sor A. Haim for his crucially important assistance with the stopped-flow measurements. We derived much benefit from discussions with Dr. H. E. Simmons and with Professors E. M. Kosower and I. Lengyel. The work was generously supported by the National Science Foundation.

Metal–Ammonia Reduction. XII. Mechanism of Reduction and Reductive Alkylation of Aromatic Hydrocarbons[1]

Donald F. Lindow, Cecilia N. Cortez, and Ronald G. Harvey*

Contribution from the Ben May Laboratory, The University of Chicago, Chicago, Illinois 60637.

Received October 30, 1971

Abstract: The mechanism of reduction of biphenyl with alkali metals in liquid ammonia is shown to involve formation of a dianion rapidly protonated by the medium at 4 position (in accord with HMO theory) to afford a stable phenylcyclohexadienyl anion (**6**). Evidence for the intermediacy of **6** rather than the unprotonated dianion **5** or the related radical-anion **4** (or their ion pairs) includes demonstration of efficient *hydride transfer* from the product of interaction of lithium with 4,4′-dideuteriobiphenyl in ammonia to anthracene; *electron transfer* from **4** or **5** fails to compete to significant extent. Analogous reductive alkylation follows a similar mechanism, with dialkylated products arising *via* back reaction involving proton abstraction by amide ion on the initially formed 1-alkyl-1,4-dihydrobiphenyl rather than dialkylation of **6**. The extent of di- and trialkylation parallels the solubility of the corresponding amides (Na > Li > Ca). The radical-anion **4**, like **6**, is stable in ammonia, undergoing neither protonation nor alkylation efficiently. Related investigations with anthracene demonstrate considerable similarity between the two systems, and the following general mechanism is proposed: (1) formation of a dianion which protonates rapidly with lithium or calcium, but more slowly with sodium; (2) facile alkylation of the monoprotonated anion and the dianion (if present); and (3) further alkylation of these products through back reaction involving proton abstraction by amide ion.

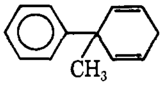
Reduction of polycyclic aromatic hydrocarbons by means of solutions of alkali metals in liquid ammonia has proven remarkably regiospecific[1–4] (*i.e.*, only a single dihydro isomer formed at each stage), in accord with predictions of molecular orbital theory.[5] However, greater complexity of mechanism than assumed in the theoretical treatment is indicated by the recent demonstration of important counterion and solvent effects in reductive methylation of naphthalene.[6] Also, little is known regarding the nature of the anionic intermediates, the existence and structure of which has largely been inferred from the structure of products of reduction and reductive alkylation.[6–8]

We report now investigations into the mechanisms of reduction and reductive alkylation of aromatic hydrocarbons. Evidence will be presented relating to the stability of the intermediate anionic species, the relative importance of ion-pair association and protonation by the medium, and the relative rates and significance of the various possible reaction pathways.

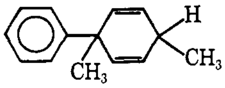
Initial studies were conducted with the biphenyl system. Although interaction of biphenyl with alkali metals was first described over 40 years ago,[9] product structure has been the subject of controversy until recently. Grisdale, *et al.*,[10] utilizing modern techniques of separation (glc) and analysis (nmr) established that the calculated dihydro derivative, 1,4-dihydrobiphenyl, is the initial product; rapid protonation is necessary to prevent its isomerization and further reduction. With sodium, some biphenyl is always recovered;[10] with lithium and rapid product isolation, transformation is virtually quantitative.[3]

Results

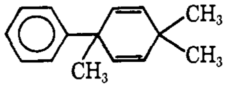
Reductive methylation of biphenyl with lithium in ammonia and methyl bromide proceeded virtually quantitatively to afford 1-methyl-1,4-dihydrobiphenyl (**1**). The integrated nmr spectrum was consistent with only the assigned structure (sharp methyl singlet at δ 1.42, benzylic protons absent); the vinylic protons appeared as an apparent singlet (δ 5.61) resembling those of 1,4-dihydrobiphenyl and differing from the more complex patterns of the isomeric phenylcyclohexadienes.[10] Analogous reaction with calcium also furnished **1** as the sole product. With sodium, however, the major products were **1** and *cis*- and *trans*-1,4-dimethyl-1,4-dihydrobiphenyl (**2**); these were accompanied by minor amounts of 1,4,4-trimethyl-1,4-dihydrobiphenyl (**3**).



1



2



3

---

[1] Paper XI: R. G. Harvey, *J. Org. Chem.*, **36**, 3306 (1971).

[2] R. G. Harvey and P. W. Rabideau, *Tetrahedron Lett.*, 3695 (1970).

[3] R. G. Harvey, *Synthesis*, 161 (1970).

[4] R. G. Harvey, L. Arzadon, J. Grant, and K. Urberg, *J. Amer. Chem. Soc.*, **91**, 4535 (1969).

[5] A. Streitwieser, Jr., and S. Suzuki, *Tetrahedron*, **16**, 153 (1961); A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961, p 425.

[6] P. W. Rabideau and R. G. Harvey, *Tetrahedron Lett.*, 4139 (1970).

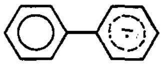
[7] R. G. Harvey and L. Arzadon, *Tetrahedron*, **25**, 4887 (1969).

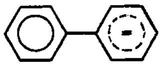
[8] R. G. Harvey and C. C. Davis, *J. Org. Chem.*, **34**, 3607 (1969).

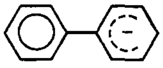
[9] W. Schlenk and E. Bergmann, *Ann.*, **463**, 92 (1928).

[10] P. J. Grisdale, T. H. Regan, J. C. Doty, J. Figueras, and J. L. Williams, *J. Org. Chem.*, **33**, 1116 (1968).

The observed metal effect is open to several interpretations, with decision between the alternatives turning on the identity of the anionic intermediate in solution immediately prior to alkylation. The species to be distinguished are the radical-anion **4**, the dianion **5**, the protonated monoanion **6**, and their respective ion pairs.

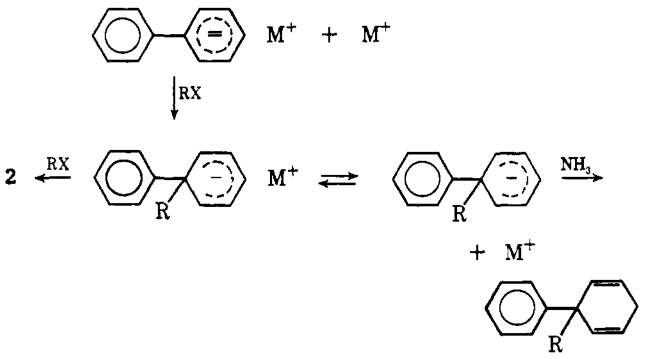

4


5

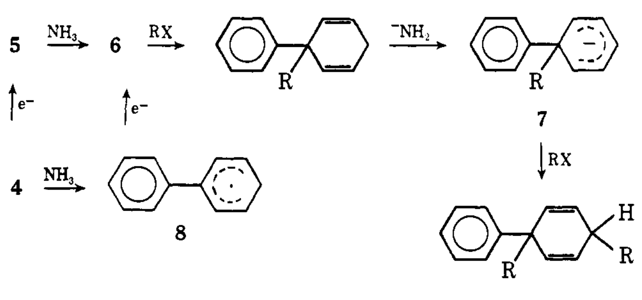

6

According to HMO theory,[5] initial reaction of **4** or **5** is predicted at the 4 position, the site of calculated highest electron density. However, formation of **1** as a major product and the complete absence of any detectable quantity of 4-methyl-1,4-dihydrobiphenyl would appear to support, instead, initial methylation in the 1 position. Therefore, if **4** or **5** is the predominant species, either the theory is incorrect, or not applicable due to solvation or other factors neglected in the calculations. In the latter view (mechanism A), contact ion pair association at the relatively unhindered 4 position of **5** could diminish reactivity at this site[11] while permitting reaction at the presumably less tightly associated 1 position. The observed metal effect is consistent with this hypothesis, since methylation at the 1 position would furnish a monoanion whose degree of association would be dependent upon the counterion[12,13] with the lithium aggregate expected to be more dissociated and, hence, more susceptible to protonation by the medium.

Mechanism A



Mechanism B



The alternative possibility (mechanism B) is that protonation by ammonia precedes methylation.[14] In this interpretation, the protonated species **6** (arising directly from **5**, or from **4** with subsequent addition of a second electron) is the direct precursor of **1** which, in turn, is the precursor of **2** *via* proton abstraction from the 4 position by amide ion, followed by a second methylation. The observed metal effect may be rationalized, in this view, as a consequence of the much higher solubility[15] of sodamide than the corresponding lithium or calcium amides. A relatively high concentration of amide ion in solution is essential for efficient proton abstraction during the brief time available following initial methylation.

Since ion-pairing is generally sensitive to solvent, temperature, concentration, etc.,[11–13] the influence of these variables on the course of reductive methylation was investigated. Although some correlation between extent of dialkylation and solvent polarity is apparent in the data in Table I, the effect is not dramatic.

Table I. Reductive Methylation of Biphenyl (Effect of Metal and Cosolvent)[a]

Metal	Cosolvent	% conversion	% yield[b] 1	2	3
Li		93	99	1	0
Ca		91	100	0	0
Na		96	50	41	10
Na	Toluene[c]	100	68	32	0
Na	TMEDA	97	51	43	3
Na	Ether	98	43	52	5
Na	THF	96	38	54	7
Na	DME	96	45	46	9

[a] The metal (5.5 mmol) was added to a suspension of biphenyl (2.5 mmol) in 75 ml of cosolvent and 150 ml of NH_3 at −33°. After a suitable interval, usually 20 min, excess CH_3Br was passed into the deeply colored solution. [b] Yields based on biphenyl converted and measured by peak area on glpc on a 15 ft 20% DEGS column. [c] Reaction is heterogenous.

It is worthy of note that, except with toluene, reactions were generally homogeneous after dissolution of the metal (and concurrent solubilization of the hydrocarbon by anion formation), even in the absence of a cosolvent. Conversion remained consistently high (generally >90%) under all conditions, even at low temperature, apparently independent of the proportion of the hydrocarbon initially in solution. A significant temperature effect was detected (Table II), with a markedly diminished degree of dimethylation being found at lower reaction temperature (−78°). Product distribution was also influenced by concentration (Table II), with higher concentration (metal–biphenyl ratio constant) tending to favor methylation beyond the monomethyl stage. Finally, no significant common ion effect could be detected even in reactions conducted in the presence of relatively massive quantities of sodium bromide (Table II).

---

(11) Solvent-separated ion pairs generally exhibited greater reactivity than the related contact ion pairs.[12]

(12) T. E. Hogen-Esch and J. Smid, *J. Amer. Chem. Soc.*, **90**, 4654 (1968); N. H. Velthorst and G. J. Hoijtink, *ibid.*, **87**, 4529 (1965).

(13) In this connection, it is worthy of note that 9-lithio-9,10-dihydroanthracene exists as a tight ion pair in tetrahydrofuran while its 10-methyl derivative is, according to Nicholls and Szwarc, dissociated into solvent separated ions; D. Nicholls and M. Szwarc, *Proc. Roy. Soc. Ser., A*, **301**, 223 (1967).

(14) Both mechanisms may conceivably be operative, with the nature of the metal cation and its degree of association with the biphenyl dianion determining the extent to which protonation precedes alkylation. Also, associated intermediates may be involved in mechanism B, but are assumed not to play an essential role in determining product structure.

(15) E. C. Franklin, "The Nitrogen System of Compounds," Reinhold, New York, N. Y., 1935; F. W. Bergstrom and W. C. Fernelius, *Chem. Rev.*, 20, 413 (1937).

Table II. Reductive Methylation of Biphenyl with Sodium and Methyl Bromide (Effect of Concentration, Temperature, and Added Salt)[a]

Concn of biphenyl, $M \times 10^3$	Concn of Na, $M \times 10^3$	Concn of NaBr, $M \times 10^3$	Temp, °C	% conversion	% yield[b] 1	2	3
17	37	0	−33	96	50	41	10
17	73	0	−33	94	32	44	24
33	37	0	−33	52	50	40	10
67	147	0	−33	95	48	33	19
4	9	0	−33	85	53	43	4
17	37	0	−78	94	73	26	0
17[c]	37	0	−78	85	98	2	0
17	37	20[d]	−33	94	49	44	7
17	37	120[d]	−33	97	51	43	5

[a] Conditions were similar to those in Table I except where stated otherwise and cosolvent was not employed. [b] Yields calculated as in Table I. [c] Methyl bromide introduced at maximum flow rate; in other experiments a lower standard flow rate was employed. [d] Sodium bromide was added after 10 min.

Although observed concentration and temperature effects are consistent with intermediacy of an associated ion pair, the solvent effect is considerably smaller than encountered earlier with naphthalene[6] and is in the opposite direction. All effects, however, are readily understandable in terms of mechanism B, principally in terms of their effect on amide ion concentration. Thus, lower temperature and less polar solvents may be expected to diminish amide concentration, thereby decreasing the rate of proton abstraction.[16] Also, high reactant concentrations (metal–biphenyl ratio constant) should lead to an enhanced rate of proton removal (due to higher concentration of both hydrocarbon and amide) resulting in di- and trimethylation.[17] Certain other observations may also be encompassed in this explanation. Thus, increased overmethylation with employment of excess metal may be understood as a consequence of generation of additional amide ion from reduction of excess alkyl halide: $RX + 2Na + NH_3 \rightarrow RH + NaNH_2 + NaX$. Also, the higher proportion of trimethylated derivatives resulting from slower rates of introduction of gaseous methyl bromide into the reaction vessel (Table III) is the expected consequence of the longer time available for proton abstraction.

Table III. Reductive Methylation of Biphenyl (Effect of Rate of Introduction of Methyl Bromide)[a]

Flow rate, mmol/min	Decoloration, min	% yield[b] 1	2	3	Biphenyl
0.6	13	48	26	22	3
3.9	2	41	43	10	6
3.9	2	41.5	41.5	11	6
>20	0.25	49	36	1	13

[a] Reactions were conducted as those in Table I without a cosolvent (Na = 62.5 g-atom). [b] Yields determined by glpc.

The proton abstraction mechanism was verified experimentally by demonstration that reaction of **1** with metal amides and methyl bromide under conditions approximating those of reductive methylation led to formation of much higher proportions of **2** and **3** with the amide of sodium than with those of either lithium or calcium (Table IV). The effect is particularly evident with short reaction time; at 0.5 min the yield of **2** was 95% for sodium and 10% for lithium. With use of higher ratios of sodamide, conversion to **2** and **3** was virtually complete. Also, reaction of 1,4-dihydrobiphenyl (**9**) with somewhat greater than 2 equiv of these same metal amides furnished products whose degree of methylation related directly to the solubility of the corresponding amide (*i.e.*, Na > Li > Ca) (Table IV). Product distribution from these back reactions was virtually identical with that from reductive methylation.

Table IV. Methylation of 1-Methyl-1,4-dihydrobiphenyl (**1**) and 1,4-Dihydrobiphenyl (**9**)[a]

1 or 9, mmol	Metal amide[b] (mmol)	Time, min	% yield[c] 1	2	3
2.3	Na (2.75)	0.5	3	95	2
2.3	Li (2.75)	0.5	90	10	0
2.6	Na (5.6)	10	1	86	13
2.3	Na (5.6)	10	1	89	10
4.5	Na (10.7)	10	2	70	28
2.6	Li (5.6)	10	61	39	0
2.6	Li (5.4)	60	61	38	1
2.4	Ca (2.65)	20	99	1	0
	Methylation of 9				
2.9	Na (6.25)	20	37	43	17
2.2	Na (6.25)	20	30	45	23
2.2	Li (5.5)	10	96	1	1
1.3	Ca (2.7)	20	6	0	0
1.6	Ca (2.2)	240	46	0	0

[a] Conditions duplicate those of reductive methylation as closely as practicable (no cosolvent, 150 ml of NH_3, −33°). [b] The metal amide was generated *in situ* by iron-catalyzed reaction of the metal with ammonia (see Experimental Section) before addition of the hydrocarbon. [c] Yields calculated as before.

More direct evidence for **6** as the major, and probably sole, stable intermediate species in liquid ammonia comes from studies with deuterium-labeled biphenyl and anthracene. These experiments are based on the concept that radical anions or dianions undergo *electron transfer* to hydrocarbons of greater electron affinity,[18] whereas cyclohexadienyl anions interact with suitable acceptors such as anthracene *via hydride transfer*[19] (Chart I). The two processes are distinguishable, in principle, on the basis of the deuterium content of the products.

It was initially established in a control experiment that lithium–ammonia reduction of 4,4′-dideuteriobiphenyl afforded the corresponding 1,4-dihydro derivative in which the deuterium label was completely retained. Therefore, protonation of the intermediate by ammonia is either irreversible or fails to take place to significant extent; the alternative possibility, equilibration involving stereospecific proton addition and loss, would appear improbable. The 4,4′-dideuterio-1,4-dihydrobiphenyl was then treated with lithium amide in ammonia, anthracene was added, and finally the reaction was quenched with ammonium chloride. Bi-

---

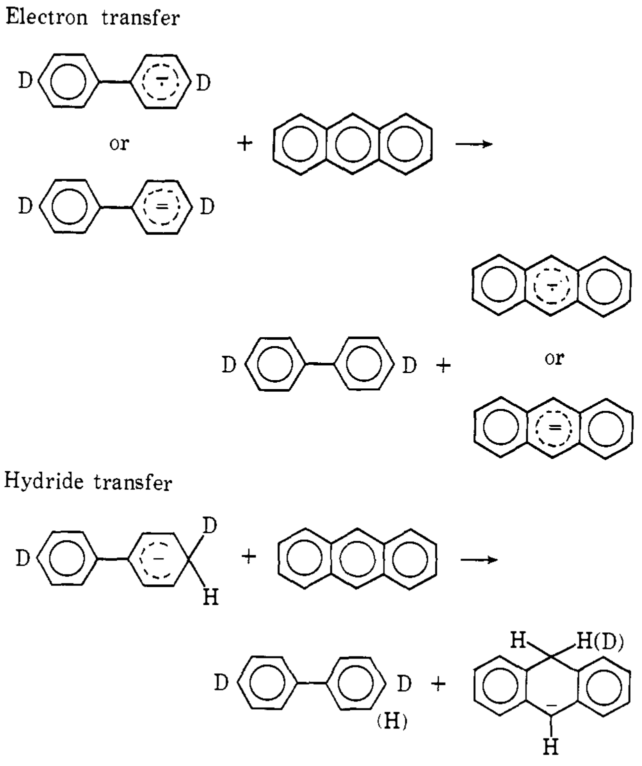
(16) Decreased rate of methylation at lower temperature should be partially compensated by increased steady-state concentration of methyl bromide.

(17) Methylation required visibly longer for decolorization at higher concentrations, presumably due to the larger absolute amount of the monoalkyl monoanion present.

(18) G. J. Hoijtink, E. DeBoer, P. H. van der Meij, and W. P. Weijland, *Recl. Trav. Chim. Pays-Bas*, **75**, 487 (1956).

(19) J. E. Hofmann, P. A. Argabright, and A. Schriesheim, *Tetrahedron Lett.*, 1005 (1964).

Chart I. Reactions with Anthracene



phenyl and 9,10-dihydroanthracene were recovered as the sole products in agreement with the expected stoichiometry for hydride transfer to anthracene. Also, the per cent deuterium loss from dihydrobiphenyl was consistent with a normal isotope effect ($k_H/k_D = 5.5 \pm 0.5$) and equivalent to the level of deuterium incorporation in the dihydroanthracene. Exactly the same results (±1%) were observed from lithium–ammonia reduction of 4,4′-dideuteriobiphenyl with treatment of the product with anthracene. Results of all experiments were consistent with hydride transfer from a monoanion, rather than electron transfer from a dianion. We conclude, therefore, that a protonated anion rather than an associated dianion is the stable intermediate formed upon addition of alkali metals to biphenyl in ammonia, and that methylation occurs at the benzylic position of this intermediate.

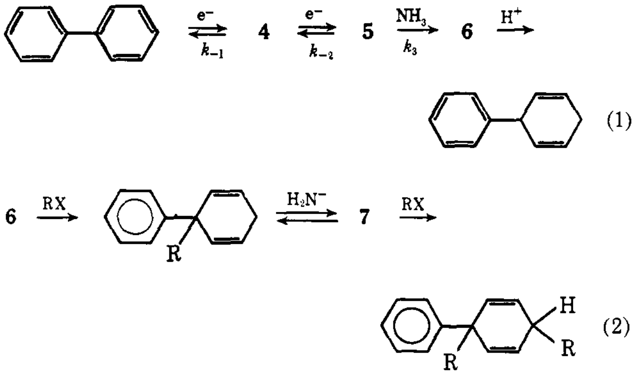
The second fundamental question concerns the stage at which protonation takes place during formation of the monoanion **6**. Is the radical-anion **4** protonated by the medium as rapidly as formed, or does it persist until acquisition of a second electron? Interaction of 4,4′-dideuteriobiphenyl with 1 equiv of lithium metal in THF–ammonia affords a green solution, distinctly different from the red solutions of **6** obtained with 2 equiv of the metal. Presumably the green intermediate is either the radical-anion **4** or its protonated form **8**.[20] Treatment of the reaction mixture with methyl bromide furnishes on work-up 4,4′-dideuteriobiphenyl (87%), a result consistent with **4** as the predominant intermediate species in solution. This follows, since radical anions are known to be both poor nucleophiles and efficient electron transfer reagents capable of reduction of alkyl halides.[22] Equilibrium between **4** and **8** involving protonation–deprotonation is ruled out by observed retention of the deuterium label essentially completely (>98%) in the recovered deuterated biphenyl. It may be concluded, therefore, that **4** is a stable intermediate in liquid ammonia, undergoing neither protonation nor disproportionation to any significant extent under the conditions of these experiments.

The position of the equilibrium $\mathbf{1} + H_2N^- \rightleftharpoons \mathbf{7} + NH_3$ must also be considered. The forward reaction exhibits a strong metal ion dependency, that with sodamide being 95% complete in 0.5 min, while comparable reaction involving lithium amide attains only 10% completion in the same period[23] (Table IV). Analogous reaction with the 4,4′-dideuterio derivative of **1** (**1**-d_2) gave after 30 min with sodamide 12% loss of deuterium in the 4 position and with lithium amide ≤2% deuterium loss. Mobile equilibrium requires deuterium loss to exceed 14% assuming a normal maximum isotope effect of about 7.[24] Since sodamide is completely soluble under the conditions of these experiments, while the lithium salt is not, experiments with sodamide are most informative regarding the position of the equilibrium. From the results, the equilibrium appears to be far to the right, with the forward reaction relatively fast and the return reaction (*i.e.*, protonation) slow. In other words, the monanion **7**, like **6**, appears to be relatively stable in ammonia at −33°.

Finally, Petrov, *et al.*,[25] claimed to have isolated 4-alkyl-1,4-dihydrobiphenyl (*ca.* 10%) and 1,4-dialkyl-1,4-dihydrobiphenyl (*ca.* 5%) from prolonged reaction (80 hr) of biphenyl with lithium in ether. Though the monoalkyl compounds were designated as 4-alkyl rather than 1-alkyl isomers, this result is not inconsistent with the findings reported herein for reaction in ammonia. This follows, since a radical anion rather than a protonated monoanion is the likely predominant intermediate in ether.

Discussion

The foregoing results support the following mechanisms for *reduction* (eq 1) and *reductive alkylation* (eq 2).



---

[20] The radical anion of biphenyl and the radical anion and dianion of anthracene are blue in THF.[21] The extent to which solvation, ion pair association, and related phenomena may shift the absorption maxima is unknown.

[21] P. Balk, G. J. Hoijtink, and J. Schreurs, *Recl. Trav. Chim. Pays-Bas*, 76, 813 (1957).

[22] J. F. Garst, J. T. Barbas, and F. E. Barton, II, *J. Amer. Chem. Soc.*, **90**, 7159 (1968); G. D. Sargent and G. A. Lux, *ibid.*, **90**, 7160 (1968); J. F. Garst and J. T. Barbas, *Tetrahedron Lett.*, 3125 (1969).

[23] Yield determined by methylation with methyl bromide.

[24] K. B. Wilberg, *Chem. Rev.*, **55**, 713 (1955); Y. Pocker and J. H. Exner, *J. Amer. Chem. Soc.*, **90**, 6764 (1968).

[25] A. Petrov, E. Kaplan, Z. Letina, and I. Egorov, *J. Gen. Chem. USSR*, 28, 609 (1958).

Table V. Reductive Methylation of Anthracene[a]

Metal	Time, min	Temp, °C	% yield[b] DHA[c]	MDHA	DMDHA	TMDHA	A
Na	10	−33	1	24	46	27	0
Li	10	−33	1	62	34	3	0
Ca	10	−33	96	1	1	0	2
Na	10	−78	1	29	64	5	1
Li	10	−78	0	91	9	0	0
Ca	10	−78	28	50	10	2	10
Na	60	−78	1	46	49	4	0
Li	60	−33	0	60	37	2	0
Li[d]	30	−33	2	33	18	4	42
Li[e]	8	−33	7	30	16	3	44[f]
Li[e]	3	−78	14	7	7	2	70[g]

[a] Conditions were similar to those in Table I except where stated otherwise. [b] Yields determined by peak area on glpc on a 6-ft 10% SE 30 column at 150°. [c] DHA = 9,10-dihydroanthracene; MDHA = 9-methyl-DHA; DMDHA = *cis*-9,10-dimethyl-DHA; TMDHA = 9,9,10-trimethyl-DHA; A = anthracene. [d] Only 2.75 g-atoms of lithium was employed in 75 ml of NH_3 and 150 ml of THF. [e] Anthracene (5 mmol) in 225 ml of THF was employed with 5.5 g-atoms of lithium in 75 ml of NH_3. [f] A control experiment with 11 g-atoms of lithium gave 7% of A. [g] A control experiment with 11 g-atoms of lithium gave 42% of A.

The alternative reduction sequence

$$\mathbf{4} \xrightarrow{NH_3} \mathbf{8} \xrightarrow{e^-} \mathbf{6}$$

which previously could not be distinguished, has now been excluded as an important pathway.

Although kinetic data are lacking, it may readily be deduced that $k_1 > k_2$. Aside from the fact that the second electron adds to an already charged species, the solution remains green until more than 1 equiv of the metal is present, whereupon it becomes dark red. Also, formation of **5** by disproportionation of **4** apparently fails to occur to any significant extent (*i.e.*, reduction rather than formation of **1** occurs on interaction of solutions of **4** with methyl bromide), despite the driving force of protonation of **5** by the medium. Although the relative rate of protonation, k_3, is less certain, it is clear that proton addition is essentially irreversible (*i.e.*, no deuterium loss) under the conditions of our experiments.

The high basicity of the dianion contrasts with the relatively weak basicity of the radical anion **4** or the protonated monoanion **6**, both of which persist unchanged in ammonia. Although the properties of hydrocarbon radical anions are the subject of current active investigations in several laboratories,[22,26] only spectroscopic studies are available on the dianions,[21,27] and no studies on the relative reactivity of dianions compared with radical anions have been published. Failure of **4** to undergo alkylation contrasts with observed facile alkylation of **6**, and is consistent with the reported nucleophilicity of the corresponding ions of naphthalene.[26]

Numerous questions may now be raised regarding other systems. Existence of dianions of naphthalene,[6] anthracene,[3,4,7] benz[*a*]anthracene,[7,28] tetracene,[4] and dibenz[*a,h*]anthracene[7] in ammonia, earlier proposed to explain formation of dialkylated products on reductive alkylation of these hydrocarbons, must be reexamined in the light of the foregoing information; the facts would appear equally consistent with a mechanism analogous to eq 1 and 2.

Accordingly, a series of experiments were conducted with anthracene in order to examine the general applicability of the mechanism established for biphenyl. Considerable similarity between the two systems was, indeed, observed, and evidence was obtained that all the same processes occur, though at somewhat different relative rates. Thus, a pronounced metal effect was noted, with the extent of methylation at −33° paralleling the solubility of the corresponding amides (*i.e.*, Na > Li > Ca) (Table V).[29] Temperature also influenced product distribution, a lower proportion of di- and trimethylated dihydroanthracene bing formed at −78° than at −33° with lithium, but not with sodium or calcium for which the reverse was true. An increased time interval between metal addition and methylation (with sodium only) also resulted in a lower di- to monomethyl ratio; no significant influence of reaction time on the course of reaction was noted earlier with biphenyl. This time effect is quite interesting, since it would appear to indicate relatively slow protonation of a disodioanthracene dianion; this difference is consistent with the lower basicity expected of a dibenzylic *vs.* a diallylic anion. On the other hand, reaction with lithium proved time independent, so that protonation of the dilithio dianion must be relatively rapid. This difference is most simply explicable in terms of ion pair association being greater with sodium than with lithium,[6,11,12] resulting in slower protonation of the intermediate containing the former cation.

That some of the methylated products may arise *via* back reaction with amide ion was confirmed by demonstration of efficient methylation of dihydroanthracene with sodamide and methyl bromide at −78° under the conditions of reductive methylation; there were obtained 47% mono-, 46% di-, and 4% trimethyldihydroanthracene (average of two runs). Analogous reaction with lithium amide at −33° gave 70% mono-, 27% di-, and 2% trimethyldihydroanthracene.

Interaction of anthracene with slightly more than 1 equiv of lithium gave a blue color, changing after *ca.* 5 min to green which persisted until discharged with methyl bromide. Major products were anthracene (40–50%)

---

(26) S. Bank and B. Bockrath, *J. Amer. Chem. Soc.*, **93**, 430 (1971).

(27) R. G. Lawler and C. V. Ristagno, *ibid.*, **91**, 1534 (1969).

(28) R. G. Harvey and K. Urberg, *J. Org. Chem.*, **33**, 2206 (1968).

(29) Conditions employed for these reactions resemble those for biphenyl and differ from those reported in earlier studies[7] in that greater dilution and generally shorter reaction time are used. Reductive methylation of anthracene by the previous procedure gave *cis*-DMDHA (78%) and TMDHA (18%); the latter was erroneously reported to be *trans*-DMDHA earlier. The rate of introduction of methyl bromide, maintained at *ca.* 24 mmol/min in the reactions reported herein, was not measured in previous studies; however, it is estimated from a reaction conducted under similar conditions to be *ca.* 10 mmol/min.

and methylated dihydroanthracenes, in approximately equal proportion (Table V). This stoichiometry, coupled with the relatively minor amounts of dihydroanthracene formed, would suggest that the radical anion of anthracene spontaneously disproportionates to anthracene and its dianion, driven by protonation of the latter. However, this is conjectural, since it cannot be ruled out that the radical anion, unlike that of biphenyl, undergoes facile alkylation and/or protonation to furnish the corresponding radicals (AR· or AH·) which gain a second electron from another molecule of the radical anion to form the related anions (AR^- or AH^-), further reaction of which would lead to the methylated products.

On the basis of the foregoing evidence, we propose a mechanism for reductive alkylation of anthracene analogous to that established for biphenyl (eq 1 and 2), and consisting of the following steps: (1) formation of a dianion which undergoes protonation rapidly with lithium or calcium, but more slowly with sodium; (2) facile monomethylation of the protonated monoanion and dimethylation of the dianion; and (3) further methylation of the mono- and dimethyl products through back reaction involving proton abstraction by amide ion. Similar processes presumably are operative for analogous reactions of benz[*a*]anthracene, tetracene, naphthalene, and other related hydrocarbons.

Experimental Section

Physical Data. Proton nmr spectra were obtained on a Varian A-60 spectrometer; chemical shifts are reported relative to TMS in CCl_4. Integration was consistent with all assignments. Glpc analyses were performed on an F & M Model 500 chromatograph employing one of the following columns: (A) 15 ft × 0.25 in. 20% DEGS at 140°, (B) 6 ft × 0.25 in. 20% DEGS at 150°, or (C) 6 ft × 0.25 in. 5% DEGS at 100°, all on 60–80 mesh Chromosorb W. The cis and trans isomers of 1,4-dimethyl-1,4-dihydrobiphenyl were not separable even on column A on which separation of the mono-, di-, and trimethylbiphenyls was achieved. Mass spectra were determined on a Finnigan 1015 mass spectrometer at 70 eV, except the deuterium analyses for which 8–10 eV was employed.

Reactions in Liquid Ammonia. Precautions for the exclusion of impurities (moisture, air, peroxides, ferrous metals in ammonia) were scrupulously observed, and all reactions were carried out under helium (passed through a drying tower containing Drierite and Ascarite) rather than nitrogen to avoid formation with lithium of lithium nitride. Polycyclic hydrocarbons were recrystallized from alcohol and carefully dried *in vacuo*. Tetrahydrofuran (THF) and 1,2-dimethoxyethane (DME) were freshly distilled from $LiAlH_4$ before use. Ammonia was distilled into the reaction vessel (a three-neck flask fitted with a Dewar condenser) through a column of barium oxide (10–20 mesh). Lithium wire and sodium metal were freshly cut and washed free of oil with hexane before use.

Work-up procedures were conventional with the important exception that *products were isolated as rapidly as possible* by partition between ether (or other organic solvent) and water. The common practise of allowing ammonia to evaporate in a hood before isolation of products tends to permit isomerization and other secondary processes to occur, and is not recommended. The method described in the following paragraph for reduction of biphenyl is the *standard method* now employed in our laboratory for most reductions.

1,4-Dihydrobiphenyl (9). A solution of biphenyl (770 mg, 5 mmol) in ether (75 ml) was added to 150 ml of refluxing ammonia, followed by lithium wire (11 g-atom), and 20 min later the color was discharged by addition of solid NH_4Cl (20 g). To avoid isomerization, products were isolated rapidly by partition between water and ether followed by conventional work-up procedures. Glpc analysis on column A gave **9** (97%) and biphenyl (1%), relative retention time 0.49 and 1.00, respectively. The nmr spectrum of **9** matched that reported earlier.[3,10] A similar reaction, in which reactant quantities were increased fivefold and solvent volumes doubled, afforded 94% of **9** and 5% of recovered biphenyl.

4,4′-Dideuterio-1,4-dihydrobiphenyl (9-d_2). Analogous reduction of 4,4′-dideuteriobiphenyl in the absence of cosolvent afforded deuterated **9**-d_2 (99%) in which the deuterium label was essentially completely retained. Mass spectral analysis of the starting material gave 92% d_2, 6% d_1, and 2% d_0; nmr analysis of **9**-d_2 gave the same result, which was further confirmed by mass spectral analysis of the products of a hydride transfer experiment (see below) for which this compound was employed as the starting material. The nmr spectrum had δ 7.17 (s, 4, aromatic), 5.71 (s, 4, vinylic), 3.88 (broad d, 1, benzylic, $J = 8.5$), and 2.69 (very broad apparent s, 1, allylic).

Reductive Methylation of Biphenyl. Reactions were conducted as for reduction except that after the appropriate time, usually 20 min, gaseous methyl bromide was introduced relatively rapidly to decolorize the solution in approximately 2 min. Then NH_4Cl (20 g) was added immediately and products were isolated by the usual procedure.

Glpc analysis on column A gave **1**, **2**, and **3**, having retention times 0.49, 0.44, and 0.35, respectively, relative to biphenyl (1.00). Reaction with lithium under optimum conditions (Table I) afforded **1** (93%) and recovered biphenyl (4%). The structure of **1** is supported by the nmr spectrum: δ 7.17 (m, 5, aromatic), 5.61 (s, 4, vinylic), 2.62 (broad s, 2, CH_2), and 1.43 (s, 3, CH_3).

Anal. Calcd for $C_{13}H_{14}$: C, 91.71; H, 8.29. Found: C, 91.74; H, 8.42.

The nmr spectrum of **2** isolated off the glpc column showed δ 7.18 (m, 5, aromatic), 5.56 (s, 4, vinylic), 2.74 (q, 1, $J = 7.5$ Hz, CH), 1.43 (s, 3, CH_3), and 1.11 (d, 3, $J = 7.5$ Hz, CH_3); at 100-MHz sweep width the apparent methyl doublet at δ 1.11 was revealed as a pair of doublets, $J = 7.3$ Hz, $\Delta\nu = 0.7$ Hz, interpreted as due to equivalent concentrations of *cis*- and *trans*-**2**. The mass spectrum of **2** exhibited the expected molecular ion *m/e* (rel intensity) at 184 (31) and characteristic peaks at 169 (100) and 154 (46) indicative of loss of one and two methyl groups, respectively.

The nmr spectrum of **3** showed δ 7.18 (m, 5, aromatic), 5.48 (s, 4, vinylic), 1.43 (s, 3, CH_3), and 1.09 (s, 6, CH_3). The mass spectrum of **2** displayed the calculated molecular ion at 198 (31), and major peaks for loss of one and two methyls at 183 (100) and 168 (35), respectively.

Reductive Methylation of 4,4′-Dideuteriobiphenyl. Analogous reductive methylation of 4,4′-dideuteriobiphenyl (2.5 mmol) with lithium (5.5 g-atoms) in the absence of solvent (30 min) afforded 1-methyl-1,4-dihydro-4,4′-dideuteriobiphenyl (**1**-d_2) (97%) and the related dimethyl derivative **2**-d_2 (3%); nmr analysis showed complete retention of the deuterium label. The nmr spectrum of **1**-d_2 showed δ 7.27 (s, 4, aromatic), 5.67 (s, 4, vinylic), 2.65 (broad peak, 1, allylic), and 1.45 (s, 3, CH_3).

Amide Induced Methylation of 1 and 9 (Table IV). The metal amide was generated *in situ* by addition of ferric chloride (30 mg) to refluxing ammonia (150 ml) followed by the metal (quantity indicated in Table IV plus 0.55 mequiv of additional metal to reduce $FeCl_3$ to Fe). When the blue color was discharged, **1** or **9** was added, and after an appropriate interval gaseous methyl bromide was introduced, and reaction was quenched and worked up in the usual manner.

Hydride Transfer from the Protonated Monoanion of Biphenyl 6. (a) Monanion Generated from 9. Treatment of dihydrobiphenyl **9** (4.7 mmol) in THF (25 ml) and ammonia (150 ml) with lithium amide (5 mmol) formed *in situ* for 20 min at −33° afforded a solution of **6**. Then a solution of anthracene (7.5 mmol) in THF (50 ml) was added and the resulting solution stirred for 40 min before quenching with NH_4Cl. Glpc analysis of the product on column A revealed biphenyl and 9,10-dihydroanthracene (yields of both 100% based on **9**) and unreacted excess anthracene. A similar experiment employing sodamide (and anthracene without cosolvent) gave essentially similar results.

(b) Monoanion Generated *via* Lithium–Biphenyl Interaction. Reaction of biphenyl (2.5 mmol) with lithium (5.5 g-atoms) in THF (50 ml) and 150 ml of refluxing ammonia by the standard procedure furnished a solution of **6**. To this, after 40 min, a solution of anthracene (5 mmol) in THF (25 ml) was added and the solution was stirred for 40 min before quenching with NH_4Cl. Glpc analysis indicated quantitative hydride transfer, as in a.

Hydride Transfer from 6-d_2. (a) Monanion from 9-d_2. Reaction of the 4,4′-dideuterio derivative of dihydrobiphenyl **9**-d_2 (1.1 mmol) with lithium amide (5.6 mmol) without cosolvent in refluxing ammonia furnished a solution of the monoanion **6**-d_2. Treatment of the latter with anthracene (5 mmol) in THF (75 ml) for 40 min followed by NH_4Cl provided a product, glpc analysis of which showed quantitative conversion to biphenyl and 9,10-dihydroanthracene. Mass spectral analysis gave biphenyl (78% d_2, 20% d_1, 2% d_0), dihydroanthracene (2% d_2, 9% d_1, 89% d_0), and anthracene (0% d_2, 1% d_1, 99% d_0); the starting material had 92% d_2, 6% d_1, 2% d_0. The percentage of deuterium loss from **9**-d_2 was equivalent to the level of deuterium incorporation in anthracene, indicative of essentially quantitative hydride transfer.

(b) **Monanion from Biphenyl-d_2.** Lithium–ammonia reduction of 4,4′-dideuteriobiphenyl and treatment of the product with anthracene by the same method employed with unlabeled biphenyl afforded quantitatively biphenyl, dihydroanthracene, and recovered excess anthracene. Deuterium distribution matched closely (±1%) that observed in a.

Equilibration of 1-d_2. Treatment of the deuterium-labeled 1-methyl derivative of dihydrobiphenyl (**1**-d_2) (0.88 mmol) with lithium amide (4.9 mmol) for 30 min at −33° in liquid ammonia (150 ml) in the absence of a cosolvent led to recovery of **1**-d_2 with ≤2% loss of deuterium by nmr analysis.

Analogous reaction with sodamide proceeded similarly to furnish **1**-d_2 with *ca.* 12% deuterium loss.

Attempted Methylation of the Radical Anion of Biphenyl-d_2. Reaction of biphenyl-d_2 (5 mmol) with lithium (5.5 g-atom) and methyl bromide under the usual conditions for reductive methylation led to recovery of biphenyl-d_2 (87%) and the mono- and dimethyl compounds **1**-d_2 (11%) and **2**-d_2 (1%). The latter two components apparently arise *via* dianion formation with the excess lithium (10 ± 2%). Net loss of deuterium was <2%, ruling out a mobile equilibrium involving protonation of **4**.

Acknowledgment. This investigation was supported in part by U. S. Public Health Service Research Grants CA-11,968 and CA-05246 from the National Cancer Institute and by the Louis Block Fund, The University of Chicago.

Metal–Ammonia Reduction. XIII. Regiospecificity of Reduction and Reductive Methylation in the Terphenyl Series[1]

Ronald G. Harvey,* Donald F. Lindow, and Peter W. Rabideau

Contribution from the Ben May Laboratory, The University of Chicago, Chicago, Illinois 60637. *Received October 30, 1971*

Abstract: Interaction of alkali metals with *p*-terphenyl in liquid ammonia affords both the theoretically predicted *cis*- and *trans*-1′,4′-dihydro-*p*-terphenyl (**2**) and the outer ring dihydro isomer, 1,4-dihydro-*p*-terphenyl (**1**). The relative ratios of **1** and **2** are dependent upon reaction variables, *e.g.*, metal, temperature, solvent, quenching agent (NH_4Cl or H_2O), etc., and under appropriate conditions product distribution may be shifted to favor exclusively the outer ring dihydro product **1**. This discrepancy from HMO theoretically predicted regiospecific reduction, the first encountered to date, may be rationalized in terms of an equilibrium between associated and free forms of a dianionic intermediate, protonation of which leads to **1** and **2**, respectively. Analogous reductive methylation of *p*-terphenyl furnishes products of both inner and outer ring attack. In contrast, metal–ammonia reduction and reductive alkylation of both *m*- and *o*-terphenyl proceeds regiospecifically in accord with theory in the central ring. The site of initial protonation of the *o*-terphenyl dianion appears nonregiospecific, occurring in both the 1′ and 4′ positions, while initial proton addition to the *m*-terphenyl dianion takes place exclusively in the 4′ position. Evidence is presented concerning the stability of the intermediate anionic species, their extent of association with the counterion, the relative importance of possible reaction pathways, and the stereochemistry of the 1,4-cyclohexadiene products.

According to Hückel molecular orbital theory,[2] reduction of polycyclic aromatic hydrocarbons (PAH) by alkali metals in liquid ammonia is predicted to occur at the regions of highest electron density in the intermediate anionic species, independent of the pathway. Careful reinvestigation of earlier work employing improved techniques of reaction, product characterization, and analysis has revealed a remarkable regiospecificity (*i.e.*, only a single dihydro isomer formed) for these reactions. Of the PAH investigated to date, which include biphenyl,[1] naphthalene,[3] anthracene,[4] phenanthrene,[5,6] chrysene,[7] benz[*a*]anthracene,[4,8] tetracene,[4] dibenz[*a*,*h*]anthracene,[4] pyrene,[9] and numerous alkyl derivatives of these, the only discrepancy between theory and experimental finding was detected with pyrene. The later compound, upon treatment with lithium in liquid ammonia, afforded, contrary to earlier claims, 1,9-dihydropyrene as the primary reduction product: the latter isomer is only one of at least five theoretically predicted equivalent structures.

We now wish to report studies on reduction and reductive methylation in the terphenyl series, including the first example of reduction nonregiospecific and partially contrary to theoretical prediction, and evidence for ion pair formation as an important factor in the determination of product structure.

In the only previous investigation of terphenyl, Hückel and Bretschneider reported[10] transformation of *p*-terphenyl upon treatment with sodium or calcium in liquid ammonia to a 2:1 mixture of a dihydroter-

---

(1) Part XII: D. F. Lindow, C. N. Cortez, and R. G. Harvey, *J. Amer. Chem. Soc.*, **94**, 5406 (1972). For review on metal–ammonia reduction of aromatic molecules *cf.* R. G. Harvey, *Synthesis*, 161 (1970).

(2) A. Streitwieser, Jr., and S. Suzuki, *Tetrahedron*, 16, 153 (1961); A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961, p 425.

(3) P. W. Rabideau and R. G. Harvey, *Tetrahedron Lett.*, 4139 (1970).

(4) R. G. Harvey, L. Arzadon, J. Grant, and K. Urberg, *J. Amer. Chem. Soc.*, 91, 4535 (1969).

(5) P. W. Rabideau, R. G. Harvey, and J. B. Stothers, *Chem. Commun.*, 1005 (1969).

(6) P. W. Rabideau and R. G. Harvey, *J. Org. Chem.*, **35**, 25 (1970).

(7) R. G. Harvey, *ibid.*, **36**, 3306 (1971).

(8) R. G. Harvey and K. Urberg, *ibid.*, **33**, 2206 (1968).

(9) R. G. Harvey and P. W. Rabideau, *Tetrahedron Lett.*, 3695 (1970).

(10) W. Hückel and H. Bretschneider, *Justus Liebigs Ann. Chem.*, **540**, 157 (1939).