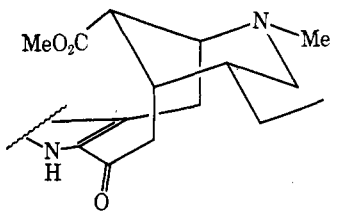
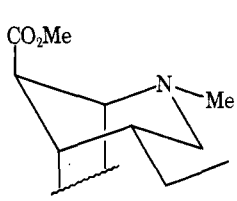
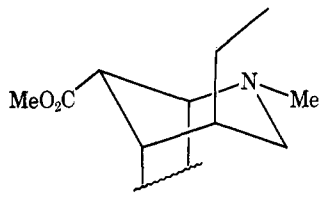
shielding on C(20). This γ effect is possible only in the presence of an axial H(20) and constrains the ethyl group to an equatorial orientation, as illustrated in partial structures **4** and **5**, respectively. As a consequence, tabernaemontanine (**1b**) must possess an axial ethyl function (**6**). This is confirmed by the loss and gain of γ effects in **1b** relative to **1a** at C(14) and C(16), respectively. Furthermore, the chemical shift of the methyl component of the ethyl group reflects the conformation of the two-carbon side chain.[7]



4



5



6

While the shifts of the carbomethoxy group of 16-epidregamine (**3, 5**) are characteristic of methyl cyclohexanecarboxylates,[3b,8] the carbonyl and methoxy groups of compounds **1, 2a,** and **2b** are shielded anomalously by 2.7 ± 0.4 and 1.8 ± 0.2 ppm, respectively. These shift perturbations reflect the close proximity of the carbomethoxy group in substances **1** and **2** to the α-acylindole moiety and are diagnostic of the C(16) stereochemistry. The indole α carbon and neighboring keto carbon respond likewise by being shielded by 1.2 ± 0.1 and 2.0 ± 0.1 ppm, respectively. Since strong anisotropic shielding (0.89 ppm) of the methoxy hydrogens of vobasine (**2a**), relative to 16-isovobasine, by the indole ring was observed some time ago,[5] the shift perturbation of the methoxy carbon may be due to the same effect. Anisotropic shielding of carbon centers has been predicted to be comparable in magnitude to such shielding observed in ^{1}H NMR spectroscopy[9] and therefore has been difficult to isolate as a unique contribution to the chemical shift.[10]

The methyl ester carbonyl shift of vobasinyl acetate (**2d**) is similar to that of the 3-keto systems **1, 2a,** and **2b,** while that of vobasinol (**2c**) is downfield 4.3 ppm owing to hydrogen bonding with the 3β-hydroxy group.[8]

Conjugation of a carbonyl group with the indole ring through its α carbon causes shift alteration throughout the aromatic system. The strong deshielding of the customarily high-field indole β carbon[3,11] is especially characteristic of the α-acyl attachment.

Experimental Section

The ^{13}C NMR spectra were recorded on Bruker HX90E and Varian XL-100-15 spectrometers operating at 22.6 and 25.2 MHz in the Fourier transform mode, respectively. The shifts indicated on formula i are from a deuteriochloroform solution [$\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm] and the stars thereon represent interchangeable signals.

Acknowledgment. The authors express their sincere thanks to Aline and Henri-Philippe Husson for the preparation of 21-deuteriotabernaemontanine, Abbas Shafiee for the deuterated derivatives of **1a** and **3**, Pierre Mangeney and Yves Langlois for a sample of i, and Jean-Pierre Cosson and B. C. Das for a sample of **2b**.

Registry No.—**1a,** 2299-26-5; **1b,** 2134-98-7; **2a,** 2134-83-0; **2b,** 2134-97-6; **2c,** 7168-77-6; **2d,** 58324-78-0; **3,** 52389-31-8.

References and Notes

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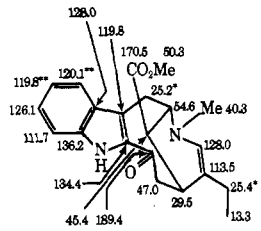
(2) Address correspondence to Department of Chemistry, Rice University, Houston, Texas 77001.
(3) (a) M. C. Koch, M. M. Plat, N. Préaux, H. E. Gottlieb, E. W. Hagaman, F. M. Schell, and E. Wenkert, *J. Org. Chem.*, **40**, 2836 (1975); (b) E. Wenkert, C.-J. Chang, H. P. S. Chawla, D. W. Cochran, E. W. Hagaman, J. C. King, and K. Orito, *J. Am. Chem. Soc.*, in press; and preceding papers.
(4) The recent conversion of tabernaemontanine (**1b**) into ervatamine and the latter's x-ray analysis[1a] indicated the necessity of the revision of the alkaloid's heretofore accepted stereostructure [U. Renner, D. A. Prins, A. L. Burlingame, and K. Biemann, *Helv. Chim. Acta*, **46**, 2186 (1963)].
(5) M. P. Cava, S. K. Talapatra, J. A. Weisbach, B. Douglas, and G. O. Dudek, *Tetrahedron Lett.*, 53 (1963).
(6) The carbon shifts of this substance are delineated on formula i.



i

(7) The ca. 1 ppm difference of C(18) shifts has been shown earlier to be diagnostic of the C(20) stereochemistry in corynantheoid alkaloids.[3a]
(8) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
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A Convenient Method for Estimation of Alkyllithium Concentrations

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Alkyllithium reagents have become increasingly important in organic synthesis. Commercial alkyllithium reagents are usually accompanied with a lot analysis, but often even freshly obtained solutions have obviously deteriorated, being dark colored and cloudy, and most alkyllithium solutions deteriorate after the container is opened. For use in metalation reactions and alkylations, an excess or a deficiency of alkyllithium is often detrimental, especially where dilithio intermediates are formed.[1] Thus analysis of an alkyllithium reagent is often desirable.

The standard procedure for such an analysis requires a double titration—total alkali, which includes the alkyllithium and such species as alkoxides formed by reaction of the reagent with air, from which is subtracted that portion which does not react rapidly with certain halides. The method is said not to be useful for certain alkyllithium reagents.[2]

Since the organolithium compound is so often used for metalation, we offer a convenient method of analysis which is based on the reaction for which the reagent is intended, namely carbon lithiation, and which produces a color at the end point and is thus independent of indicator. A similar acid–indicator system has been proposed; however, solvent plays a critical role, and there is some difference from the values determined by the double titration procedure.[3]

We noticed in the metalation of certain pyridine esters that the red dianion color was not observed until the butyllithium

Table I. Standardization of Alkyllithium Solutions[a]

Sample	Label	Method	Concn
BuLi[b]	1.6 M	$(C_6H_5)_2CHCOOH$	1.47
		Double titration	1.48
BuLi[c]	1.66 M	$(C_6H_5)_2CHCOOH$	1.12
		Double titration	1.14
CH_3Li[d]	1.56 M	$(C_6H_5)_2CHCOOH$	1.06
		Double titration[e]	1.12
CH_3Li[f]	2.1 M	$(C_6H_5)_2CHCOOH$	1.78
		Double titration	1.80

[a] At least two determinations in agreement. [b] The bottle had previously been opened but there was no discoloration or sediment. [c] The bottle had previously been opened, there was much sediment, and the solution was dark brown. [d] The bottle had previously been opened and there was much sediment. [e] The double titration is said not to be useful for methyllithium when benzyl chloride is used; we used dibromoethane in all our double titrations. [f] The bottle had not previously been opened.

was considerably in excess of that calculated (from the lot analysis) for complete formation of the yellow monoanion.[4] Careful standardization of the butyllithium indicated a low titer. However if the lot analysis was ignored, the volume of a molar equivalent was indicated by initial formation of the red dianion color, and it was sufficient to add a second equal volume to form the dianion completely.

$$\underset{}{\text{H–P–H}} \rightarrow \underset{\text{(yellow)}}{\text{H–P–Li}} \rightarrow \underset{\text{(red)}}{\text{Li–P–Li}}$$

The involved synthesis of the pyridine ester precludes its widespread use for this purpose,[5] but many compounds produce dianions differently colored from the monoanion, and one of these, cheap and readily available, is proposed.

Diphenylacetic acid has the advantage of being a solid, stable on storage and easily weighed. A sample of diphenylacetic acid (typically 0.50 g) is weighed into an Erlenmeyer flask and dissolved in tetrahydrofuran (10 ml), and the alkyllithium solution is run in from a syringe until the yellow end point is reached. The yellow color indicates formation of lithium α-lithiodiphenylacetate after all the carboxyl proton is consumed.

$$(C_6H_5)_2CHCOOH \rightarrow \underset{\text{(colorless)}}{(C_6H_5)_2CHCOO^-Li^+} \rightarrow \underset{\text{(yellow)}}{(C_6H_5)_2CLiCOO^-Li^+}$$

Table I summarizes results from several commercial samples of alkyllithium reagents.

Registry No.—BuLi, 109-72-8; CH_3Li, 917-54-4; $(C_6H_5)_2CHCOOH$, 117-34-0.

References and Notes

(1) See, for example, W. G. Kofron and M. K. Yeh, *J. Org. Chem.*, **41**, 438 (1976).
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