 3,3-dimethyl-1-decen-4-ol, which was purified by filtration through silica gel, eluting with 10% ethyl acetate/hexane, (0.874 g, 95%). GC (3 ft): 4.32 min. TLC: silica gel, 10% ethyl acetate/hexane, R_f = 0.49. NMR: δ 0.82–0.97 (m, 5 H), 0.99 (s, 6 H), 1.27 (br s, 9 H), 3.24 (d, J = 9.87, 1 H), 5.00–5.20 (m, 2 H), 5.81 (dd, J = 17.74, 11.16, 1 H). GC–MS (relative abundance): 138.1 (5.6), 82.1 (11.3), 70.1 (16.6), 69.1 (100.0), 67.1 (8.8), 41.1 (70.5)

3-Methyl-1-decen-4-ol. Method A was followed with use of 2.27 g (19.9 mmol) of heptaldehyde, 2.36 mL (24 mmol) of crotyl chloride, and 1.56 g (24 mmol) of zinc in 20 mL of saturated aqueous NH_4Cl solution and 4 mL of THF. The reaction mixture was stirred overnight to yield, after filtration through silica gel, 2.97 g (87.8%) of 3-methyl-1-decen-4-ol as 1:1 mixture of erythro to threo products. GC (3 ft): 4.4 min. TLC: silica gel, 10% ethyl acetate/hexane, R_f = 0.5. NMR: δ 0.85–0.95 (br s), 1.04 (d, J = 2.92, $^3/_2$ H), 1.06 (d, J = 2.96, $^3/_2$ H), 1.22–1.4 (br s), 3.35–3.45 (m, $^1/_2$ H), 3.47–3.56 (m, $^1/_2$ H), 5.05–5.2 (m, 2 H), 5.7–5.9 (m, 1 H). GC–MS (relative abundance): 97.1 (22.6), 69.0 (12.6), 57.1 (17.9), 56.1 (95.4), 55.1 (100.0), 43.1 (49.9), 41.0 (54.7).

Method B, using 0.570 g (5 mmol) of heptaldehyde, 1 mL (10 mmol) of 3-chloro-1-butene (Aldrich), 0.650 g (10 mmol) of zinc, and 0.5 g of C_{18} silica gel, in 5 mL of saturated NH_4Cl solution, gave 0.860 g of 3-methyl-1-decen-4-ol.

Method B, using 120.63 mg (1.06 mmol) of heptaldehyde, 0.2 mL (2 mmol of crotyl chloride, 130 mg (2 mmol) of zinc, and 200 mg of C_{18} silica gel, gave after 16 h 0.153 g of product (85%).

Method B, using Bio-beads SX-8 (200 mg, Bio-Rad Laboratories), gave 137.9 mg of product (77%).

3-Methyl-4-phenyl-1-buten-4-ol. Method A with 0.122 g (1.16 mmol) of benzaldehyde (used without prior distillation), 0.23 mL of crotyl chloride (2.3 mmol), and 0.150 g (2.3 mmol) of zinc for 2.5 h gave 0.169 g of the homoallylic alcohol (90%) as a 57:43 mixture of erythro/threo products.[6]

(±)-Artemisia Alcohol. A sample of 36.6 mg of 3-methyl-2-butenal (0.44 mmol) was reacted with 0.1 mL of 3,3-dimethylallyl bromide and 78 mg of zinc by using method A. Artemisia alcohol[12] was obtained in 76% isolated yield (51 mg).

5-Phenyl-1-hexen-4-ol. Method A, using 0.134 g (1 mmol) of 2-phenylpropionaldehyde (Aldrich, 98%), 0.17 mL (2 mmol) of allyl bromide (Aldrich, 99%), and 0.133 g (2 mmol) of zinc gave 90% yield (GC) as an 8:2 mixture of Cram to anti-Cram products.[13]

Acetylation: A small sample was converted into the acetates (acetic anhydride, triethylamine, 4-(dimethylamino)pyridine). GC (3 ft): 5.52 min. TLC: silica gel, 10% ethyl acetate/hexane, R_f = 0.57. GC–MS (relative abundance): 158.2 (M^+ – AcOH, 13.7), 105.1 (45.6), 77.0 (6.8), 43.0 (100.0). Two isomers were recorded in a ratio of 20:80. Capillary GC (60 °C, 1 min/5 °C per min/220 °C): t_R = 20.4 and 20.8 min in a ratio 24/76.

Method B was followed with use of 0.143 09 g (1.07 mmol) of D,L-2-phenylpropionaldehyde, 0.34 mL (4 mmol) of allyl bromide, 0.260 g (4 mmol) of zinc dust, 2 mL of water, 300 mg of C_{18} silica gel (Baker for flash chromatography), and 1 g of pyridinium tosylate. The reacton mixture was stirred for 2.5 h. After workup 168.06 mg of crude product was obtained (89%). Kugelrohr distillation (73–75 °C/2 mmHg) gave 145.9 mg of 5-phenyl-1-hexen-4-ol as a colorless oil (77.5%).

6-(Benzyloxy)-5-methyl-1-hexen-4-ol. Method A was followed, using 84.22 mg (0.47 mmol) of 3-(benzyloxy)-2-methylpropionaldehyde,[14] 0.05 mL (0.59 mmol) of allyl bromide, and 38 mg (0.59 mmol) of zinc. The crude product was purified by radial chromatography on a 1 mm silica gel plate, eluting with 10% ethyl acetate/hexane. A 64% yield of pure alcohol was obtained[13] (65.99 mg) as a 56:44 mixture of Cram to anti-Cram products by comparison with an authentic sample.

1,5-Heptadien-4-ol. Method A was followed, using 0.1 mL (1.2 mmol) of crotonaldehyde, 0.12 mL (1.4 mmol) of allyl bromide, and 93.6 mg (1.4 mmol) of zinc dust. After 0.5 h the reaction mixture turned yellow and all the zinc was consumed. 1,5-Heptadien-4-ol was obtained as a yellow oil (96 mg, 72%). The product was purified by preparative TLC on a 1000 μm silica gel plate, eluting with 20% ethyl acetate/hexane to give 50.2 mg of product (37.4%). TLC: silica gel, 20% ethyl acetate/hexane, R_f = 0.52. NMR: δ 1.73 (d, J = 6.16, 3 H), 2.32 (m, 2 H), 4.14 (q, J = 6.21, 1 H), 5.10–5.25 (m, 2 H), 5.47–5.62 (m), 5.66–5.93 (m). Total area 5.47–5.93 (3 H, CH=CH_2 and C*H*=C*H*).

4,5,9-Trihydroxy-1,11-dodecadiene. Method A was followed with use of 2.6 mL (5 mmol) of 2-hydroxyhexanedial (Aldrich, 25% solution in water), 2.6 mL (30 mmol) of allyl bromide, 1.950 g (30 mmol) of zinc dust, 2.4 mL of NH_4Cl solution, and 1 mL of THF. The reaction was very exothermic, and all the zinc was consumed in 15 min. Usual workup gave 0.909 g of crude triol (85%). A sample of 250 mg was purified by radial chromatography on a 1 mm silica gel plate, eluting with 60% ethyl acetate/ligroin. Evaporation of the solvent at reduced pressure yielded 150 mg of product (60%). Bp: 180 °C (0.3 mmHg). GC (3 ft): 7.11 min. TLC: silica gel, 60% ethyl acetate/ligroin, R_f = 0.24. NMR: δ 1.51 (br s, 6 H), 2.27 (m, 4 H), 3.51 (br s), 3.68 (br s), total area 3.5–3.7 (3 H), 5.14 (d apparent, J = 14.4, 4 H), 5.86 (m, 2 H). ^{13}C: δ 21.86, 31.58, 33.43, 36.39, 38.36, 42.11, 70.63, 73.77, 118.28, 134.90 (the spectrum shows that more than one isomer is present). IR (Perkin-Elmer): 3500(s), 3000(s), 1650(m), 910(s) cm^{-1}. GC–MS (relative abundance: 155.2 (26.4), 143.1 (30.6), 125.1 (26.4), 119.1 (38.0), 113.0 (65.6), 109.2 (19.6), 108.1 (13.8), 107.2 (22.6), 101.1 (12.9), 97.2 (25.3), 95.1 (32.0), 93.2 (29.5), 91.1 (26.7), 83.1 (29.8), 81.1 (48.8), 79.1 (36.6), 71.1 (28.4), 69.1 (28.1), 67.2 (78.2), 57.1 (77.1), 55.2 (92.8), 44.1 (20.1), 43.1 (92.0), 41.1 (100.0). The triol was further characterized by acetylation. To a solution of 1.83 g (8.6 mmol) of the above triol in 10 mL of dry THF was added 5 mL (53 mmol) of acetic anhydride, 105 mg (0.9 mmol) of (*N*,*N*-dimethylamino)pyridine, and 7.2 mL (51.8 mmol) of triethylamine. The mixture was stirred at room temperature under a nitrogen atmosphere for 2 h, quenched with saturated aqueous sodium bicarbonate solution, extracted with ether, dried (Na_2SO_4), and concentrated under vacuum to give 2.09 g of the crude triacetate (71.5%). The product was purified by flash chromatography, eluting with 10% ethyl acetate in ligroin. The sample for elemental analysis was collected from preparative gas chromatography. An ether solution of the sample was filtered through Millex-HV_4 filter (0.45 micron, 4 mm, Millipore), and the ether was evaporated under vacuum. GC (3 ft): 9.52 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.23. NMR: δ 1.30 (m), 1.55 (br d), 2.00–2.15 (m), 2.30 (br m), total area 1.2–2.4 (19 H), 4.8–5.15 (m), 5.6–5.8 (m), total area 4.8–5.8 (9 H). GC–MS (relative abundance): 239.4 (6.3), 197.3 (17.0), 119.3 (8.7), 67.2 (7.7), 55.2 (7.4), 43.3 (100.0), 41.3 (6.9) (two isomeric peaks were recorded by GC–MS). ^{13}C: δ 21.20, 25.92, 29.16, 30.49, 33.29, 34.32, 35.56, 38.63, 73.28, 117.78, 133.64, 170.70 (the spectrum shows that more than one isomer was present). IR (Perkin-Elmer): 3000 (m), with shoulder at 2900, 1750 (s), 1420 (w), 1370 (m), 1220 (s), 1020 (m, broad), 910 (w) cm^{-1}. Microanalysis Calcd C, 63.53; H, 8.24. Found: C, 63.79; H, 8.32.

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(13) Heathcock, C. H.; Kiyooka, S.; Blumerkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4214.
(14) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

1-(2-Hydroxy-3-methoxyphenyl)-2-vinyl-3-buten-1-ol. Method A, using 117 mg (0.8 mmol) of *o*-vanillin, 125 mg (0.85 mmol) of 1-bromo-2,4-pentadiene, and 52 mg (0.8 mmol) of zinc, gave crude alcohol, which was purified by preparative TLC, eluting with 15% ethyl acetate/ligroin to prove 63 mg of product (36% yield). TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.17; 20% ethyl acetate/ligroin, R_f = 0.47. NMR: δ 3.32 (q, J = 7.5, 1 H), 3.92 (s, 3 H), 2 superimposed doublets 4.88 (J = 7.17) and 4.90 (J = 7.15), together (1 H, C*H*OH), 5.00–5.30 (m, 4 H), 5.71–5.85 (m, 1 H), 5.88–6.05 (m, 1 H), 6.8–6.9 (m, 3 H). The two superimposed doublets integrate roughly 1:1. When the decoupler was set at 3.322 ppm, the two superimposed doublets collapsed into two singlets at 4.88 and 4.90 ppm. They are broad and superimposed, too, and therefore integration is difficult. IR (Perkin-Elmer): 3600 (s), 3000 (m) with shoulder at 2950, 1500 (s), 1250 (s) cm^{-1}.

4-*tert*-Butyl-1-(2-propenyl)cyclohexanol. Method A with use of 0.168 g (1.1 mmol) of 4-*tert*-butylcyclohexanone, 0.1 mL (1.2 mmol) of allyl bromide, and 78 mg (1.2 mmol) of zinc gave 40% yield of the alcohol as a 60/40 axial/equatorial mixture by comparison with an authentic sample.[7]

1-Allyl-1,2-cyclohexanediol. Method A was used with 154.5 mg (1.36 mmol) of 2-hydroxycyclohexanone, 0.17 mL (2 mmol) of allyl bromide, and 130 mg (2 mmol) of zinc to produce the diol as a yellow oil (0.190 g, 89.7%). GC (3 ft): 5.12 min. TLC: silica gel, 50% ethyl acetate/ligroin: R_f = 0.6 (blue) and R_f = 0.48 (red, color indicated is obtained by visualizing the TLC plate with vanillin spray). NMR: δ 1.20–1.80 (m, 8 H), 2.06 (br s, 1 H), 2.13 (br s, 1 H), 2.26–2.47 (m, 2 H), 3.47 (d apparent, J = 7.83, 1 H), 5.15 (m, 2 H), 5.80–6.00 (m, 1 H). GC–MS (relative abundance): 115.0 (17.2), 97.0 (17.2), 79.0 (17.2), 69.9 (13.8), 69.1 (34.5), 58.1 (20.7), 57.1 (27.6), 55.1 (44.8), 43.1 (44.8), 41.1 (100.0). ^{13}C: δ 21.21, 23.37, 30.50, 34.46, 43.77, 73.43, 118.70, 133.94. IR (Nujol): 3500 (s), 3000 (s), 1650 (w), 1050 (br m), 970 (m), 910 (m) cm^{-1}. Accurate mass (EI^+): calcd for $C_9H_{16}O_2$ 156.1146, obsd 156.1150.

2-Methyl-1-decen-4-ol. Method B was used on 0.576 g (5.05 mmol) of heptaldehyde, 1 mL (10.1 mmol) of 3-chloro-2-methylpropene, 0.650 g (10 mmol) of zinc, and 0.5 g of C_{18} silica gel. The mixture was stirred for 16 h. The product was obtained in 56% yield (0.480 g). NMR data matches the reported values.[15]

(15) Hegedus, L. S.; Wagner, S. D.; Waterman, E. L.; Siirala-Hansen, K. *J. Org. Chem.* **1975**, *40*, 593.

1,8-Nonadien-4-ol. Method A was applied to 0.235 g (2.4 mmol) of 5-hexenal, 0.25 mL (2.9 mmol) of allyl bromide, and 0.199 g (3 mmol) of zinc in 2.5 mL of saturated aqueous solution of NH_4Cl and 0.5 mL of THF. After workup 0.254 g of crude product was obtained. A sample of 117.65 mg of crude product was purified by radial chromatography on a 1-mm plate, eluting with 10% ethyl acetate/ligroin to give 82.34 mg of 1,8-nonadien-4-ol as a yellow oil (70% yield). GC (3 ft): 2.34 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.30. NMR: δ 1.4–1.65 (m, 4 H), 1.65–1.75 (br s, 1 H), 2.05–2.40 (m, 4 H), 3.07 (br s, 1 H), 4.95–5.22 (m, 4 H), 5.75–5.95 (m, 2 H). GC–MS (relative abundance): 81.1 (91.3), 79.1 (13.9), 57.2 (35.7), 55.2 (70.9), 54.2 (15.9), 53.2 (18.7), 43.2 (65.2), 42.2 (21.5), 41.2 (100.0). ^{13}C: δ 25.09, 33.80, 36.37, 42.10, 70.67, 114.71, 118.23, 134.91, 138.77. IR (neat, Beckman IR-18): 3140 (s), 3060 (s), 3020 (w), 2800 (w), 1720 (s), 1650 (m), 1415 (s), 1250 (s), 990 (m), 910 (m) cm^{-1}.

1-Allylcyclohexanol. Method B was used on 0.490 g (5 mmol) of cyclohexanone, 0.86 mL (10 mmol) of allyl bromide, 0.650 g (10 mmol) of zinc, and 0.5 g of reverse-phase silica gel. The mixture was stirred for 2 h. 1-Allylcyclohexanol was obtained as a yellow oil (0.58 g, 82%). GC (3 ft): 2.16 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.52. NMR: δ 1.40–1.70 (m, 10 H), 2.25 (d, J = 7.45, 2 H), 5.08–5.24 (m, 2 H), 5.83–6.00 (m, 1 H). GC–MS (relative abundance): 99.1 (100.0), 81.0 (97.0), 79.0 (13.1), 57.1 (10.0), 55.1 (44.9), 43.0 (25.4), 41.0 (32.3).

7-Methyl-9-(trimethylsilyl)-4-hydroxy-1,7-nonadiene. Method B was used on 91.82 mg (0.5 mmol) of aldehyde, 0.09 mL (1 mmol) of allyl bromide, 65 mg (1 mmol) of zinc, and 50 mg of C_{18} silica gel. The mixture was stirred for 16 h. The crude product was purified by radial chromatography on a 1-mm plate, eluting with 7% ethyl acetate/ligroin. The product was obtained in 67.6% yield (76.4 mg). GC (3 ft): 5.28 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.42. NMR: δ 0.01 (s, 9 H, TMS), 1.59 (s, CH_3C=), 3.70 (br m, C*H*OH), 5.10–5.30 (m), and 5.60–6.00 (m), total area (4 H). GC–MS (relative abundance): 226.1 (M^+, 8.0), 95.1 (19.6), 75.1 (29.6), 73.1 (100.0), 68.1 (63.6), 67.1 (20.5), 45.0 (20.2), 43.0 (11.7), 41.0 (14.1).

Acknowledgment. We thank the National Institutes of Health (Grant GM-29259) for financial support of this work. We also acknowledge the Rockefeller University NIH-Biomedical Mass Spectrometer Lab for providing exact mass measurements.

Synthesis of the K-Region Monofluoro- and Difluorobenzo[*c*]phenanthrenes

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Received September 20, 1988

Polycyclic aromatic hydrocarbons are metabolically activated by cytochromes P-450 and epoxide hydrolase to ultimate mutagens and carcinogens. Substitution by fluorine at specific positions has been used to elucidate metabolic activation and detoxication pathways of polycyclic aromatic hydrocarbons. Substitution by fluorine at the K-region C-6 position of the weak carcinogen benzo[*c*]phenanthrene (**1**) causes a >4-fold increase in its tumorigenicity. Out of the six possible monofluorobenzo[*c*]phenanthrenes, only 5-fluorobenzo[*c*]phenanthrene (**8a**) has not been evaluated as a carcinogen, presumably because a convenient synthetic method for the 5-fluoro derivative has not been available. Hence, a new method has been developed for the synthesis of **8a** from readily available starting materials. The method consists of selective bromination of benzo[*c*]phenanthrene (**1**) to 5-bromobenzo[*c*]phenanthrene (**3**), substitution of bromine by an amino group, and a modified Schiemann reaction of 5-aminobenzo[*c*]phenanthrene (**6a**) to yield 5-fluorobenzo[*c*]phenanthrene (**8a**). An improved method for the synthesis of 6-fluorobenzo[*c*]phenanthrene (**19**) has also been developed which consists of bromofluorination of β-naphthylstyrene, followed by selective dehydrobromination and photocyclization of the fluorostyrene to the 6-fluoro derivative **19**. The above methods, with minor modifications, also provided synthetic routes for the preparation of the difluoro derivatives 5,7-, 5,8-, and 6,7-difluorobenzo[*c*]phenanthrenes.

Polycyclic aromatic hydrocarbons are widespread environmental pollutants. They are metabolically activated by cytochromes P-450 and epoxide hydrolase to bay region diol epoxides which constitute an important class of ul-

0022-3263/89/1954-3091$01.50/0