reaction mixture with 10% aqueous sodium hydroxide afforded on acidification 1.7 g (41%) of lauric acid. The neutral residue was analyzed on the following vpc columns: (a) 10% SE-30, (b) 10% diethylene glycol succinate, (c) 5% Apiezon M, and (d) 5% β,β'-oxydipropionitrile on Chromosorb W. There were isolated 20% 1-undecene, 2% other undecenes (mainly *trans*-2-undecene), and 30% 12-tricosanone of mp 68°.[16]

Registry No.—*p*-Fluorobenzoic anhydride, 25569-77-1; *p*-phenylbenzoic anhydride, 25327-57-5; 3,5-dimethylbenzoic anhydride, 25569-79-3; 2,3'-dichlorobiphenyl, 25569-80-6; 3,4'-dichlorobiphenyl, 2974-90-5; 2,3',4,5'-tetramethylbiphenyl, 25569-82-8; 1,3,-

(16) An authentic sample was prepared as described by J. C. Sauer, "Organic Syntheses," Coll. Vol. IV, Wiley, New York, N. Y., 1963, p 560.

5,7-tetramethylfluorenone, 25569-83-9; 3,5-dimethylfluorenone, 25569-84-0; 6-chloro-2-methylfluorenone, 25569-85-1; 2-chloro-6-methylfluorenone, 25569-86-2; *o*-toluic anhydride, 607-86-3; *m*-toluic anhydride, 21436-44-2; *p*-toluic anhydride, 13222-85-0; *p*-chlorobenzoic anhydride, 790-41-0; *p*-bromobenzoic anhydride, 1633-33-6; 2-thenoic anhydride, 25569-97-5; 2,4'-dimethylbiphenyl, 611-61-0; 3,3'-dimethylbiphenyl, 612-75-9; 3,4'-dimethylbiphenyl, 7383-90-6; 4,4'-dimethylbiphenyl, 613-33-2; 3,3',5,5'-tetramethylbiphenyl, 25570-02-9.

The Mechanism of the Reaction of 2'-Iodo-2-bromomethylbiphenyl with Methyllithium to Yield Fluorene

L. J. Altman* and Timothy R. Erdman

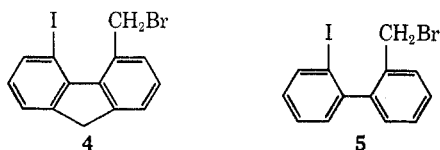*Department of Chemistry, Stanford University, Stanford, California 94305*

The mechanism of the cyclization of 2'-iodo-2-bromomethylbiphenyl to fluorene using methyllithium was investigated. Evidence that this conversion proceeds by the direct displacement of the benzylic bromine by an aromatic anion is presented.

We have been interested in the synthesis of the strained hydrocarbon **1** as a likely precursor to dibenzo-[*cd,gh*]pentalene (**2**). Compound **2** can be visualized as a perturbed [12]annulene. The recent synthesis[1] of hydrocarbon **1**, as well as the dianion of **2**, prompts us to report our results at this time.

1   2   3
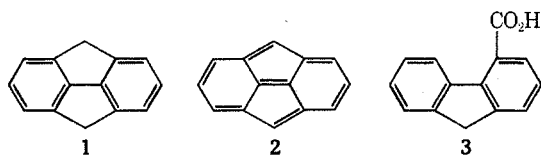
Friedel–Crafts cyclization of the readily available fluorene-4-carboxylic acid (**3**) cannot be expected to serve as a synthetic method for the preparation of **1**. This acylation would proceed through an acylium ion which must attack the aromatic ring along the π orbital,[2] an impossibility for the rigid, planar acid **3**. We therefore sought a method that would circumvent this difficulty and turned to an investigation of methods potentially capable of converting 5-iodo-4-bromomethylfluorene (**4**) to **1**. We chose to study the cyclization of 2'-iodo-2-bromomethylbiphenyl (**5**) as an easily prepared model for this cyclization. Our investigations were limited to those reactions, such as a back-side displacement of the benzylic bromine by an aromatic

4   5

anion, which would cyclize **5** in a manner that would not require large changes in geometry. Several reactions were investigated, including those with Zn, Zn–Cu couple, Mg, Ni(CO)₄,[3] and methyllithium. Methyllithium proved to be the most satisfactory reagent, affording fluorene in yields of 69–71%. In order to determine whether the cyclization of **5** with methyllithium was indeed proceeding through the desired back-side displacement of the benzylic bromine, a study of the mechanism of this reaction was undertaken and our results are reported below.

A search of the literature provides little information about the relative rates of halogen–lithium exchange for iodobenzene and benzyl bromide, except that the order of reactivity of the halides is I > Br > Cl.[4] We therefore chose to work with methyllithium, the least reactive of the alkyllithiums,[5] in order to enhance any differences in the halogen–lithium exchange rates.

An ethereal solution of **5** at 0° was treated with 2 equiv of methyllithium, allowed to come to room temperature, and worked up with ammonium chloride solution to afford fluorene in isolated yields of 69–71%. The remaining material had no iodine as shown by a lack of absorption at lower field than δ 7.80 (aromatic protons ortho to iodine) in the nmr spectrum.

A priori there are four possible mechanisms for this conversion (Scheme I). Recent work[6,7] indicates that the halogen–lithium exchange reaction proceeds by a one-electron transfer to give a caged radical pair. These radicals may complete the halogen–metal exchange by transferring a second electron or they may

* Author to whom correspondence should be addressed.

(1) B. Trost and P. Kinson, *J. Amer. Chem. Soc.,* **92**, 2591 (1970).
(2) J. von Braun, E. Danziger, and Z. Koehler, *Chem. Ber.,* **50**, 56 (1917); J. von Braun and E. Rath, *ibid.,* **61**, 956 (1928); J. von Braun and E. Anton, *ibid.,* **62**, 145 (1929).

(3) The yields of fluorene obtained from Zn or Zn–Cu couple were 1–6%, those from Mg were 30%, and those from Ni(CO)₄ were 2–46%, depending upon the solvent used. A paper on the cyclization of **5** with Ni(CO)₄ will appear at a later date.
(4) See H. Gilman, *Org. React.,* **6**, 339 (1951), and the references therein.
(5) H. Gilman and F. W. Moore, *J. Amer. Chem. Soc.,* **62**, 1843 (1940).
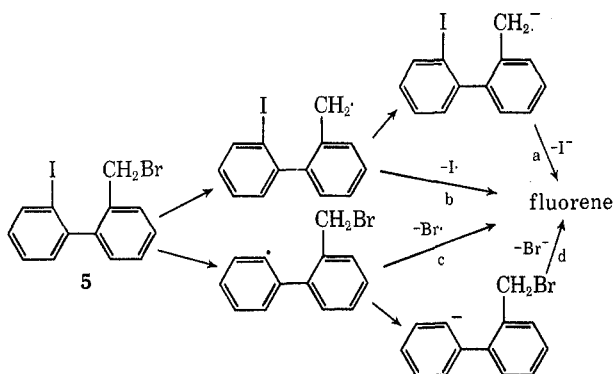(6) H. R. Ward, R. Lawler, and R. Cooper, *ibid.,* **91**, 746 (1969).
(7) A. R. Lepley and R. Landau, *ibid.,* **91**, 748, 749 (1969).

SCHEME I

undergo further reactions. Reaction of 5 with methyllithium may therefore be proceeding through the formation of either an aromatic or a benzylic radical, depending on which halogen exchanges more rapidly, and this radical might conceivably then displace the second halogen as X· (paths b and c). To test this possibility, the reduction of 5 with triphenyltin hydride, a reduction known to proceed through a radical intermediate,[8] was envisaged. In order to assure ourselves that both the radical intermediates of paths b and c would be produced, a standardized solution of benzyl bromide and iodobenzene was partially reduced with triphenyltin hydride. The ratio of the per cent disappearance of benzyl bromide to iodobenzene, as determined by glpc, was 3, while the ratio of toluene to benzene formed was 2.6. Therefore the reduction of 5 would be expected to produce both the aromatic and the benzylic radicals of paths b and c. When this reduction was carried out in dilute solution to allow the radicals sufficient time to cyclize, a 33% yield of 2'-iodo-2-methylbiphenyl (6), a 25% yield of 2-methylbiphenyl (7), and an 18% yield of 2-bromomethylbiphenyl (8), all based on a 23% recovery of starting material, were
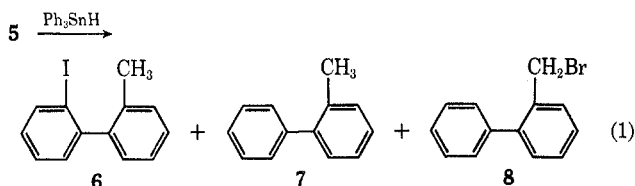

obtained. Significantly, no fluorene was produced. Since all three possible reduced products were recovered from the reduction, both of the radical intermediates in Scheme I must have been formed, but, because no fluorene was observed, these intermediate radicals do not cyclize and paths b and c are eliminated.[9]

(8) H. G. Kuivila, *Accounts Chem. Res.,* **1,** 299 (1968); H. G. Kuivila, L. W. Menapace, and C. R. Warner, *J. Amer. Chem. Soc.,* **84,** 3584 (1962); L. W. Menapace and H. G. Kuivila, *ibid.,* **86,** 3047 (1964).

(9) Furthermore, no 2'-bromo-2-methylbiphenyl (9) was detected from the reduction of 5 (as little as 0.6% could have been detected), thus eliminating the possibility of an intramolecular halogen bridge and transfer.
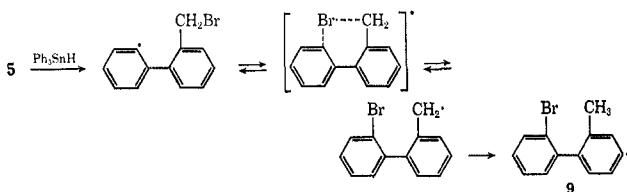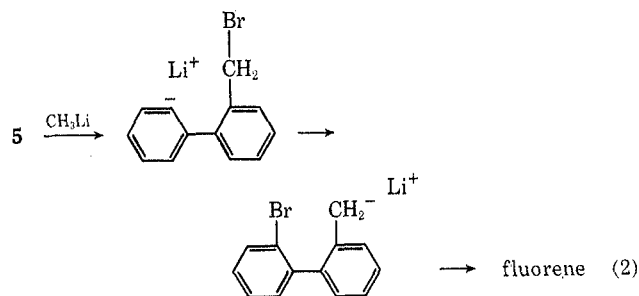

Since the cyclization does not proceed directly from the radical intermediates, it must go through either of the anionic pathways a or d. To differentiate between paths a and d, the relative rates of exchange of an aromatic iodine and a benzylic bromine with methyllithium had to be determined. As mentioned earlier, nothing conclusive pertaining to this question was found in the literature. Wittig and Witt[10] have observed that when benzyl bromide is treated with phenyllithium the products are bibenzyl and bromobenzene, presumably arising from the reaction

$$PhLi + PhCH_2Br \rightleftharpoons PhBr + PhCH_2Li$$

$$PhCH_2Li + PhCH_2Br \longrightarrow PhCH_2CH_2Ph + LiBr$$
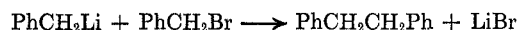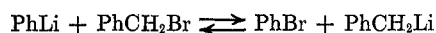
Unfortunately, these results provide no conclusive information regarding the relative rates of halogen–lithium exchange. Therefore a methyllithium competition experiment with benzyl bromide and iodobenzene to determine these relative rates was carried out. When a standardized solution of iodobenzene and benzyl bromide in ether was treated with methyllithium and analyzed by glpc, it was found that less than 1% of the benzyl bromide had disappeared, while nearly 21% of the iodobenzene disappeared; the ratio of benzene to toluene detected was greater than 90:1. Thus the rate of halogen–metal exchange is greater for CH_3Li with PhI than for CH_3Li with $PhCH_2Br$. These results indicate that it is the aromatic anion that is forming more rapidly in the reaction of 5 with methyllithium. This anion then displaces a bromide ion to form fluorene in a rapid reaction as depicted in path d.

That the consequent back-side displacement of bromide is indeed the next step and is rapid is indicated by the following observations. When the cyclization is run at −70° and worked up with acid after 50% reaction, only starting material and fluorene (69% based on reacted 5) are recovered with no detectable amount of 8. The absence of 8 indicates that the path d intermediate has a very short lifetime and cannot be trapped by H⁺.

To investigate the possibility that there was actually one more step involved in path d before final closure, namely an internal halogen–lithium exchange and subsequent cyclization as in eq 2, the reaction of 2'-

bromo-2-bromomethylbiphenyl (10) with methyllithium was carried out. The products identified from this reaction were 1,2-bis-2-(2'-bromobiphenyl)ethane (11, 44%), 2'-bromo-2-ethylbiphenyl (12, 20%), and 2'-bromo-2-methylbiphenyl (9, 2%), but no fluorene. In this reaction the benzylic anion is undoubtedly an

(10) G. Wittig and H. Witt, *Chem. Ber.,* **74,** 1474 (1941).
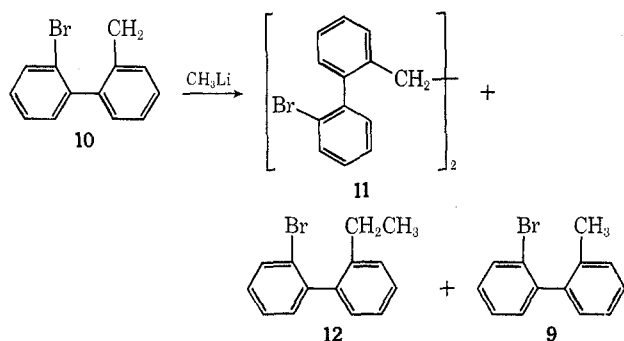
intermediate; however the absence of fluorene indicates that it does not cyclize. Instead, the expected bibenzyl formation[10] and methyl coupling[4] products are obtained. These results therefore eliminate eq 2 as a possible pathway in the reaction of **5** with CH₃Li. Hence, path d of Scheme I is the mechanism by which the cyclization of **5** with methyllithium proceeds.

Experimental Section

Melting points are uncorrected. Nmr spectra were taken in deuteriochloroform with tetramethylsilane (TMS) as internal standard. Silica gel HF₂₅₄ (E. Merck) was used for preparative thin layer chromatography (tlc). Ir spectra of solids were determined as KBr pellets; ir spectra of liquids were determined as thin films.

2'-Amino-2-methylbiphenyl.—A mixture of 4.0 g (18 mmol) of 2'-nitro-2-methylbiphenyl,[11] 5 g of mossy tin, and 12 ml of concentrated HCl were refluxed for 1 hr. The cooled reaction mixture was treated with 50 ml of a 10 M NaOH solution and the resulting solution was steam distilled. The distillate was extracted with dichloromethane and the dried extracts were evaporated. The oil that remained was distilled to give 2.4 g of clear oil, bp 94–99° (0.1 mm), which solidified into a white solid, mp 31–34° (lit.[11] 37°).

2'-Iodo-2-methylbiphenyl (6).—To a solution of 1.24 g (7.16 mmol) of 2'-amino-2-methylbiphenyl in 3 ml of concentrated HCl and 9 ml of H₂O at 0° was slowly added a solution of 0.52 g (7.5 mmol) of sodium nitrite in 2 ml of ice water. The resulting yellow solution was poured into a solution of 1.7 g of potassium iodide in 10 ml of H₂O at 0°. Gas was evolved and a dark, red tar formed. The mixture was slowly warmed to room temperature (2 hr) and then extracted with CHCl₃. The dried organic extracts were evaporated and the remaining red oil was chromatographed on 100 g of neutral alumina (Woelm, activity I, hexane); 1.30 g of a clear oil was obtained which solidified to a white solid, mp 36–38° (lit.[11] 38–39°).

2'-Iodo-2-bromomethylbiphenyl (5).—A solution of 3.94 g (13.4 mmol) of **6**, 2.48 g (13.9 mmoles) of N-bromosuccinimide, and a few milligrams of benzoyl peroxide in 90 ml of CCl₄ under nitrogen was simultaneously irradiated and refluxed by means of a 500-W incandescent light for 1 hr. The cooled reaction mixture was filtered and the filtrate concentrated to give 5.21 g of orange oil which, upon purification by preparative tlc (hexane as eluent), gave 4.38 g (11.7 mmol, 88%) of **5**: nmr δ 7.94 (d, J = 8 Hz, 1 H), δ 7.5–7.0 (m, 7 H), δ_A 4.13, δ_B 4.37 (AB quartet, J = 10 Hz, 2 H).

Anal. Calcd for C₁₃H₁₀BrI: C, 41.85; H, 2.70; I, 34.02. Found: C, 41.53; H, 2.67; I, 33.84.

2'-Bromo-2-bromomethylbiphenyl (10).—A solution of 0.925 g (3.74 mmol) of 2'-bromo-2-methylbiphenyl (9),[12] 0.661 g (3.70 mmol) of N-bromosuccinimide, and a few milligrams of benzoyl peroxide in 20 ml of CCl₄ under N₂ was simultaneously irradiated and refluxed with a 500-W incandescent light for 10 min. The cooled mixture was filtered and the filtrate concentrated to give 1.32 g of crude material which, upon purification by preparative tlc, afforded 89 mg of **9** and 1.06 g of 2'-bromo-2-bromomethylbiphenyl (10): nmr δ 7.06–7.78 (m, 8 H), δ_A 4.17, δ_B 4.37 (AB quartet, J = 10 Hz, 2 H).

(11) A. M. Sadler and G. Powell, *J. Amer. Chem. Soc.*, **56**, 2650 (1934).
(12) L. Moscarelli and D. Gatti, *Atti Reale Accad. Noz. Lincei*, **15**, 89 (1932).

Anal. Calcd for C₁₃H₁₀Br₂: C, 47.89; H, 3.09; Br, 49.02. Found: C, 48.15; H, 3.15; Br, 48.70.

Reaction of Methyllithium with Iodobenzene and Benzyl Bromide.—A standard mixture of 1 g (5 mmol) of iodobenzene, 0.85 g (5 mmol) of benzyl bromide, and 0.51 g (5 mmol) of *p*-xylene in 100 ml of ether was analyzed by vpc (20 ft × ¹/₈ in. column of 10% SE-30 on Chromosorb W at 130°). The area ratios were PhI/*p*-xylene = 0.729; PhCH₂Br/*p*-xylene = 0.654. To one-half of the standardized ether solution at 0° was added 1 ml of a 1.47 M methyllithium solution in ether (Foote Mineral Co.). A few pieces of Dry Ice were added to react with any organolithium compounds and the ether layer was analyzed by vpc.: PhI/*p*-xylene = 0.576; PhCH₂Br/*p*-xylene = 0.650. To the other half of the standardized ether solution at 0° was added 1 ml of 1.47 M methyllithium solution in ether. After 1 min, 2 ml of water was added and the ether layer analyzed by vpc for benzene and toluene: PhH/toluene > 90:1.

Reaction of 5 with Methyllithium.—To a stirred solution of 535 mg (1.43 mmol) of **5** in 50 ml ether at 0° under N₂ were added 2 ml of a 1.47 M methyllithium solution in ether. The solution was stirred at 0° for 30 min, then warmed to room temperature before adding 10 ml of a saturated NH₄Cl solution. The ether layer was separated, dried, and concentrated, leaving 231 mg of a slightly yellow solid. Fluorene (165 mg) was separated from the rest of the material by preparative tlc. An nmr of the remaining material (43 mg) had no absorption at lower field than δ 7.80 (protons *ortho* to aromatic I); this material was composed of at least eight components (tlc), the largest of which contained 6 mg. No further attempts at identification were carried out.

Reaction of 10 with Methyllithium.—To a solution of 128 mg (0.392 mmol) of **10** in 25 ml of ether under N₂ at 0° was added ¹/₂ ml of a 1.47 M solution of methyllithium in ether. After 2 hr 2 ml of a saturated NH₄Cl solution was added and the ether layer was separated. The dried ether layer was concentrated and the remaining oil (102 mg) separated by preparative tlc to afford 42 mg of 1,2-bis-2-(2'-bromobiphenyl)ethane (11): mp 182–184° (from CHCl₃); nmr δ 7.53–7.70 (m, 2 H), 6.78–7.40 (m, 14 H), 2.55 (s, 4 H).

Anal. Calcd for C₂₆H₂₀Br₂: C, 63.44; H, 4.09; Br, 32.47. Found: C, 63.64; H, 4.23; Br, 32.47.

A second fraction (20 mg) consisted of two materials (10:1 mol ratio by nmr), the smaller component being identified as **9** (singlet at δ 2.10). The larger component is tentatively identified as 2'-bromo-2-ethylbiphenyl (12) on the basis of its nmr spectrum: δ 7.05–7.80 (m, 8 H), δ 4.12 (q, J = 8 Hz, 2 H), δ 1.07 (t, J = 8 Hz, 3 H).

The remaining material (32 mg) consisted of several components (tlc) of 11 mg or less. No further attempts at identification were carried out.

Reaction of 5 with Triphenyltin Hydride.—To a stirred solution of 305 mg (0.818 mmol) of **5** and a few crystals of azobisisobutyronitrile (AIBN) in 20 ml of hexane at 50° under N₂ was added a solution of 304 mg (0.866 mmoles) of triphenyltin hydride in 20 ml of hexane over a period of 80 min. The reaction was refluxed for 26 hr, evaporated to dryness, triturated with CCl₄ to destroy excess triphenyltin hydride, and evaporated to dryness again. The remaining material was purified by preparative tlc to remove triphenyltin halides and two fractions were obtained. Fraction A (98 mg) consisted of a 5:3 mol ratio (nmr) of **5** (AB quartet at δ 4.20) and **8**. Fraction B (86 mg) consisted of a 4:3 mol ratio (nmr) of **6** (singlet at δ 2.07) and **7** (singlet at δ 2.23).

Reaction of Benzyl Bromide and Iodobenzene with Triphenyltin Hydride.—A solution of 1 ml of benzyl bromide, 1 ml of iodobenzene, and 1 ml of *o*-xylene in 10 ml of pentane was analyzed by vpc (area ratios): xylene/PhI/PhCH₂Br = 1:0.76:0.78. To 10 ml of the above solution at reflux under N₂ was added a solution of 2.5 g of triphenyltin hydride in 10 ml of pentane over 15 min. and reflux was continued for an additional 1.25 hr. The reaction mixture was then analyzed by vpc: xylene/PhI/PhCH₂Br = 1:0.67:0.50; xylene/PhH/PhCH₃ = 1:0.14:0.37.

Registry No.—**5**, 25860-20-2; **10**, 13379-29-8; **11**, 25860-22-4; methyllithium, 917-54-4.