Dimetalated Heterocycles as Synthetic Intermediates. IV. Dilithio Derivatives of 2-Methylbenzimidazole, 2-Benzylbenzimidazole, and Related Compounds[1]

JAMES V. HAY, DAVID E. PORTLOCK, AND JAMES F. WOLFE*

Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061

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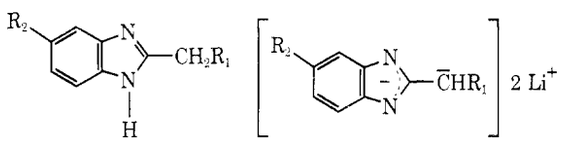
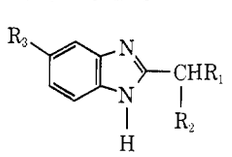
Treatment of 2-methylbenzimidazole (**1a**), 2-methyl-5-chlorobenzimidazole (**1b**), 2-benzylbenzimidazole (**1c**), and 1-(2-benzimidazolyl)-1-phenylpropane (**3g**) with 2 mol equiv of *n*-butyllithium in THF–hexane at 0° resulted in abstraction of the heterocyclic NH proton as well as an α hydrogen of the 2-alkyl substituent. Reactions of the resulting dilithio derivatives with alkyl halides, aldehydes, and ketones took place selectively at the side-chain carbanion center to produce 2-alkylbenzimidazoles and 2-(2-hydroxylalkyl)benzimidazoles, respectively. Attempted twofold deprotonation of 2-propylbenzimidazole (**3a**) with *n*-butyllithium afforded only the monolithio salt (**7**) even in the presence of TMEDA or HMPA.

The weakly acidic character of the methyl protons of 2-methylbenzimidazole (**1a**) has been demonstrated on a number of occasions.[2] For example, **1a** reacts with aromatic aldehydes in the presence of both acidic and basic catalysts to form 2-styrylbenzimidazoles.[2c] Although the base-catalyzed reactions presumably involve an intermediate possessing carbanion character at the 2-methyl position,[2a] active hydrogen condensations at this site have previously been limited to those in which unfavorable ionization of a side-chain proton is compensated for by a later, irreversible step such as dehydration of an intermediate aldol product. It occurred to us that treatment of **1a** with a suitable strong base should effect rapid ionization of the NH proton and that the benzimidazole nucleus might provide sufficient delocalization of negative charge to then allow secondary ionization of a methyl hydrogen to form dianion **2a**. If such a dual ionization process could be driven to completion by utilizing an essentially irreversible acid–base reaction, and if dianion **2a** were to possess reasonable stability in aprotic solvents, it seemed possible that this and similar intermediates might be useful for the synthesis of a variety of 2-substituted benzimidazole derivatives *via* simple carbanion condensations.



1a, $R_1 = R_2 = H$
b, $R_1 = H$; $R_2 = Cl$
c, $R_1 = C_6H_5$; $R_2 = H$

2a, $R_1 = R_2 = H$
b, $R_1 = H$; $R_2 = Cl$
c, $R_1 = C_6H_5$; $R_2 = H$



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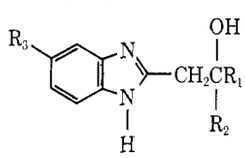

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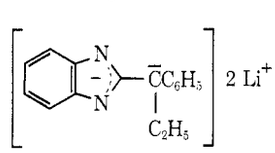

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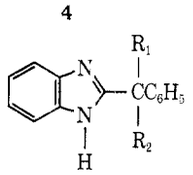

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We now wish to report that **1a** can be readily converted into dianion **2a** by means of 2 mol equiv of *n*-butyllithium in THF–hexane at 0°, as shown by deuteration and selective condensations with various electrophiles at the exocyclic carbanion site. These results represent the first example of simultaneous ring and side-chain metalation of a 2-alkylbenzimidazole.[3]

Alkylation of **2a** with a series of primary halides as well as isopropyl bromide afforded *C*-alkyl derivatives **3a–e** (Table I). These results are in contrast to alkylations of 2-alkylbenzimidazoles in the presence of weaker bases, which afford N-substituted derivatives.[4] Reactions of **2a** with a representative series of aromatic, aliphatic, and α,β-unsaturated aldehydes produced carbinols **4a–d**, rather than the styryl derivatives obtained under more vigorous conditions.[2c] Similarly, benzophenone, cyclohexanone, and acetophenone afforded tertiary alcohols **4e–f** and **4h**, while benzalacetophenone gave a mixture of 1,2 and 1,4 adducts **4g** and **3f**, respectively. Twofold lithiation of 5-chloro-2-methylbenzimidazole (**1b**) to form dianion **2b** also took place smoothly, as demonstrated by condensations with anisaldehyde and benzophenone to form **4i** and **4j**, respectively.

Exposure of 2-propylbenzimidazole (**3a**) to 2 mol equiv of *n*-butyllithium in THF–hexane at 0° afforded a light yellow slurry. Treatment of such reaction mixtures with benzyl chloride or benzophenone failed to yield the expected side-chain condensation products, and **3a** was recovered unchanged. The absence of detectable quantities of addition and/or reduction[5] products resulting from reaction of residual *n*-butyl-

(1) (a) The following papers constitute parts I–III of this series: J. F. Wolfe, G. B. Trimitsis, and D. R. Morris, *J. Org. Chem.*, **34**, 3263 (1969); J. F. Wolfe and T. G. Rogers, *ibid.*, **35**, 3600 (1970); J. D. Taylor and J. F. Wolfe, *Synthesis*, 310 (1971). (b) Abstracted in part from the Ph.D. dissertation of D. E. Portlock, Virginia Polytechnic Institute and State University, April 1972. (c) Supported by Grant No. NS-10197 from the National Institute of Neurological Diseases and Stroke. (d) Presented at the 166th National Meeting of the American Chemical Society, Chicago, Ill., Aug 30, 1973.

(2) (a) For reviews see K. Hofmann in "The Chemistry of Heterocyclic Compounds," Part I, A. Weissberger, Ed., Interscience, New York, N. Y., 1953; A. F. Pozharskii, A. D. Garnovskii, and A. M. Simonov, *Russ. Chem. Rev.*, **35**, 122 (1966). (b) For a report of H–D exchange at the methyl group of **1a** see N. N. Zatsepina, Y. L. Kaminskii, and I. F. Tupitsyr, *Reakts. Sposobnost Org. Soedin.*, 433 (1967); *Chem. Abstr.*, **69**, 85848e (1968). (c) For examples of aldol condensations involving **1a** see W. R. Sullivan, *J. Med. Chem.*, **13**, 784 (1970), and references cited therein.

(3) Several investigators have found previously that 1-alkyl- or 1-arylbenzimidazoles undergo metalation of the heterocyclic ring and/or addition to the azomethine linkage on treatment with organolithium reagents. See (a) R. C. Elderfield and V. B. Meyer, *J. Amer. Chem. Soc.*, **76**, 1891 (1954); (b) P. W. Alley and D. A. Shirley, *J. Org. Chem.*, **23**, 1791 (1958); (c) B. A. Tertov, N. A. Ivankova, and A. M. Simonov, *Zh. Obshch. Khim.*, **32**, 2989 (1962); (d) B. A. Tertov and S. E. Panchenko, *ibid.*, **33**, 3671 (1963); (e) A. V. Koblik, *Mater. Nauch. Konf. Aspir., Rostov-na-Donu Gos. Univ.*, 7th, 8th, 235 (1967) [*Chem. Abstr.*, **71**, 13061m (1969)].

(4) For example see M. Mousseron, J. M. Kamenka, and A. Stenger, *J. Med. Chem.*, **11**, 889 (1968).

(5) J. D. Buhler, *J. Org. Chem.*, **38**, 904 (1973).

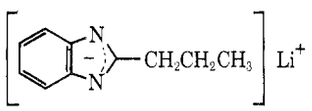
TABLE I

CONDENSATIONS OF DIANIONS 2a–e AND 5 WITH ALKYL HALIDES AND CARBONYL COMPOUNDS

Di-anion	Halide or carbonyl Registry no.	Halide or carbonyl Compd	No.	R_1	R_2	R_3	Yield, %[a]	Recrystn solvent
2a	74-96-4	CH_3CH_2Br	3a	CH_3CH_2	H	H	78	EtOH–H_2O
2a	100-44-7	$C_6H_5CH_2Cl$	3b	$C_6H_5CH_2$	H	H	44	EtOH–H_2O
2a	926-57-8	$ClCH_2CH{=}C(Cl)CH_3$	3c	$CH_3C(Cl){=}CHCH_2$	H	H	40	EtOH–H_2O
2a	106-95-6	$CH_2{=}CHCH_2Br$	3d	$CH_2{=}CHCH_2$	H	H	33	Me_2CO–hexane
2a	75-26-3	$(CH_3)_2CHBr$	3e	$(CH_3)_2CH$	H	H	43	EtOH–H_2O
2a	111-71-7	$CH_3(CH_2)_5CHO$	4a	$CH_3(CH_2)_4CH_2$	H	H	61	EtOH
2a	100-52-7	C_6H_5CHO	4b	C_6H_5	H	H	65	EtOH
2a	123-11-5	p-$CH_3OC_6H_4CHO$	4c	p-$CH_3OC_6H_4$	H	H	48	EtOH
2a	107-02-8	$C_6H_5CH{=}CHCHO$	4d	$C_6H_5CH{=}CH$	H	H	68	EtOH
2a	119-61-9	$(C_6H_5)_2C{=}O$	4e	C_6H_5	C_6H_5	H	70	EtOH
2a	108-94-1	c-$C_6H_{11}O$	4f	$-CH_2CH_2CH_2CH_2CH_2-$		H	49	EtOAc
2a	94-41-7	$C_6H_5CH{=}CHCOC_6H_5$	4g	C_6H_5	$C_6H_5CH{=}CH$	H	59	Me_2CO–hexane
	779-51-1	Benzalacetophenone	3f	$C_6H_5COCH_2CH(C_6H_5)$	H	H	32	Me_2CO–hexane
2a	98-86-2	$C_6H_5COCH_3$	4h	C_6H_5	CH_3	H	65	EtOAc–hexane
2b		p-$CH_3OC_6H_4CHO$	4i	p-$CH_3OC_6H_4$	H	Cl	46	EtOH
2b		$(C_6H_5)_2C{=}O$	4j	C_6H_5	C_6H_5	Cl	62	EtOH
2c		CH_3CH_2Br	3g	CH_3CH_2	C_6H_5	H	69	EtOH–H_2O
2c		$C_6H_5CH_2Cl$	3h	$C_6H_5CH_2$	C_6H_5	H	70	EtOH–H_2O
5	105-65-9	$CH_3(CH_2)_2CH_2Br$	6	$CH_3(CH_2)_2CH_2$	CH_3CH_2		88	EtOAc–hexane

[a] Yields are based on isolated, constant-melting material and have not been subjected to optimization.

lithium with benzophenone raised the question as to whether the precipitate was the desired dianion or perhaps an insoluble complex consisting of monoanion **7**



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and 1 equiv of lithium reagent.[6] The first of these possibilities was eliminated by deuterium oxide quenching, which returned **3a** containing no side-chain deuterium. The second premise was shown to be suspect by isolation of valeric acid (17%) upon treatment of the inhomogeneous reaction mixture with excess, gaseous carbon dioxide. However, this experiment was complicated by rapid dissolution of the precipitate as carbon dioxide was added. The identity of the precipitate was established as uncomplexed monoanion **7** by separating it from the reaction mixture, followed by hydrolysis and titration of the resulting aqueous solution against standard hydrochloric acid.

Several subsequent attempts were made to effect side-chain metalation of **3a** utilizing *n*-butyllithium complexed with *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA)[7] and by solubilizing monoanion **7** with hexamethylphosphoric triamide (HMPA). The first of these approaches again gave only the insoluble monoanion as shown by deuterium oxide quenches. Use of HMPA resulted in the production of a homogeneous solution, but addition of benzyl chloride to the reaction mixture afforded a nearly quantitative recovery of **3a** and a 64% yield of stilbene. Excess *n*-butyllithium (3 mol equiv/mol equiv of **3a**) effected a small amount of metalation at the α-methylene position of **3a** as evidenced by incorporation of 0.29 D per α-methylene group of **3a**. However, these experimental conditions appear to offer limited possibilities for the synthesis of benzimidazoles bearing α-alkyl substituents in the 2 position.

Although substitution of alkyl groups larger than methyl at the 2 position of the benzimidazole nucleus appears to surpress, almost completely, side-chain metalation, the α-phenyl substituent of 2-benzylbenzimidazole (**1c**) is compatible with formation of dianion **2c** as shown by alkylations with ethyl bromide and benzyl chloride to afford **3g** and **3h** in yields of 69 and 70%, respectively. The α-phenyl substituent of **3g** provides sufficient activation to allow abstraction of the methinyl hydrogen to form tertiary dianion **5**, which underwent alkylation with butyl bromide to form **6** in 88% yield.

In conclusion, it should be pointed out that the present reactions involving dianions **2a–c** and **5** represent a mild and seemingly versatile alternative to more classical methods[8] for the synthesis of 2-substituted benzimidazoles. Moreover, such dianions should prove to be useful intermediates for introduction of the biologically interesting[2,4] 2-benzimidazolemethyl and related moieties into various molecules containing appropriate electrophilic centers.

Experimental Section

General.—Melting points were obtained on a Thomas-Hoover apparatus in open capillaries and are uncorrected. All evaporations were carried out *in vacuo*.

Materials.—Tetrahydrofuran (THF) was distilled from lithium aluminum hydride immediately before use. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) and hexamethylphosphoric triamide (HMPA) were distilled from calcium hydride and stored over Linde type 3A molecular sieves. *n*-Butyllithium (as a solution in hexane) was obtained from Ventron Corp., Beverly, Mass. 5-Chloro-2-methylbenzimidazole (**1b**) was obtained from Aldrich Chemical Co., Inc., Milwaukee, Wis., and was recrystallized from water. All other commercial reagents were used without further purification.

(6) R. G. Harvey and L. N. H. Cho, *J. Amer. Chem. Soc.*, **95**, 2376 (1973), have recently proposed such a 1:1 complex between the monolithio salt of 9,10-dihydrophenanthrene and *n*-butyllithium.

(7) A. W. Langer, Jr., *Trans. N. Y. Acad. Sci.*, **27**, 741 (1965).

(8) For examples of such methods, which normally involve condensations of *o*-phenylenediamines with acids, aldehydes, and imino ethers, respectively, see (a) M. A. Phillips, *J. Chem. Soc.*, 2393 (1928); (b) D. Jerchez, H. Fischer, and M. Kracht, *Justus Liebigs Ann. Chem.*, **575**, 162 (1952); (c) F. E. King and R. M. Acheson, *J. Chem. Soc.*, 1396 (1949).

2-Methylbenzimidazole (**1a**) was prepared in 43% yield by condensation of acetic acid with *o*-phenylenediamine according to the procedure of Phillips,[8a] and had mp 178–179° (lit.[8a] mp 176°); pmr (DMSO-d_6) δ 2.63 (s, 3, CH_3), 7.02 (m, 2, aromatic), and 7.32 ppm (m, 2, aromatic).

2-Benzylbenzimidazole (**1c**) was prepared by the method of King and Acheson[8c] from *o*-phenylenediamine and the hydrochloride salt of methyl iminophenylacetate in 55% yield: mp 190–191° (lit.[8c] mp 191°); pmr (DMSO-d_6) δ 4.16 (s, 2, CH_2), 7.04 (m, 2, aromatic), and 7.30 ppm (m, 8, aromatic and NH).

General Procedure for Preparation of Dianions 2a–c and 5.—The 2-alkylbenzimidazole **1a–c** and **3g** (1–15 mmol) was dissolved in 50–75 ml of THF under nitrogen. The magnetically stirred solution was cooled to 0° in an ice bath, and *n*-butyllithium (2.1–32.0 mmol) was added *via* syringe. The resulting reaction mixture was stirred for 1 hr at 0° to ensure complete formation of the respective dianion. Dianion **2a** appeared as a tan slurry; dianions **2b** and **2c** formed red-brown solutions, while dianion **5** formed a blood-red solution.

Deuteration of Dianion 2a.—A slurry of **2a** in THF was quenched with 0.5 ml of D_2O. The precipitated lithium deuterioxide was removed by filtration, the filtrate was diluted with ether and dried over $MgSO_4$ and the solvent was evaporated, giving deuterated **1a**. Analysis of the pmr spectrum of this material ($CDCl_3$) indicated incorporation of 0.84 D per methyl group of **1a**.

Alkylations of Dianions 2a–c and 5.—A solution of the appropriate alkyl halide (5–15 mmol) in 10–15 ml of THF was added to the respective dianion. The reaction mixture was stirred for 2 hr while warming to room temperature. The reaction was processed by quenching with 50 ml of water, neutralization with concentrated HCl, and extraction with ether. The crude isolated products were recrystallized from the appropriate solvent (Table I). The following 2-alkyl benzimidazoles were prepared by this method.

2-Propylbenzimidazole (**3a**) had mp 156–157.5° (lit.[9] mp 152–153°); pmr (DMSO-d_6) δ 0.96 (s, 3, CH_3), 1.81 (m, 2, CH_2), 2.80 (t, 2, CH_2), 7.01 (m, 2, aromatic), and 7.36 ppm (m, 2, aromatic).

2-Phenethylbenzimidazole (**3b**) had mp 190–191° (lit.[10] mp 189–190°); pmr (DMSO-d_6) δ 3.16 (m, 4, CH_2) and 7.25 ppm (m, 9, aromatic).

5-(2-Benzimidazolyl)-2-chloro-2-pentene (**3c**) had mp 143–144°; pmr (DMSO-d_6) δ 2.05 (s, 3, CH_3), 2.63 (t, 2, CH_2), 2.82 (m, 2, CH_2), 5.61 (t, 1, =CH), 7.04 (m, 2, aromatic), and 7.41 ppm (m, 2, aromatic).

Anal. Calcd for $C_{12}H_{13}N_2Cl$: C, 65.30; H, 5.93; N, 12.70. Found: C, 65.38; H, 5.80; N, 12.62.

4-(2-Benzimidazolyl)-1-butene (**3d**) had mp 165–166°; pmr (DMSO-d_6) δ 2.51 (t, 2, CH_2), 2.86 (m, 2, CH_2), 4.94 (m, 2, $=CH_2$), 5.78 (m, 1, =CH), 7.01 (m, 2, aromatic), and 7.37 ppm (m, 2, aromatic).

Anal. Calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.03; N, 16.27. Found: C, 76.89; H, 6.77; N, 16.35.

2-Isobutylbenzimidazole (**3e**) had mp 185.5–187° (lit.[11] mp 186–187°); pmr (DMSO-d_6) δ 0.97 (d, 6, CH_3), 2.21 (m, 1, CH), 2.72 (d, 2, CH_2), 7.13 (m, 2, aromatic), and 7.52 ppm (m, 2, aromatic).

4-(2-Benzimidazolyl)-1,3-diphenyl-1-butanone (**3f**)[12] had mp 194–195.5°; pmr (DMSO-d_6) δ 3.19 (m, 2, CH_2), 3.48 (m, 2, CH_2), 3.92 (m, 1, CH), 7.21 (m, 12, aromatic), and 7.81 ppm (d, 2, aromatic).

Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 80.85; H, 5.96; N, 8.27.

1-(2-Benzimidazolyl)-1-phenylpropane (**3g**) had mp 189–191° (lit.[13] mp 189–190°); pmr (DMSO-d_6) δ 0.87 (t, 3, CH_3), 2.14 (m, 2, CH_2), 4.07 (t, 1, CH), and 7.29 ppm (m, 10, aromatic and NH).

1-(2-Benzimidazolyl)-1,2-diphenylethane (**3h**) had mp 244–245°; pmr (DMSO-d_6) δ 3.31 and 3.62 (2 AB, 2, CH_2), 4.52 (t, 1, CH), and 7.29 ppm (m, 15, aromatic and NH).

Anal. Calcd for $C_{21}H_{18}N_2$: C, 84.53; H, 6.05; N, 9.39. Found: C, 84.25; H, 6.19; N, 9.44.

3-(2-Benzimidazolyl)-3-phenylheptane (**6**) had mp 211–213°; pmr (DMSO-d_6) δ 0.96 (m, 10, CH_2 and CH_3), 2.30 (m, 4, CH_2), 7.23 (m, 8, aromatic), and 7.62 ppm (m, 1, aromatic).

Anal. Calcd for $C_{20}H_{24}N_2$: C, 82.14; H, 8.27; N, 9.58. Found: C, 82.43; H, 8.56; N, 9.27.

Carbonyl Condensations of Dianions 2a–b.—A solution of the aldehyde or ketone (5–15 mmol) in 10–15 ml of THF was added to the respective dianion. After 2 hr the reaction mixture was poured into 100 ml of iced water, and the crude product was isolated by ether extraction, or, in cases where a precipitate formed, filtration. The crude product was purified by recrystallization from the appropriate solvent (Table I). The following carbinols were prepared in this manner.

1-(2-Benzimidazolyl)-2-octanol (**4a**) had mp 192–193°; pmr (DMSO-d_6) δ 0.85 (t, 3, CH_3), 1.30 (m, 10, CH_2), 2.50 (s, 1, OH), 2.90 (d, 2, CH_2), 4.03 (t, 1, CH), 7.03 (m, 2, aromatic), and 7.38 ppm (m, 2, aromatic).

Anal. Calcd for $C_{15}H_{22}N_2O$: C, 73.12; H, 9.02; N, 11.37. Found: C, 73.26; H, 8.86; N, 11.24.

1-Phenyl-2-(2-benzimidazolyl)ethanol (**4b**) had mp 213.5°; pmr (DMSO-d_6) δ 3.18 (d, 2, CH_2), 5.18 (t, 1, CH), 5.72 (s, 1, OH), and 7.36 ppm (m, 9, aromatic).

Anal. Calcd for $C_{15}H_{14}N_2C$: C, 75.61; H, 5.93; N, 11.76. Found: C, 75.72; H, 6.08; N, 11.88.

1-*p*-Anisyl-2-(2-benzimidazolyl)ethanol (**4c**) had mp 212.5–213°; pmr (DMSO-d_6) δ 3.06 (d, 2, CH_2), 3.67 (s, 3, OCH_3), 5.04 (t, 1, CH), 5.50 (broad, 1, OH), 6.82 (d, 2, aromatic), 7.05 (m, 2, aromatic), 7.25 (d, 2, aromatic), and 7.38 ppm (m, 2, aromatic).

Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.65; H, 5.85; N, 10.26.

1-(2-Benzimidazolyl)-4-phenyl-3-buten-2-ol (**4d**) had mp 214.5–215°; pmr (DMSO-d_6) δ 3.03 (d, 2, CH_2), 4.67 (2 d, 1, CH), 5.43 (s, 1, OH), 6.30 (2 d, 1, =CH), 6.58 (d, 1, =CH), and 7.26 ppm (m, 9, aromatic).

Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.61. Found: C, 76.93; H, 6.18; N, 10.37.

1,1-Diphenyl-2-(2-benzimidazolyl)ethanol (**4e**) had mp 199–201°; pmr (DMSO-d_6) δ 3.36 (broad, 1, OH), 3.85 (d, 2, CH_2), and 7.29 ppm (m, 14, aromatic).

Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.22; H, 5.78; N, 8.91. Found: C, 80.03; H, 5.91; N, 9.15.

2-(1-Hydroxycyclohexylmethyl)benzimidazole (**4f**) had mp 200–201.5°; pmr (DMSO-d_6) δ 1.44 (s, 10, CH_2), 2.85 (s, 2, CH_2), 4.72 (s, 1, OH), 7.04 (m, 2, aromatic), and 7.42 ppm (m, 2, aromatic).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 73.28; H, 8.08; N, 12.13.

1-(2-Benzimidazolyl)-2,4-diphenyl-3-buten-2-ol (**4g**) had mp 139.5–140.5°; pmr (DMSO-d_6) δ 3.51 (s, 2, CH_2), 6.49 (s, 1, OH), 6.60 (d, 1, =CH), and 7.22 ppm (m, 15, aromatic and =CH).

Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.25; H, 5.75; N, 8.52.

1-(2-Benzimidazolyl)-2-phenyl-2-propanol (**4h**) had mp 157.5–159°; pmr (DMSO-d_6) δ 1.53 (s, 3, CH_3), 3.27 (s, 2, CH_2), 5.91 (s, 1, OH), and 7.38 ppm (m, 9, aromatic).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.11. Found: C, 76.44; H, 6.09; N, 11.20.

1-*p*-Anisyl-2-(5-chloro-2-benzimidazolyl)ethanol (**4i**) had mp 235–236°; pmr (DMSO-d_6) δ 3.08 (d, 2, CH_2), 3.70 (s, 3, OCH_3), 5.04 (t, 1, CH), 5.64 (s, 1, OH), 6.84 (d, 2, aromatic), 7.01 (m, 1, aromatic), 7.28 (d, 2, aromatic), and 7.47 ppm (d, 2, aromatic).

Anal. Calcd for $C_{16}H_{15}ClN_2O_2$: C, 63.47; H, 4.99; N, 9.25. Found: C, 63.28; H, 5.06; N, 9.28.

2-(5-Chloro-2-benzimidazolyl)-1,1-diphenylethanol (**4j**) had mp 204.5–206°; pmr (DMSO-d_6) δ 3.89 (s, 2, CH_2), 6.89 (s, 1, OH), and 7.36 ppm (m, 13, aromatic).

Anal. Calcd for $C_{21}H_{17}ClN_2O$: C, 72.30; H, 4.91; N, 8.03. Found: C, 72.51; H, 4.76; N, 8.16.

Attempted Dimetalation of 2-Propylbenzimidazole (**3a**) **with *n*-Butyllithium.**—*n*-Butyllithium (2.1–21.0 mmol) was added *via* syringe to a solution of 2-propylbenzimidazole (**3a**, 1–10 mmol) in 25–50 ml of THF at 0° under nitrogen. After stirring for 1 hr, the yellow slurry was quenched with one of the following electrophiles.

(9) R. Sera and R. H. Müller, *Monatsh. Chem.*, **57**, 97 (1931).

(10) B. A. Porai-Koshits and G. M. Kharkhova, *Zh. Obshch. Khim.*, **25**, 2138 (1955).

(11) R. Weidenhagen, *Ber.*, **69B**, 2263 (1936).

(12) **3f** was obtained from reaction of **2a** with benzalacetophenone and was separated from the 1,2-addition product **4g** by column chromatography on silica gel, employing ether–hexane as the eluent.

(13) A. Hunger, J. Kerble, A. Rossi, and K. Hoffman, *Helv. Chim. Acta*, **43**, 800 (1960).

A. Deuterium Oxide.—The reaction slurry formed from 2 mmol of **3a** was quenched with 0.5 ml of deuterium oxide. The precipitated lithium deuterioxide was removed by filtration; the filtrate was diluted with ether, dried over $MgSO_4$, and concentrated. Analysis of the pmr spectrum (DMSO-d_6) of the residue indicated no deuterium incorporation at the α-methylene position of **3a**.

B. Benzyl Chloride.—To a reaction slurry formed from 10 mmol of **3a** was added a 1:1 v/v solution of benzyl chloride (11 mmol) in THF, and the resulting mixture was stirred for 2 hr. The reaction mixture was poured into 50 ml of water and neutralized with concentrated HCl. The organic phase was separated, and the aqueous phase was extracted with two 50-ml portions of ether. The organic solution was dried over $MgSO_4$, and the solvent was evaporated. Tlc analysis (benzene–acetone–hexane, 1:1:1) of the resulting gummy solid indicated the presence of only unreacted **3a** and benzyl chloride.

C. Butyl Bromide.—Butyl bromide (1 mmol) in 2 ml of THF was added to the slurry formed from 1 mmol of **3a**. After 2 hr, the reaction mixture was processed in a manner similar to that of the preceding experiment. Tlc analysis (benzene–acetone–hexane, 1:1:1) of the crude reaction product indicated the presence of only unreacted **3a**.

D. Benzophenone.—To a reaction slurry formed from 10 mmol of **3a**, benzophenone (11 mmol) in 25 ml of THF was added. After 2 hr, the reaction was processed in the usual manner. Tlc analyses (benzene–acetone–hexane, 1:1:1, and ether) showed only the presence of unreacted **3a** and benzophenone in the crude reaction product; no diphenylbutylcarbinol could be detected.

E. Carbon Dioxide.—Carbon dioxide was bubbled through a slurry formed from 3.5 mmol of **3a** and 7.1 mmol of *n*-butyllithium for 3 min, causing dissolution of the yellow slurry. The reaction mixture was poured into 50 ml of iced water. The organic phase was separated, and the aqueous phase was extracted with two 50-ml portions of ether. The organic solution was dried over $MgSO_4$ and the solvent was evaporated, giving 0.55 g (98% recovery) of **3a**. The alkaline aqueous solution was acidified to pH ~2 and was continuously extracted with ether for 22 hr. The ethereal solution was dried over $MgSO_4$, and the solvent was evaporated to afford 0.06 g (17%) of valeric acid; ir and pmr spectra were identical with those of authentic material.

F. Water.—The precipitate formed from 1 mmol of **3a** was allowed to settle, and the yellow supernatant solution was withdrawn with a syringe and added to 25 ml of water. The precipitate was washed with 5 ml of THF, and the washing was added to the hydrolyzed supernatant. The basic solution was titrated with 0.05 *M* HCl to the end point of phenolphthalein, 29.50 ml of acid being required to reach the end point. This volume of acid represents 1.475 mmol of total base present in the supernatant.

The precipitate was suspended in 5 ml of THF and hydrolyzed with 25 ml of water. Titration of this solution with 0.05 *M* HCl to the end point of phenolphthalein required 23.45 ml, indicating that hydrolysis of the precipitate liberated 1.173 mmol of hydroxide ion.

Attempted Dimetalation of 2-Propylbenzimidazole (3a) with 2 Mol Equiv of *n*-Butyllithium–TMEDA Complex.—*n*-Butyllithium (1.1 ml of 1.9 *M* hexane solution, 2.1 mmol) was added *via* syringe to a solution of **3a** (0.160 g, 1 mmol) and TMEDA (0.232 g, 2 mmol) in 15 ml of THF at 0° under nitrogen. The resulting yellow slurry was stirred for 1 hr before the addition of 0.5 ml of deuterium oxide. After stirring for 1 min, lithium deuteroxide was removed by filtration, the filtrate was diluted with 50 ml of ether and dried over $MgSO_4$, and the solvent was evaporated. The recovered **3a** was dried at 50° (3 mm) for 3 hr to remove residual TMEDA. Analysis of the pmr spectrum (DMSO-d_6) of this material indicated no deuterium incorporation at the α-methylene group of **3a**.

Attempted Benzylation of 2-Propylbenzimidazole (3a) with 2 Mol Equiv of *n*-Butyllithium in the Presence of HMPA.—*n*-Butyllithium (5.8 ml of 1.9 *M* hexane solution, 11 mmol) was added *via* syringe to a solution of **3a** (0.800 g, 5 mmol) in 20 ml of THF and 2 ml of HMPA at 0° under nitrogen. The yellow-brown solution was stirred for 1 hr, and benzyl chloride (0.633 g, 5 mmol) in 5 ml of THF was added. The reaction solution immediately became deep red-black. After approximately 30 sec, this color was discharged, being replaced by the original yellow-brown color. The reaction solution was stirred for 2 hr before being poured into 100 ml of iced water containing 2.5 ml of concentrated HCl. The organic phase was separated, and the acidic aqueous phase was extracted with two 50-ml portions of ether. The organic solution was dried over $MgSO_4$, and the solvent was evaporated. The resulting tan, oily solid was recrystallized from ethanol, giving 0.29 g (64%) of stilbene, mp 119–121° (lit.[14] mp 124°).

The acidic solution was neutralized with concentrated NH_4OH and then was extracted with two 50-ml portions of ether. The organic solution was dried over $MgSO_4$ and the solvent was evaporated, giving 0.77 g (96.5% recovery) of **3a**.

Attempted Dimetalation of 2-Propylbenzimidazole (3a) with 3 Mol Equiv of *n*-Butyllithium.—*n*-Butyllithium (3.3 ml of 1.9 *M* hexane solution, 6.3 mmol) was added *via* syringe to a solution of **3a** (0.320 g, 2 mmol) in 25 ml of THF at 0° under nitrogen. The resulting yellow slurry was stirred for 1 hr before the addition of 1 ml of deuterium oxide. The resulting reaction mixture was processed as in other deuteration experiments. Analysis of the pmr spectrum (DMSO-d_6) of the recovered material indicated incorporation of 0.29 D per α-methylene group of **3a**.

Registry No.—**1a**, 615-15-6; **1b**, 2818-69-1; **1c**, 621-72-7; **3a**, 5465-29-2; **3b**, 5805-30-1; **3c**, 42449-70-7; **3d**, 5838-57-3; **3e**, 5851-45-6; **3f**, 42449-72-9; **3g**, 24893-44-5; **3h**, 42449-74-1; **4a**, 42449-75-2; **4b**, 42449-76-3; **4c**, 42449-77-4; **4d**, 42449-78-5; **4e**, 42449-79-6; **4f**, 42449-80-9; **4g**, 42449-81-0; **4h**, 42449-82-1; **4i**, 42449-83-2; **4j**, 42449-84-3; **6**, 42449-85-4.

(14) T. W. J. Taylor and A. R. Murray, *J. Chem. Soc.*, 2079 (1938).