Anal. Calcd for $C_{11}H_{19}ClNS$: C, 59.05; H, 4.51; Cl, 15.85; N, 6.26. Found: C, 58.97; H, 4.34; Cl, 16.05; N, 6.37.

1-(4,5-Dimethyl-2-thiazolyl)ethanol (18).—Metalation of 4,5-dimethylthiazole with *n*-butyllithium at −80° was followed by addition of a threefold excess of acetaldehyde. Isolation in the usual fashion afforded **18** in 71% yield: bp 186–188° (150 mm) [lit.[21] bp 120–123° (10 mm)]; mp 53–55°; nmr ($CDCl_3$) δ 1.52 (d, 3, J = 6.5 Hz, $CHCH_3$), 2.22 (s, 3, 4-CH_3), 2.27 (s, 3, 5-CH_3), 5.00 (q, 1, J = 6.5 Hz, $CHCH_3$), 5.70 (s, 1, OH).

Anal. Calcd for $C_7H_{11}NOS$: C, 53.47; H, 7.05; N, 8.91. Found: C, 53.29; H, 7.02; N, 8.85.

1-(4,5-Dimethyl-2-thiazolyl)ethyl chloride (19) was prepared from **18** using phosphorus pentachloride: bp 151–157° (44 mm); nmr ($CDCl_3$) δ 1.88 (d, 3, J = 6.5 Hz, $CHCH_3$), 2.30 (6, 4-CH_3 and 5-CH_3), 5.23 (q, 1, J = 6.5 Hz, $CHCH_3$).

Anal. Calcd for $C_7H_{10}ClNS$: C, 47.86; H, 5.74; Cl, 20.18; N, 7.94; S, 18.25. Found: C, 47.98; H, 5.97; Cl, 20.32; N, 8.08; S, 18.10.

Kinetic procedures have been described previously.[5]

Registry No.—**3**, 41029-77-0; **4**, 41029-78-1; **5**, 20949-81-9; **6**, 41029-80-5; **7**, 41029-81-6; **8**, 41029-82-7; **9**, 5198-80-1; **10**, 41029-84-9; **11**, 41029-85-0; **12**, 41029-86-1; **13**, 41029-87-2; **14**, 41029-88-3; **15**, 41029-89-4; **16**, 41029-90-7; **17**, 41029-91-8; **18**, 7531-72-8; **19**, 41029-93-0; 2-methyl-4-formylthiazole, 20949-84-2; 4-formylthiazole, 3364-80-5; ethylene glycol, 107-21-1; *p*-toluenesulfonic acid, 104-15-4; 1-(4-methyl-2-thiazolyl)ethanol, 7586-99-4; 4,5-dimethylthiazole, 3581-91-7; *n*-butyllithium, 109-72-8; thioacetal i,[18] 41029-97-4.

(21) J. Okimaya, *Nippon Kagaku Zasshi*, **87**, 594 (1966); *Chem. Abstr.*, **65**, 15362*C* (1966).

Syntheses with N-Protected 2-Lithioindoles

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A series of potential N-protecting groups which would permit syntheses *via* N-protected 2-lithioindoles has been investigated. These include the methoxymethyl, benzyloxymethyl, benzyl, benzenesulfonyl, trimethylsilyl, and *tert*-butyldimethylsilyl groups. The methoxymethyl and benzenesulfonyl derivatives of indole have been shown to be satisfactorily lithiated and to give addition reactions with typical carbonyl and cyano compounds. The benzenesulfonyl group has a major advantage over the methoxymethyl group for subsequent removal. A number of new 2-acylindoles and 2-indolylcarbinols prepared by these reactions are described. Certain competing reactions leading to by-products have also been detected and are described.

It was demonstrated some years ago[1] that 1-methylindole could be efficiently converted to the 2-lithio derivative by lithiation with *n*-butyllithium. Although there has subsequently been some use of this reaction in synthetic work,[2-4] the utility of this particular lithium derivative is restricted to *N*-alkylindoles, since there is no suitable means for subsequently dealkylating the reaction products. Since 2-lithioindoles could provide a quite general synthetic route to 2-substituted indoles, we have undertaken efforts to develop a procedure for lithiation of indoles substituted by a group which could subsequently be removed under relatively mild conditions. We report here our examination of the methoxymethyl, benzyloxymethyl, benzyl, benzenesulfonyl, trimethylsilyl, and *tert*-butyldimethylsilyl groups for this purpose.[5]

Synthesis of N-Protected Indoles.—The data of Cardillo, *et al.*, indicate that syntheses of 1-alkylated indole could be expected to proceed very efficiently in dipolar aprotic solvents.[6] We found it convenient to effect the alkylations in dimethyl sulfoxide. The sodium salt of dimethyl sulfoxide was generated in the usual way,[7] and indole was then added, forming the sodium salt. The alkylating agent was then added. The yields of **1a**, **1b**, **1c**, and **1d** by this procedure were excellent.[8] Others[9] have recommended hexamethylphosphoramide as a solvent or cosolvent for indole alkylations. The *N*-silyl compounds **1e** and **1f** were prepared in tetrahydrofuran solution because of the reactivity of the silyl chlorides toward dimethyl sulfoxide.

Lithiation.—The extent of lithiation was determined by treating a solution of the N-substituted indole in ether, THF, or tetramethylethylenediamine (TMEDA) with *tert*-butyllithium, quenching with D_2O, and determination of the extent and location of deuterium incorporation by analysis of the mass spectrum. Details of the mass spectral analysis are given in the Experimental Section. The results are summarized in Table I. Of the systems studied only **1a** and **1d** gave relatively clean-cut 2 deuteration. Only these two systems were, therefore, subjected to study with respect to use as a protecting group in subsequent synthetic transformations.

Our studies have given some insight into the course of the reaction of the other four systems with *tert*-butyllithium, which we will summarize here briefly. Not surprisingly, the benzyl compound **1c** is lithiated competitively at the benzyl methylene group. The mass spectrum of recovered **1c** indicates 55% incorporation of D at that position with only 15% lithiation at

(1) D. A. Shirley and P. A. Roussel, *J. Amer. Chem. Soc.*, **75**, 375 (1953).

(2) F. E. Ziegler and E. B. Spitzner, *J. Amer. Chem. Soc.*, **92**, 3492 (1970).

(3) J. Kebrle and K. Hoffmann, *Gazz. Chim. Ital.*, **93**, 238 (1963).

(4) J. Kebrle, A. Rossi, and K. Hoffmann, *Helv. Chim. Acta*, **42**, 907 (1959).

(5) Some previous work using these or similar groups on indole or related heterocycles follows. (a) Methoxymethyl: M. H. Karger and Y. Mazur, *J. Amer. Chem. Soc.*, **91**, 5663 (1969). (b) Benzyloxymethyl: H. J. Anderson and J. K. Groves, *Tetrahedron Lett.*, 3165 (1971). (c) Arenesulfonyl: R. E. Bowman, D. D. Evans, and P. J. Islip, *Chem. Ind. (London)*, 33 (1971); R. E. Bowman, D. D. Evans, J. Guyett, H. Nagy, J. Weale, D. J. Weyell, and A. C. White, *J. Chem. Soc., Perkin Trans. 1*, 1926 (1972); W. A. Remers, R. H. Roth, G. J. Gibs, and M. J. Weiss, *J. Org. Chem.*, **36**, 1232 (1971); R. E. Bowman, D. D. Evans, J. Guyett, H. Nagy, J. Weale, and D. J. Weyell, *J. Chem. Soc., Perkin Trans. 1*, 438 (1973). (d) Trialkylsilyl (previous preparation of N-silated indole has been recorded but we are not aware of examples where the group has been employed specifically as a protecting group): R. Fessenden and D. F. Crowe, *J. Org. Chem.*, **26**, 4638 (1961).

(6) B. Cardillo, G. Casnati, A. Pochini, and A. Ricca, *Tetrahedron*, **23**, 3771 (1967).

(7) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **84**, 866 (1962); **87**, 1353 (1965).

(8) Excellent results in dimethyl sulfoxide using potassium hydroxide as the base have been reported recently: H. Heaney and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 498 (1973).

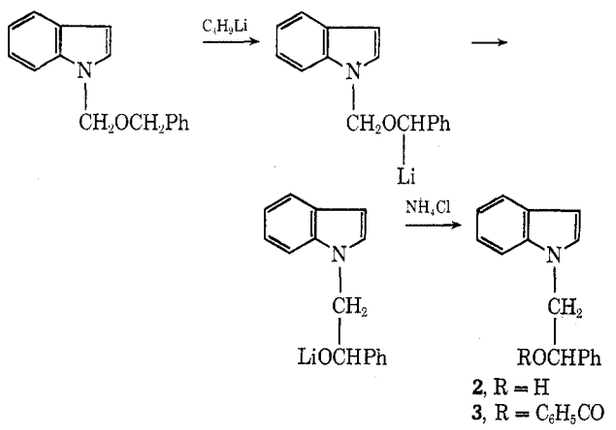
(9) (a) G. M. Rubottom and J. C. Chabala, *Synthesis*, 566 (1972); (b) M. G. Reinecke, J. F. Sebastian, H. W. Johnson, and C. Pyun, *J. Org. Chem.*, **37**, 3066 (1972).

TABLE I

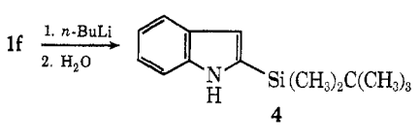
LITHIATION OF 1-SUBSTITUTED INDOLE BY *tert*-BUTYLLITHIUM

Compd	1 substituent	Solvent for lithiation	Yield of recovered indole, %	Total D incorporation, %	D incorporation at C-2, %
1a	CH_3OCH_2	Et_2O	77	95	95
1b	$PhCH_2OCH_2$	Et_2O	35	40	30
1c	$PhCH_2$	THF	90	70	15
1d	$PhSO_2$	THF	90	97	86
		TMEDA	85	90	88
1e	$(CH_3)_3Si$	TMEDA	0		
1f	$(CH_3)_3C(CH_3)_2Si$	THF	85	0	0
		TMEDA	60	0	0

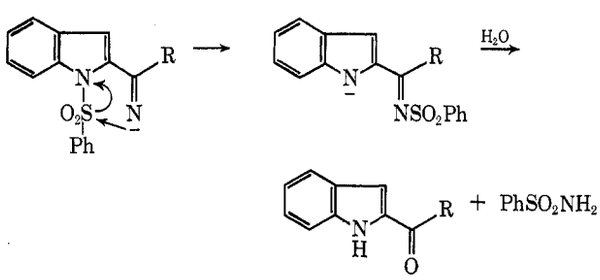
the C-2 position of the ring. The nitrogen–silicon bond in 1-trimethylsilylindole is cleaved by *tert*-butyllithium and only unsubstituted indole is found after lithiation. The situations with **1b** and **1f** are not quite so straightforward. The problem with **1b** is a competing lithiation at the benzyl group followed by Wittig rearrangement.[10] The rearranged alcohol **2** was isolated in ~65% yield after lithiation and D_2O quench. The derived benzoate ester **3** was isolated after treatment of the lithiation mixture with benzoyl chloride.



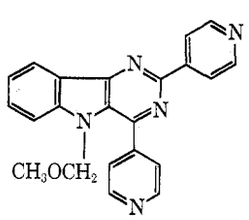
The very bulky silyl substituent in **1f** exerts a strong steric influence and we did not observe any lithiation on reaction with *tert*-butyllithium. With *n*-butyllithium reaction occurred but a rearrangement of the 2-lithio derivative ensued and after deuteration the product was found to be 2-[dimethyl-(1,1-dimethylethyl)silyl]indole (**4**). The rearrangement is an example of anionic rearrangement of silane derivatives which have been studied extensively by West and coworkers.[11]



Synthetic Transformations of Protected 2-Lithioindoles.—Reactions of the lithio derivatives of **1a** (2-LiMMI) and **1d** (2-LiBSI) were run with typical substrates used in organometallic synthetic procedures including aldehydes, ketones, acid chlorides, esters, and nitriles. In most instances these reactions proceeded to give the expected product in moderate yields. In a few cases efforts were made to optimize individual reaction conditions. In these cases some improvement in yields was noted but yields seldom exceeded 70%, indicating that some, as yet unidentified, competitive reactions are occurring. The data are summarized in Table II and the spectral properties of the products are given in the Experimental Section. This data normally was sufficient to corroborate the identity of the products. In other cases the products were known compounds and the physical constants were in satisfactory agreement with literature data. One point of interest is the fact that the benzenesulfonyl substituent was cleaved during the reaction or work-up in the case of reactions with esters and nitriles. The 2-acyl substituent, which increases the stability of the indolyl anion, may be at least partially responsible for this facile removal of protecting group. In reactions involving nitriles, benzenesulfonamide was isolated in several instances. Its formation indicates that transfer of the benzenesulfonyl substituent to the imine nitrogen may precede hydrolysis of the intermediate imine.



Identifiable by-products were noted in only a few of the reactions. In the reaction of 2-LiMMI with 4-cyanopyridine, a yellow solid, **26**, mp 251.5–252.5°, having the formula $C_{22}H_{17}N_5O$ was isolated in up to 84% yield. The mass spectrum consisted of only a few ions, suggesting a highly aromatic structure for this material. The available data is in accord with assigning the structure 5-methoxymethyl-2,4-di(4-pyridyl)pyrimido[5,6-*b*]indole to this material. It is formally derived from a two-electron oxidation of a 2:1 adduct of 4-cyanopyridine with 2-LiMMI. Its formation may involve aromatization by elimination of LiH.



26

(10) H. E. Zimmerman, "Molecular Rearrangements," P. de Mayo, Ed., Interscience, New York, N. Y., 1963, pp 372–377; D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 230–233; U. Schöllkopf, *Angew. Chem., Int. Ed. Engl.*, **9**, 763 (1970).

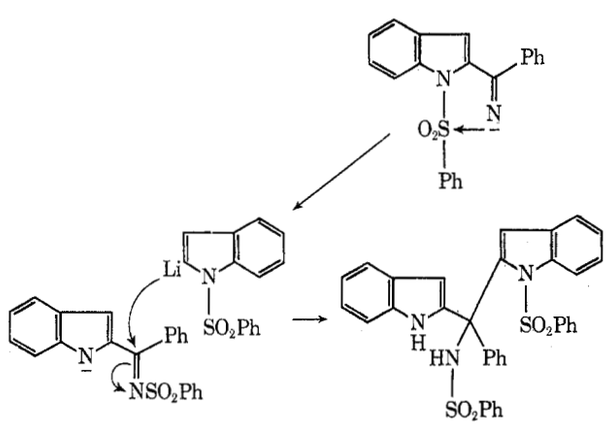
(11) A. Wright, D. Ling, P. Boudjouk, and R. West, *J. Amer. Chem. Soc.*, **94**, 4784 (1972), and preceding papers.

TABLE II

REACTIONS OF 1-PROTECTED 2-LITHIOINDOLES WITH TYPICAL FUNCTIONAL GROUPS

Reactant	Reaction product	Isolated yield, %
	A. 2-LiMMI	
Benzaldehyde	(1-Methoxymethylindol-2-yl)phenylmethanol (5)	40
Carbon dioxide	1-Methoxymethyl-2-indolecarboxylic acid (6)	80
N-Methylformanilide	1-Methoxymethyl-2-indolecarboxaldehyde (7)	46
Benzonitrile	1-Methoxymethyl-2-indolyl phenyl ketone (8)	84
4-Methoxybenzonitrile	1-Methoxymethyl-2-indolyl 4-methoxyphenyl ketone (9)	70
2-Cyanopyridine	1-Methoxymethyl-2-indolyl 2-pyridyl ketone (10)	56
4-Cyanopyridine	1-Methoxymethyl-2-indolyl 4-pyridyl ketone (11)	56
	B. 2-LiBSI	
Benzaldehyde	(1-Benzenesulfonylindol-2-yl)phenylmethanol (12)	55
4-Methoxybenzaldehyde	(1-Benzenesulfonylindol-2-yl)(4-methoxyphenyl)methanol (13)	65
2-Pyridinecarboxaldehyde	(1-Benzenesulfonylindol-2-yl)-2-pyridylmethanol (14)	32
Acetophenone	1-(1-Benzenesulfonylindol-2-yl)-1-phenylethanol (15)	64
4-Methoxyacetophenone	1-(Benzenesulfonylindol-2-yl)-1-(4-methoxyphenyl)ethanol (16)	35
4-Acetylpyridine	1-(1-Benzenesulfonylindol-2-yl)-1-(4-pyridyl)ethanol (17)	35
Benzoyl chloride	1-Benzenesulfonyl-2-indolyl phenyl ketone (18)	65
Nicotinyl chloride	1-Benzenesulfonyl-2-indolyl 3-pyridyl ketone (19)	60
Ethyl chloroformate	Ethyl 1-benzenesulfonylindole-2-carboxylate (20)	75
Carbon dioxide	1-Benzenesulfonylindole-2-carboxylic acid (21)	63
Ethyl benzoate	2-Indolyl phenyl ketone (22)	26
Ethyl isonicotinate	2-Indolyl 4-pyridyl ketone (23)	31
Ethyl nicotinate	2-Indolyl 3-pyridyl ketone (24)	22
Benzonitrile	2-Indolyl phenyl ketone (22)	30
2-Cyanopyridine	2-Indolyl 2-pyridyl ketone (25)	36
4-Cyanopyridine	2-Indolyl 4-pyridyl ketone (23)	26

Several of the reactions of aromatic nitriles, especially benzonitrile, with 2-LiBSI gave a solid which had the composition corresponding to addition of two benzenesulfonylindole moieties to the nitrile. Structural investigation of the product from benzonitrile indicated that the compound is **27**, perhaps formed by the mechanism shown from the 1:1 adduct.

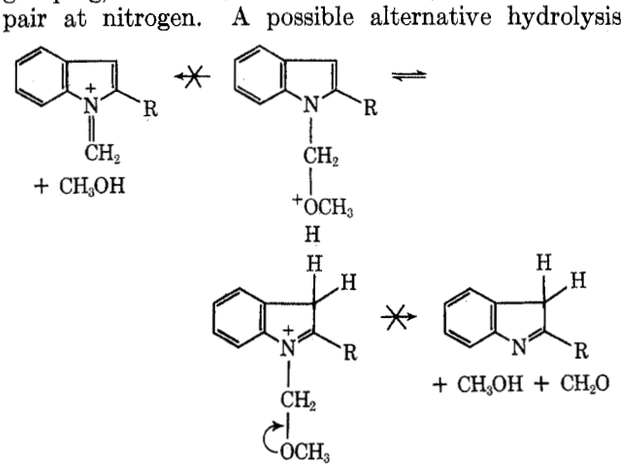


27

The mass spectrum of the compound near 200° is essentially identical with that of benzenesulfonamide. This fact is compatible with the rearrangement of the benzenesulfonyl group to a nitrogen atom derived from the nitrile. Peaks corresponding to elimination of benzenesulfonamide are not prominent in the mass spectra of compounds containing the benzenesulfonyl group as a 1 substituent on the indole ring.

In reactions of 2-LiBSI with ethyl nicotinate a pale yellow solid, mp 182–184°, having the formula $C_{22}H_{16}N_2O_2S$ was isolated in 11% yield. The mass spectrum showed a single major fragmentation with loss of the benzenesulfonyl moiety (*m/e* 141) and the nmr spectrum is in good agreement with the structure 1-benzenesulfonyl-2,2′-biindole (**28**). Hydrolysis of this compound with methanolic base gave a solid with spectral properties in accord with those expected for 2,2′-biindole (**29**), mp 301–305° (lit.[12] mp 308–310°).

Substituent Cleavage.—The methoxymethyl substituent was completely resistent to hydrolytic cleavage in acidic aqueous media. This result, which is surprising if the NCH_2OCH_3 is considered a typical carbinolamine grouping, reflects the delocalized nature of the electron pair at nitrogen. A possible alternative hydrolysis



mechanism *via* elimination of the 3*H*-indole tautomer is also evidently energetically demanding. The substituent could be cleaved in acetic anhydride utilizing lithium bromide and boron trifluoride as coreactants, but these vigorous conditions were restricted to 2-acylindoles since 2-indolylcarbinols are too sensitive to survive such vigorous conditions.[13]

The benzenesulfonyl group can be removed by relatively mild alkaline hydrolysis.[5c,14] These conditions

(12) S. A. Faseeh and J. Harley-Mason, *J. Chem. Soc.*, 4141 (1957).

(13) F. E. Ziegler, E. B. Spitzner, and C. K. Wilkins, *J. Org. Chem.*, **36**, 1759 (1971).

(14) C. D. Jones, *J. Org. Chem.*, **37**, 3624 (1972).

were successfully tested with compounds **12**, **13**, **18**, and **24** and the substituent cleavage was found to occur in excellent yield (80–95%).

These results indicate that the benzenesulfonyl group meets the necessary requirements as an N-protecting group in syntheses *via* 2-lithioindoles. It can be conveniently introduced and removed and does not usually interfere with either lithiation or subsequent reactions of the intermediate.

Experimental Section

General.—All reactions involving indole derivatives were run under nitrogen. All lithium compounds were transferred by syringe. Unless otherwise indicated the infrared bands quoted are for KBr pellets.

Preparation of N-Substituted Indoles.—A general procedure was applicable to **1a**, **1b**, **1c**, and **1d**. Sodium methylsulfinylmethide was prepared from sodium hydride and dimethyl sulfoxide as described by Corey and Chaykovsky.[7] The solution was cooled with an ice bath and 1 equiv of indole in ether solution was added dropwise, followed by stirring for 0.5 hr while warming to room temperature. The suspension which resulted was cooled to 0° and a solution of the appropriate chloride (1.1 equiv) was added dropwise with stirring. The reaction mixture was allowed to stir at room temperature for 0.5 hr and then a small amount of water was added. The reaction mixture was then poured into excess water, extracted thoroughly with ether, and evaporated to give the crude product. Specific purification procedures are described below.

1-Methoxymethylindole (1a).—The crude product from alkylation of indole (30 mmol) by methoxymethyl chloride was distilled to give a colorless oil (4.3 g, 90%): bp 69–71° (0.1 mm); nmr ($CDCl_3$) δ 3.15 (s, 3), 5.32 (s, 2), 6.45 (d, 1, J = 4 Hz), and 7.0–7.7 (m, 5).

Anal. Calcd for $C_{10}H_{11}NO$: C, 74.53; H, 6.83; N, 8.69. Found: C, 74.75; H, 6.90; N, 8.63.

1-Benzyloxymethylindole (1b).—The crude product from alkylation of indole (30 mmol) with benzyloxymethyl chloride[15] was purified by chromatography on Florisil using 2:1 hexane–benzene to elute **1b** as a pale yellow oil (8.5 g, 80%). Small quantities could be further purified by vacuum distillation: bp 156–158° (1.0 mm); nmr ($CDCl_3$) δ 4.3 (s, 2), 5.4 (s, 2), 6.48 (d, 1), 7.0–7.7 (m, 10).

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.73; H, 6.49; N, 5.84.

1-Benzylindole (1c).—Vacuum distillation of the crude product from a 50-mmol run gave **1c** (9.18 g, 89%), bp 141–143° (0.3 mm) [lit.[16] bp 172° (2 mm)].

1-Benzenesulfonylindole (1d).—The crude product from a 0.30-mol run was obtained as a pale orange-yellow oil which solidified on trituration with 2:1 hexane–ether. Recrystallization from methylene chloride–hexane using charcoal gave **1d** as white needles (70 g, 92%): mp 77.5–79°; nmr ($CDCl_3$) δ 6.53 (d, 1, J = 4 Hz), 7.0–8.1 (m, 10); $\lambda_{max}^{95\%\ EtOH}$ 252 nm (log ϵ 4.17), 275 (sh, 3.60), 285 (sh, 3.51), 292 (sh, 3.48).

Anal. Calcd for $C_{14}H_{11}NO_2S$: C, 65.36; H, 4.31; N, 5.44; S, 12.44. Found: C, 65.34; H, 4.33; N, 5.45; S, 12.55.

1-Trimethylsilylindole[17] (1e).—A solution of indole (2.34 g, 20 mmol) in THF was cooled to −12°. *n*-Butyllithium (9.5 ml of 2.1 *M* solution) was added and the reaction mixture was allowed to warm to room temperature with stirring. The solution was again cooled to −10° and a solution of trimethylchlorosilane (3.25 ml) in THF was added dropwise. The reaction mixture was stirred overnight at room temperature. After removal of a white precipitate by filtration, the solvent was evaporated and the residue was distilled to give **1e** (2.2 g, 60%) as a clear liquid: bp 82–84° (0.4 mm); ν_{NH} none; nmr (CCl_4) δ 0.56 (s, 9), 6.47 (d, J = 3 Hz, 1), and 6.9–7.6 (m, 5).

1-[Dimethyl(1,1-dimethylethyl)silyl]indole (1f).—The procedure described for **1e** using *tert*-butyldimethylchlorosilane[18] provided **1f** (3.5 g, 86%) as a liquid, bp 116–117° (1.0 mm), which solidified on standing: mp 38–39°; ν_{NH} none; nmr (CCl_4) δ 0.6 (s, 6), 0.95 (s, 9), 6.45 (d, 1, J = 4 Hz), and 6.85–7.6 (m, 5).

Anal. Calcd for $C_{14}H_{21}NSi$: C, 72.66; H, 9.15; N, 6.05. Found: C, 72.68; H, 9.21; N, 6.06.

2-Lithio-1-methoxymethylindole (2-LiMMI).—A solution of 2.3 *M* *tert*-butyllithium in hexane (12 mmol) was cooled to 0° and a solution of **1a** (1.61 g, 10 mmol) in ether was added. The orange solution was allowed to stir at room temperature for 30 min–1 hr and then used as outlined for the individual reactions.

1-Benzenesulfonyl-2-lithioindole (2-LiBSI).—A solution of 10 mmol of **1d** in ether, THF, or TMEDA was cooled to −12°. A pentane solution of *tert*-butyllithium (11–12 mmol) was added from a syringe at a moderate rate. The resulting deep red-orange solution was allowed to warm to room temperature over 15–20 min. Such solutions were used for the individual reactions described below.

Attempted Lithiation of 1-Benzyloxymethylindole (1b).—A solution of **1b** (1.185 g, 5 mmol) in THF was cooled in an ice–salt bath and 14.3 ml of 1.4 *M* *tert*-butyllithium was added. After 10 min D_2O (0.2 ml) was added and the solution was stirred for 15 min. An ether solution of the product was dried and evaporated. Chromatography of the product on Florisil gave 0.77 g (65%) of **2** having ir and nmr spectral properties similar to those of pure **2**. Further purification by preparative layer chromatography gave pure **2** which was recrystallized from chloroform–hexane: mp 83–85°; ν_{OH} 3650–3200 cm^{-1}; nmr (benzene-d_6) δ 1.85 (broad singlet), 3.75 (d, 2, J = 6 Hz), 4.4 (broad t, 1, J = 6 Hz), 6.35 (d, 1, J = 3 Hz), 6.68 (d, 1, J = 3 Hz), 6.9–7.7 (multiplet with prominent singlet at 7.0, 9).

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.82; H, 6.39; N, 5.95.

Benzoylation in pyridine gave the *O*-benzoyl derivative **3**: ν_{OH} none; ν_{CO} 1730 cm^{-1}; nmr ($CDCl_3$) δ 4.4–4.6 (AB portion of an ABX system with δ_a 4.60, δ_b 4.44, J_{ax} = 7, J_{bx} = 5, and J_{ab} = 14 Hz), 6.1–6.4 (m, 2, consists of t, 6.25, J = 6 Hz, and d, 6.35, J = 3.5 Hz), 6.82 (d, 1, J = 3.5 Hz), 6.9–7.7 (multiplet with prominent singlet at δ 7.25, 12), and 7.85–8.1 (m, 2). This compound was also isolated when the lithiation solution (prior to hydrolysis) was treated with benzoyl chloride.

2-[Dimethyl(1,1-dimethylethyl)silyl]indole (4).—A solution of **1f** (0.93 g, 4.0 mmol) in TMEDA was treated with 2.2 *M* *n*-butyllithium (1.85 ml, 4.07 mmol) and stirred at 100° for 2 hr. The reaction mixture was diluted and the product was isolated by extraction. The ether extract was washed with 1% hydrochloric acid, dried, and evaporated. Tlc showed the product to be a mixture of **1f** and **4**, mainly the latter. Pure **4** was isolated by preparative layer chromatography: mp 28–30°; ν_{NH} 3440 cm^{-1}; nmr (CCl_4) δ 0.3 (s, 6), 0.95 (s, 9), 6.5 (d, 1, J = 3 Hz), 6.8–7.8 (m, 5).

Anal. Calcd for $C_{14}H_{21}NSi$: C, 72.66; H, 9.15; N, 6.05. Found: C, 72.72; H, 9.23; N, 6.10.

Determination of Extent of Lithiation.—A solution of 5 mmol of the 1-substituted indole in 10 ml of anhydrous solvent (ether, THF, or TMEDA as noted in Table I) was cooled in an ice–acetone bath. To this solution was added 5.1 mmol of *tert*-butyllithium as a 1–2 *M* solution in pentane. The cooling bath was removed and the solution was warmed to room temperature during 15–20 min. Deuterium oxide (10 mmol) was added *via* syringe and the solution was stirred for 10 min. Ether and THF solutions were diluted with additional ether, dried over potassium carbonate, and evaporated. Reactions run in TMEDA were poured into a tenfold excess of water and extracted with ether. The combined ether extracts were washed with dilute hydrochloric acid, dried, and evaporated. In either case the crude product obtained by solvent evaporation was purified by preparative layer chromatography on silica gel and then analyzed for deuterium content by mass spectrometry. Total deuterium incorporation was derived from the parent peak region and the location was determined by measuring per cent deuteration of one or more appropriate fragment ions, using the method of calculation described by Biemann.[19] Good internal consistency of the results was found, indicating that no serious complications are arising from hydrogen migrations in the mass spectrometer.

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(16) I. Heilbron, "Dictionary of Organic Compounds," Vol. 1, Oxford University Press, New York, N. Y., 1965, p 376.

(17) A brief description of a preparation of this compound by heating indole with hexamethyldisilazane has been published: ref 5d.

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(19) K. Biemann, "Mass Spectrometry; Organic Chemical Applications," McGraw-Hill, New York, N. Y., 1962, pp 223–235.

(1-Methoxymethylindol-2-yl)phenylmethanol (5).—To a solution of 2-LiMMI (20 mmol) in TMEDA was added dropwise at room temperature a THF solution of benzaldehyde (20 mmol) and the resulting solution was stirred at room temperature for 0.5 hr. The reaction mixture was poured into water and extracted with ether. The extract was washed with 1% hydrochloric acid, dried, and evaporated. Chromatography on silica gel gave **5** (2.15 g, 40%) as an oily solid. After distillation (195–196°, 3 mm) the oil was recrystallized from ether–hexane: mp 69–71°; nmr ($CDCl_3$) δ 3.1 (s, 3), 5.25 (s, 2), 5.92 (broad s, 1), 6.18 (s, 1), 6.95–7.6 (m, 10).

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.33; H, 6.48; N, 5.19.

1-Methoxymethylindole-2-carboxylic Acid (6).—A solution of 2-LiMMI (15 mmol) was poured into an ether–Dry Ice slurry. After evaporation of the Dry Ice and solvent, the residue was refluxed for 15 min with an aqueous oxalic acid solution and then extracted with methylene chloride. The product was purified by elution from silicic acid by 1:1.5 ether–benzene (2.5 g, 80%): mp 153–154° after recrystallization from ether–hexane; nmr (DMSO-d_6) δ 3.20 (s, 3), 6.00 (s, 2), 7.07–7.8 (m, 5).

Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.42; H, 5.52; N, 6.90.

1-Methoxymethylindole-2-carboxaldehyde (7).—A solution of 2-LiMMI (10 mmol) was allowed to warm to room temperature and treated dropwise with an ether solution of *N*-methylformanilide (1.35 g, 10 mmol). The resulting suspension was refluxed for 3 hr, cooled, and hydrolyzed with 5% hydrochloric acid. The product was isolated by extraction with ether and purified by elution from Florisil with 1:1 hexane–benzene to give **7** (0.9 g, 46%) as an oil: bp 110–112° (0.1 mm); ν_{CO} 1680 cm^{-1} (neat); nmr ($CDCl_3$) δ 3.22 (s, 3), 5.86 (s, 2), 7.0–7.8 (m, 6), and 9.8 (s, 1).

Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.59; H, 5.95; N, 7.20.

1-Methoxymethyl-2-indolyl Phenyl Ketone (8).—An ether solution of benzonitrile (1.03 g, 10 mmol) was added dropwise at 0° to 2-LiMMI (10 mmol) and then stirred overnight at room temperature. After hydrolysis with aqueous ammonium chloride, the product was isolated by extraction with ether. Pure **8** was eluted from silicic acid by 1:9 benzene–hexane (2.24 g, 84%) and recrystallized from hexane: mp 56–57.5°; ν_{CO} 1640 cm^{-1}; nmr ($CDCl_3$) δ 3.30 (s, 3), 5.98 (s, 2), and 7.0–8.0 (m, 10).

Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Fund: C, 76.88; H, 5.72; N, 5.32.

A minor amount of 2,4,6-triphenyl-*s*-triazine, mp 234.5–235.5° (lit.[20] mp 234°), was identified as a by-product of this reaction.

1-Methoxymethyl-2-indolyl 4-Methoxyphenyl Ketone (9).—An ether solution of 4-methoxybenzonitrile (1.99 g, 15 mmol) was added dropwise at 0° to a solution of 2-LiMMI (15 mmol). The solution was then stirred for 1 hr at room temperature. After hydrolysis and extraction with ether, **9** was purified by elution from alumina with 1:5 ether–hexane (3.16 g, 70%) and recrystallized from chloroform–hexane: mp 97–98.5°; ν_{CO} 1640 cm^{-1}; nmr ($CDCl_3$) δ 3.28 (s, 3), 3.80 (s, 3), 5.90 (s, 2), 6.93 (d, 2, J = 8 Hz), 7.0–7.8 (m, 5), and 7.92 (d, 2, J = 8 Hz).

Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 72.78; H, 5.85; N, 4.81.

1-Methoxymethyl-2-indolyl 2-Pyridyl Ketone (10).—A solution of 2-cyanopyridine (1.04 g, 10 mmol) was added to 2-LiMMI (10 mmol) and stirred for 1 hr at room temperature. After hydrolysis with ammonium chloride, the product was isolated by extraction with ether and purified by elution from silicic acid with 1:9 ether–benzene (1.5 g, 56%): mp 92–93.5° after recrystallization from benzene–hexane; ν_{CO} 1645 cm^{-1}; nmr ($CDCl_3$) δ 3.35 (s, 3), 6.06 (s, 2), 7.0–8.15 (m, 8), and 8.7 (d, 1, J = 5 Hz).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.04; H, 5.33; N, 10.47.

1-Methoxymethyl-2-indolyl 4-Pyridyl Ketone (11).—A solution of 4-cyanopyridine (1.04 g, 10 mmol) in ether was added slowly to an ice-cooled solution of 2-LiMMI (10 mmol). The resulting suspension was stirred for 1 hr at room temperature and then hydrolyzed with ammonium chloride solution. The product mixture was extracted with ether and separated by chromatography on silicic acid. Ether–benzene (1:9) eluted **11** (1.5 g, 56%): mp 90–91° after recrystallization from hexane; ν_{CO} 1645 cm^{-1}; nmr ($CDCl_3$) δ 3.35 (s, 3), 6.0 (s, 2) 7.0–7.5 (m, 7), and 8.75 (d, 2, J = 5 Hz).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.03; H, 5.30; N, 10.51.

This was followed by variable amounts of up to 10% of 5-methoxymethyl-2,4-bis(4-pyridyl)pyrimido[5,6-*b*]indole (**26**): mp 251.5–252.5° after recrystallization from chloroform–hexane; $\lambda_{max}^{95\%\ EtOH}$ 237 nm (sh, log ε 4.25), 249 (4.38), 255 (4.39), 287 (sh, 3.85), 388 (3.89); mass spectrum *m/e* (rel intensity) 367 (49), 352 (73), 337 (47), 324 (100), 45 (58).

Anal. Calcd for $C_{22}H_{17}N_5O$: C, 71.92; H, 4.66; N, 19.06. Found: C, 71.69; H, 4.73; N, 19.01.

When the reaction was run in THF, **26** was the major product (84% yield).

1-(1-Benzenesulfonylindol-2-yl)phenylmethanol (12).—A solution of benzaldehyde (1.15 g, 10.1 mmol) in TMEDA was added dropwise to 2-LiBSI (10 mmol) in TMEDA at −10°. The solution was stirred overnight at room temperature. After isolation by extraction the product was purified by elution from a silica gel column with 5% ether in benzene. The compound solidified on trituration with ether (1.97 g, 55%) and was recrystallized from chloroform–hexane: mp 115.5–117°; ν_{OH} 3540 cm^{-1}; nmr ($CDCl_3$) δ 2.5 (s, 1), 6.3 (s, 1), 6.4 (s, 1), 7.1–8.2 (m, 14).

Anal. Calcd for $C_{21}H_{17}NO_3S$: C, 69.41; H, 4.72; N, 3.86. Found: C, 69.45; H, 4.79; N, 3.84.

1-(1-Benzenesulfonylindol-2-yl)-4-methoxyphenylmethanol (13).—A procedure analogous to that for **12** gave **13** (2.55 g, 65%) as a white solid: mp 126–127° after recrystallization from methylene chloride–hexane; ν_{OH} 3560 cm^{-1}; nmr ($CDCl_3$) δ 3.75 (s, 3), 6.3 (s, 1), 6.38 (s, 1), 6.78 (d, 2, J = 8 Hz), 7.0–8.15 (m, 11).

Anal. Calcd for $C_{22}H_{19}NO_4S$: C, 67.17; H, 4.87; N, 3.56. Found: C, 67.25; H, 4.91; N, 3.59.

1-(1-Benzenesulfonylindol-2-yl)-2-pyridylmethanol (14).—A solution of 2-LiBSI (5 mmol) was prepared in THF and brought to room temperature. A solution of pyridine-2-carboxaldehyde (0.54 g, 5 mmol) in THF was added dropwise. The resulting solution was stirred at room temperature for 15 min and then poured into water. After isolation by extraction, **14** was purified by elution from a Florisil column with 10% ether in benzene (0.59 g, 32%) and recrystallized from methanol: mp 145–147°; ν_{OH} 3180 cm^{-1}; nmr (DMSO-d_6) δ 6.42 (s, 1), 6.53 (s, 1), 6.2–6.7 (broad, 1), 7.0–8.1 (m, 12), and 8.45 (d, 1, J = 4 Hz).

Anal. Calcd for $C_{20}H_{16}N_2O_3S$: C, 65.92; H, 4.43; N, 7.69. Found: C, 65.97; H, 4.49; N, 7.61.

1-(1-Benzenesulfonylindol-2-yl)-1-phenylethanol (15).—To a solution of 2-LiBSI (10 mmol) in TMEDA was added acetophenone (1.3 g, 11 mmol). After 10 min the reaction mixture was poured into water and the product (2.42 g, 64%) was isolated by extraction: mp 129–131° after recrystallization from methylene chloride–hexane; ν_{OH} 3520 cm^{-1}; nmr ($CDCl_3$) δ 1.92 (s, 3), 5.42 (s, 1), 6.87 (s, 1), 7.0–8.2 (m, 14).

Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.02; H, 5.07; N, 3.71. Found: C, 70.04; H, 5.10; N, 3.73.

1-(1-Benzenesulfonylindol-2-yl)-1-(4-methoxyphenyl)ethanol (16).—To a solution of 2-LiBSI (10 mmol) in TMEDA was added dropwise a THF solution of 4-methoxyacetophenone (1.6 g, 11 mmol) and the reaction mixture was stirred at room temperature for 4 hr. After isolation by extraction with ether, **16** was purified by elution from silica gel with benzene (1.4 g, 35%) and recrystallized from methylene chloride–hexane: mp 137–139°; ν_{OH} 3520 cm^{-1}; nmr ($CDCl_3$) δ 1.9 (broad s, 3), 2.72 (s, 3), 5.38 (broad s, 1), 6.55–7.7 (m, 13), and 7.8–9.1 (m, 1).

Anal. Calcd for $C_{23}H_{21}NO_4S$: C, 67.81; H, 5.20; N, 3.44. Found: C, 67.86; H, 5.21; N, 3.50.

1-(1-Benzenesulfonylindol-2-yl)-1-(4-pyridyl)ethanol (17).—A solution of 4-acetylpyridine (1.3 g, 11 mmol) was added at room temperature to a solution of 2-LiBSI in TMEDA. The suspension which resulted was stirred at room temperature overnight and then poured into water. After isolation by extraction with methylene chloride, the product was obtained as a solid by trituration with ether (1.31 g, 35%) and recrystallized from chloroform–hexane: mp 229–230°; ν_{OH} 3140 cm^{-1}; nmr (DMSO-d_6) δ 1.8 (s, 3), 3.32 (s, 1), 6.02 (s, 1), 7.0–8.15 (m, 12), and 8.15–8.7 (broad, 2).

Anal. Calcd for $C_{21}H_{18}N_2O_3S$: C, 66.66; H, 4.80; N, 7.40. Found: C, 66.44; H, 4.89; N, 7.34.

1-Benzenesulfonyl-2-indolyl Phenyl Ketone (18).—A solution of benzoyl chloride (1.41 g, 10 mmol) in THF was cooled to

(20) E. Eitner and F. Krafft, *Chem. Ber.*, **25**, 2263 (1892).

−60° and a THF solution of 2-LiBSI was added rapidly. The cooling bath was then removed and the solution was allowed to come to room temperature and stirred for 1 hr. After extraction with ether and evaporation, **18** was obtained as a solid (2.35 g, 65%) by trituration with ether and recrystallized from chloroform–hexane: mp 142–144°; ν_{CO} 1660 cm^{-1}; nmr ($CDCl_3$) δ 6.87 (s, 1), 7.15–7.65 (m, 9), and 7.8–8.2 (m, 5).

Anal. Calcd for $C_{21}H_{15}NO_3S$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.85; H, 4.24; N, 3.83.

1-Benzenesulfonyl-2-indolyl 3-Pyridyl Ketone (19).—A solution of nicotinoyl chloride[21] (12.0 g, 85 mmol) in THF was cooled to −60° and 2-LiBSI (80 mmol) was added. The reaction mixture was allowed to warm to room temperature over 1 hr and then hydrolyzed by pouring into 0.04 *N* sodium hydroxide. The product was extracted with ether and purified by elution from silica gel with 1:2 ether–benzene, giving **19** (17.5 g, 60%) after trituration with ether: mp 128–129° after recrystallization from methylene chloride–hexane; ν_{CO} 1670 cm^{-1}; nmr ($CDCl_3$) δ 6.97 (s, 1), 7.2–7.65 (m, 8), 7.85–8.3 (m, 4), 8.75 (d of d, 1, J = 2, 5 Hz), 9.1 (d, 1, J = 2 Hz).

Anal. Calcd for $C_{20}H_{14}N_2O_3S$: C, 66.29; H, 3.89; N, 7.73. Found: C, 66.41; H, 3.96; N, 7.59.

Ethyl 1-Benzenesulfonylindole-2-carboxylate (20).—A THF solution of ethyl chloroformate (0.82 ml, 11 mmol) was treated at −60° with a THF solution of 2-LiBSI (10 mmol). The reaction mixture was poured into dilute alkaline brine and extracted with methylene chloride. Evaporation and trituration of the residue gave **20** (2.37 g, 75%): mp 89–91° after recrystallization from methanol; nmr (DMSO-d_6) δ 1.3 (t, 3), 4.35 (q, 2), and 7.2–8.2 (m, 10).

Anal. Calcd for $C_{17}H_{15}NO_4S$: C, 62.00; H, 4.59; N, 4.25. Found: C, 61.85; H, 4.65; N, 4.29.

1-Benzenesulfonylindole-2-carboxylic Acid (21).—A solution of 2-LiBSI (10 mmol) in THF was poured into an ether slurry of Dry Ice. The resulting mixture was acidified and the product was isolated by extraction with methylene chloride and evaporation (1.9 g, 63%): mp 188° dec after recrystallization from methylene chloride–hexane; ν_{OH} 3300–2300, ν_{CO} 1720 cm^{-1}; nmr (CH_3OH) δ 6.8–7.3 (m) and 7.45–7.8 (m).

Anal. Calcd for $C_{15}H_{11}NO_4S$: C, 59.80; H, 3.68; N, 4.65. Found: C, 59.89; H, 3.70; N, 4.64.

2-Indolyl Phenyl Ketone (22) from 2-LiBSI and Ethyl Benzoate.—A solution of ethyl benzoate (0.9 g, 6 mmol) in THF cooled in an ice–acetone bath was treated with a solution of 2-LiBSI (5 mmol) in TMEDA. After the addition, the solution was stirred for 0.5 hr, then poured into excess water. After isolation by extraction with ether, **22** was purified by elution from a silica gel column with 30% ether in hexane (0.29 g, 26%). The product was identified by melting point and comparison of its infrared spectrum with that of an authentic sample.[22]

2-Indolyl Phenyl Ketone (22) from 2-LiBSI and Benzonitrile.—A solution of 2-LiBSI (10 mmol) in ether was treated at room temperature with benzonitrile (1.03 g, 10 mmol) in ether solution. After 30 min at room temperature the reaction mixture was hydrolyzed with ammonium chloride solution. The product was isolated by extraction with ether. Trituration of the crude product gave a solid **27** described below. Chromatography of the ether-soluble portion of the product gave **22** (0.65 g, 30%), mp 147–148°, having an infrared spectrum identical with that of an authentic sample.

The maximum yield of **27** (1.6 g, 52%) was obtained when 2-LiBSI was added to a THF solution of benzonitrile at −60°. Recrystallization from methylene chloride–hexane gave pure material: mp 140–142°; ν_{NH} 3410, 3270 cm^{-1}; nmr ($CDCl_3$) δ 5.60 (d, 1, J = 2 Hz), 6.58 (s, 1), 7.1–7.7 (m, ~18–20), 8.0–8.2 (m, 2), 9.1 (broad s, 1). At 200° the mass spectrum was essentially identical with that of benzenesulfonamide, m/e 157, 141, 93, 77, and 51. At higher temperatures a weak peak at 460 (P^+ − 157) was observed.

Anal. Calcd for $C_{35}H_{27}N_3O_4S_2$: C, 68.06; H, 4.41; N, 6.80. Found: C, 67.94; H, 4.54; N, 6.74.

2-Indolyl 4-Pyridyl Ketone (23) from 2-LiBSI and Ethyl Isonicotinate.—A solution of 2-LiBSI in TMEDA (5 mmol) was added to a solution of ethyl isonicotinate (1.51 g, 10 mmol) in THF. The reaction mixture was stirred at 35° for 4 hr and then poured into water. After isolation by extraction with ether **23** was purified by elution from a silica gel column with 3:5 ether–hexane (0.34 g, 31%). The product was identified by melting point and comparison of the infrared spectrum with that of authentic material.[23]

2-Indolyl 4-Pyridyl Ketone from 2-LiBSI and 4-Cyanopyridine.—A solution of 4-cyanopyridine (0.52 g, 5 mmol) in ether was added dropwise at room temperature to a solution of 2-LiBSI (5 mmol) in ether. The solution was refluxed for 8 hr and then hydrolyzed with ammonium chloride solution. The product was isolated by extraction with methylene chloride and purified by elution from Florisil by 1:9 ether–benzene (0.58 g, 26%). The infrared spectrum was identical with that of an authentic sample.[23]

2-Indolyl 3-Pyridyl Ketone (24).—A solution of ethyl nicotinate (1.8 g, 12 mmol) in THF at 45° was treated with 2-LiBSI (10 mmol) in THF. After stirring at 45° for 1 hr the product was isolated by extraction with ether and purified by elution from silica gel with 1:2:2 chloroform–ether–benzene (0.50 g, 22%). Recrystallization from 95% ethanol gave **24**: mp 171–173°; ν_{CO} 1630 cm^{-1}; nmr ($CDCl_3$) δ 6.95–7.85 (m, 7), 8.28 (d, 1, J = 7 Hz), 8.5–9.5 (broad, 1), and 12.15 (broad s, 1).

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.65; H, 4.54; N, 12.61. Found: C, 75.44; H, 4.65; N, 12.47.

In one run in which a higher 2-LiBSI concentration was employed, elution of the column with 10% ether–benzene gave 1-benzenesulfonyl-2,2′-biindole, **28** (1.0 g, 11%): mp 182–184° after recrystallization from ethanol; ν_{NH} 3450, 3000 cm^{-1}; nmr (acetone-d_6) δ 6.8 (d, 1, J = 2 Hz), 7.0–7.9 (m, 14), 8.4 (broad s, 1).

Anal. Calcd for $C_{22}H_{16}N_2O_2S$: C, 70.96; H, 4.33; N, 7.52. Found: C, 70.89; H, 4.40; N, 7.45.

Refluxing a suspension of **28** (180 mg, 0.48 mmol) for 4 hr with 5 ml of methanol and 1 ml of 2 *N* sodium hydroxide resulted in the formation of **29**, which was isolated by filtration. Spectral evidence suggested the assigned 2,2′-biindole structure: ν_{NH} 3420 cm^{-1}; P^+ in mass spectrum, m/e 232; nmr (DMSO-d_6) δ 6.8–7.8 (m), 11.45 (s); $\lambda_{max}^{95\%\ EtOH}$ 224, 334, 352 nm (lit.[12] 224, 270, 333, 351 nm). Recrystallization from ethyl acetate gave a colorless solid, mp 301–305° (lit.[12] mp 308–310°).

2-Indolyl 2-Pyridyl Ketone (25).—A solution of 2-cyanopyridine (1.04 g, 10 mmol) in ether was added dropwise at room temperature to a solution of 2-LiBSI (10 mmol) in ether. The mixture was refluxed for 8 hr and then hydrolyzed with ammonium chloride solution. The product was isolated by extraction with chloroform, purified by elution from a silicic acid column with 1:9 ether–benzene (0.81 g, 36%), and crystallized from ether–hexane, mp 132–135° (lit.[23] mp 134.5–136°). The infrared spectrum was identical with that of an authentic sample.

Cleavage of the Methoxymethyl Substituent. 23 from 11.—A mixture of **11** (100 mg, 0.36 mmol), acetic anhydride (10 ml), lithium bromide (0.5 g), and boron trifluoride etherate (1 ml) was stirred at room temperature for 48 hr. The reaction mixture was cautiously hydrolyzed using crushed ice and extracted thoroughly with ether. The ether extracts were washed with sodium bicarbonate solution, dried, and evaporated leaving **23** (66 mg, 86% yield), identified by melting point and infrared comparison with an authentic sample.

Hydrolysis of the Benzenesulfonyl Group. 1-(2-Indolyl)-phenylmethanol (30) from 12.—A solution of **12** (0.18 g, 0.50 mmol) was heated at steam bath temperature with a 5:1 methanol–2 *N* sodium hydroxide mixture for 8 hr. The product was isolated by extraction with ether and purified by preparative layer chromatography (0.098 g, 88%): ν_{OH} 3650–3150 cm^{-1}; nmr ($CDCl_3$) δ 2.7 (broad s, 1), 5.7 (s, 1), 6.15 (d, 1, J = 3 Hz), 6.9–7.6 (m with prominent s at 7.25, 9), and 8.15 (broad s, 1).

Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.96; H, 5.82; N, 6.31.

1-(2-Indolyl)-1-(4-methoxyphenyl)methanol (31) from 13.—A solution of **13** (1.97 g, 5.0 mmol) was heated at steam-bath temperature for 12 hr in methanol (50 ml) and 2 *N* sodium hydroxide (10 ml). The product was isolated by extraction with ether and evaporation (1.03 g, 81%): mp 98–100° after recrystallization from methylene chloride–hexane; ν_{NH} 3430, ν_{OH} 3350 cm^{-1} (broad); nmr ($CDCl_3$) δ 3.0 (broad s, 1), 3.7 (s, 3), 5.7 (broad s, 1), 6.15 (d, 1, J = 3 Hz), 6.75 (d, 2, J = 8 Hz), 6.9–7.6 (m, 6), and 8.2 (broad s, 1).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.81; H, 6.01; N, 5.62.

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(22) R. J. Sundberg, *J. Org. Chem.*, **30**, 3604 (1965).
(23) R. J. Sundberg, H. F. Russell, W. V. Ligon, Jr., and L.-S. Lin, *J. Org. Chem.*, **37**, 719 (1972).

2-Indolyl Phenyl Ketone (22) from 18.—A suspension of **18** (0.18 g, 0.50 mmol) in 8 ml of ethanol and 2 ml of 2 *N* sodium hydroxide was refluxed for 2 hr. The reaction mixture was diluted with water and **22** was isolated by extraction with chloroform (0.107 g, 97%). The melting point and infrared spectrum were identical with those of pure **22**.

2-Indolyl 3-Pyridyl Ketone (24) from 19.—A suspension of **16** (7.6 g, 21 mmol) in a solution of 200 ml of methanol and 40 ml of 2 *N* sodium hydroxide was refluxed until hydrolysis was complete (20 hr). The solution was adjusted to pH 8 and the methanol was evaporated. Extraction with methylene chloride gave **24** (6.3 g, 83%), mp 166–171°, having an infrared spectrum identical with that of pure **24**.

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Registry No.—**1a**, 40899-68-1; **1b**, 40899-69-2; **1c**, 3377-71-7; **1d**, 40899-71-6; **1e**, 17983-42-5; **1f**, 40899-73-8; **2**, 40899-74-9; **3**, 40899-75-0; **4**, 40899-76-1; **5**, 40899-77-2; **6**, 40899-78-3; **7**, 40899-79-4; **8**, 40899-80-7; **9**, 40899-81-8; **10**, 40899-82-9; **11**, 40899-83-0; **12**, 40899-84-1; **13**, 40899-85-2; **14**, 40899-86-3; **15**, 40899-87-4; **16**, 40899-88-5; **17**, 40899-89-6; **18**, 40899-90-9; **19**, 40899-91-0; **20**, 40899-92-1; **21**, 40899-93-2; **22**, 1022-86-2; **24**, 40899-94-3; **25**, 24512-42-3; **26**, 40899-96-5; **27**, 40899-97-6; **28**, 40899-98-7; **29**, 40899-99-8; **30**, 40900-00-3; **31**, 40900-01-4; 2-LiMMI, 40900-02-5; 2-LiBSI, 40900-03-6; indole, 120-72-9; methoxymethyl chloride, 107-30-2; benzyloxymethyl chloride, 3587-60-8; benzyl chloride, 100-44-7; benzenesulfonyl chloride, 98-09-9; trimethylchlorosilane, 75-77-4; *tert*-butyldimethylchlorosilane, 18162-48-6; *N*-methylformanilide, 93-61-8; benzonitrile, 100-47-0; 4-methoxybenzonitrile, 874-90-8; 2-cyanopyridine, 100-70-9; 4-cyanopyridine, 100-48-1; benzaldehyde, 100-52-7; 4-methoxybenzaldehyde, 123-11-5; pyridine-2-carboxaldehyde, 1121-60-4; acetophenone, 98-86-2; 4-methoxyacetophenone, 100-06-1; 4-acetylpyridine, 1122-54-9; benzoyl chloride, 98-88-4; nicotinoyl chloride, 10400-19-8; ethyl chloroformate, 541-41-3; ethyl benzoate, 93-89-0; ethyl nicotinate, 614-18-6.

Syn–Anti Isomerization of *N*-(*p*-Tolyl)imines of Ferrocenyl, Ruthenocenyl, and (Cyclobutadienyliron Tricarbonyl) Phenyl Ketones

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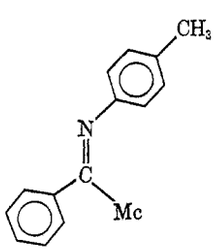
The *N*-(*p*-tolyl)imines of ferrocenyl, ruthenocenyl, and (cyclobutadienyliron tricarbonyl) phenyl ketones were prepared in moderately good yield. Studies of their syn–anti isomerization using the dnmr technique allowed the determination of their free energies of activation. The validity of approximate equations to determine free energies of activation as well as the conditions necessary for successful complete line-shape analysis are discussed.

Recently we reported[1] evidence for the syn–anti isomerization of imines I and II. In that report we

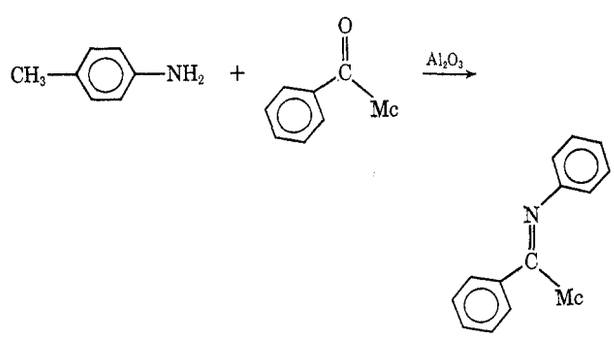


I, Mc = ferrocenyl
II, Mc = ruthenocenyl
III, Mc = cyclobutadienyliron tricarbonyl

drew attention to the approximate nature of the dnmr measurements used as supporting evidence for the isomerization. In this paper we not only extend our measurements to compound III, but also bring to light our attempts to apply complete line-shape analysis to the dynamic nuclear magnetic resonance (dnmr) data. In addition, the preparations of compounds I, II, and III are discussed.

Results and Discussion

The three compounds used in this study were prepared using the method of Hetnarski and Grabowski[1,2] in which *p*-toluidine and the appropriate phenone compound were condensed in the presence of aluminum oxides. This method originally had been successfully applied[2] only to ferrocene derivatives. We have expanded the method's utility and it appears to be fairly



general for the reaction of metallocene and metallocene-like ketones with aromatic amines. The beauty of the method is that it can be carried out under mild conditions (refluxing toluene), that it is quite clean (followed by thin layer chromatography), and that work-up is fairly simple. Purified yields range from 40 to 50%.

Characterization of I–III was accomplished using infrared, mass, and nuclear magnetic resonance spectroscopy and elemental analysis. Examination of both ir and nmr spectra made it clear that a mixture of isomers had been obtained. As examples: Compound I and II have doubled signals of unequal intensity assigned to the *p*-methyl group and to the unsubstituted cyclopentadienyl hydrogens. Compound III has two signals for its *p*-methyl group as well as doubled signals in the cyclobutadienyl group. It should be noted that we have observed other signal doubling, but that it occurs with protons of low intensity and high splitting and is consequently less dramatic. In Table I we have compiled the nmr data for compounds I–III. The unequal intensities of the signals indicated in Table I show that in compounds I and II one isomer predominates by six- to tenfold while the isomer ratio in III is

(1) R. Damrauer and T. E. Rutledge, *J. Organometal. Chem.*, **29**, C 9 (1971).

(2) B. Hetnarski and Z. Grabowski, *Bull. Acad. Pol. Sci.*, **17**, 391 (1969).