(30), 320 (64), 307 (100); HRMS calcd for $C_{37}H_{40}O_2$ 516.3028, found 516.3046.

7c: oil; NMR (400 MHz) δ 7.80–7.11 (13 H, m), 7.06 (1 H, s) and 6.88 (1 H, s) for aromatic protons, 2.91 (2 H, sep, J = 7.1 Hz, CH), 2.72 (2 H, t, J = 7.7 Hz, CH_2), 2.67 (2 H, t, J = 7.6 Hz, CH_2), 2.52 (1 H, broad s, OH), 1.99 (2 H, quin, J = 7.7 Hz, CH_2), 1.45 (3 H, s, CH_3), 1.27 (6 H, d, J = 7.1 Hz, CH_3), 1.23 (3 H, d, J = 7.1 Hz, CH_3), 1.17 (3 H, d, J = 7.1 Hz, CH_3), 0.81 (3 H, s, CH_3); UV (cyclohexane) λ 344 (ϵ 151) nm; MS, m/e (relative intensity) 530 (M^+, 12), 487 (100), 307 (64), 105 (51); HRMS calcd for $C_{38}H_{42}O_2$ 530.3184, found 530.3092.

Quantum Yields. Solutions containing diketones **6a–c** in benzene (0.001–0.05 M) were placed in 17 × 120 mm Pyrex tubes and degassed by four freeze–thaw cycles below 10^{-2} mmHg. These samples were irradiated on a merry-go-round apparatus at 25 °C. The light that was isolated from a 400-W high-pressure mercury lamp with a K_2CO_3 (1.3%)–K_2CrO_4 (0.13%) filter solution (mainly 313 nm) was employed. The benzocyclobutenols **7a–c** produced (conversion <5%) were analyzed by HPLC by using diphenylsulfone as an internal standard. The benzocyclobutenol formation from **3** in benzene solution (0.1 M) was used as actinometry (Φ_{CB} = 0.60). The light absorbed by each sample was corrected by a factor ($1 - 10^{-A}$), where A is the absorbance of the solution ($A = \epsilon cl$: $\epsilon = \epsilon$ at 313 nm, c = the initial concentration of **6a–c** or **3**, l = 1 cm).

Simple Direct Titration of Organolithium Reagents Using *N*-Pivaloyl-*o*-toluidine and/or *N*-pivaloyl-*o*-benzylaniline

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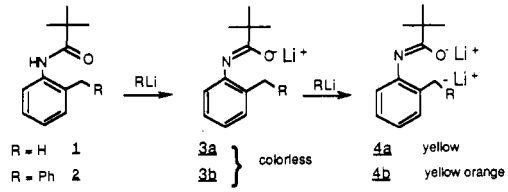
During the last decade, the use of alkyl- and aryllithium reagents in organic synthesis has increased as the result of important developments of the chemistry of many organometallic species. Accurate determination of the concentration of the reagents is generally necessary to generate reactive intermediates. Several methods[2-10] of titration have been described; some of them use the formation of a colored dianion species at the end point. The Gilman and Cartlege[2] and the diphenylacetic[7] methods are the most widely used. Recently, Juaristi et al.[10] reported a method for the determination of alkyllithium concentration based on the use of 4-biphenylmethanol as reagent indicator.

We report here a new and efficient method for the accurate determination of organolithium species by direct titration. We noticed that when **1**[1] or **2**[1] in THF is treated with organolithium reagents, the initial reaction produces a colorless solution of the enamide **3a** or **3b**, but when the formation of the enamide is complete, a drop of the organolithium species immediately gives an intense yellow or yellow-orange color due to the formation of the dianion **4a** or **4b** (Scheme I). We emphasize that the solution containing the reagent indicator **1** or **2** is completely colorless, even after addition of 0.992 equiv of the alkyllithium species. This is not the case for the simple methods described in the literature. *N*-pivaloyl-*o*-toluidine and *N*-pivaloyl-*o*-benzylaniline are easily accessible from commercially available compounds in one step in gram quantities. They are crystalline compounds, nonhygroscopic, stable, and may be stored without any special precautions.

Scheme I



The visible spectra of the colored solutions obtained when **1** and **2** were treated with 1.05 equiv of BuLi (THF, room temperature) show an absorption with λ_{max} = 435 and 440 nm, respectively. By comparison, the dianion of 4-biphenylmethanol shows an absorption at λ_{max} = 483 nm in THF at 20 °C.[10]

The titration results are summarized in Table I. In the case of tBuLi, addition of 1 equiv of tBuOLi did not change the result, indicating that there is no interaction between the reagent and a strong lithium alkoxide. The titration of MeLi with **1** does not display an as intensly colored end point as that of BuLi or tBuLi. Nevertheless, satisfactory results are obtained. We noticed that when **1** is used for the titration of PhLi, the end point is not sharp. This fact is probably due to the lower basicity of PhLi compared to the other alkyllithium reagents. Thus although **1** is not suitable for titration of PhLi, good results are obtained with reagent **2**. In all titrations attempted thus far, with the sole exception of PhLi and **1**, good agreement was found between this method and other commonly used analytical procedures.

Experimental Section

Tetrahydrofuran was distilled from sodium/benzophenone, and dichloromethane was distilled from CaH_2 prior to use. Organolithium reagents were purchased from Aldrich Chemical Co. and Janssen Chemicals. Compounds **1** and **2** were synthesized as describe below. *o*-Toluidine, *o*-benzylaniline, and pivaloyl chloride were purchased from Aldrich Chemical Co. and were not purified

Table I. Comparative Titrations of Organolithium Reagent[i]

RLi	1	2	ref 2	ref 7	ref 3	ref 10	total base[k]	nom value
BuLi[a]	1.64	1.65	1.71	1.61	1.69	1.65	1.87	1.60[g]
BuLi[b]	2.37	2.35	2.38	2.36	2.49	2.29	2.50	1.60[g]
sBuLi[c]	1.31	1.30	1.24	1.32	1.09	1.20	1.46	1.30[g]
tBuLi[a]	1.88	1.87	1.90	1.88	1.61	1.62	2.09	1.70[g]
tBuLi[d] + tBuOLi	1.88							
MeLi[e]	1.42	1.47	1.48	1.49	1.51	1.46	1.56	1.60[h]
MeLi[f]		1.43	1.50	1.51	1.68		1.86	1.60[h]
PhLi		0.94	1.05	0.95	1.04	0.89[j]	2.05	2.00[g]

[a] New bottle without any sediment. [b] The bottle had previously been opened and some solvent had evaporated. [c] New bottle, brown solution. [d] One equivalent of tBuOLi was added to the THF solution containing the reagent 1. [e] Clear solution, the bottle has been opened and used, no sediment. [f] Old bottle but never opened and containing a lot of sediment. [g] From Aldrich C[ie]. [h] From Janssen C[ie]. [i] Average of three determinations. [j] The end point was not very clear. [k] Titration using 0.1 N hydrochloric acid solution with phenolphthalein as indicator after hydrolysis of 5-mL aliquot of the organolithium solution by 10 mL of distilled water.

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prior to use. All glassware was dried in an oven at 140 °C and purged with argon before titration.

***N*-Pivaloyl-*o*-toluidine (1).** In a 250-mL flask, *o*-toluidine (10 g, 0.093 mol) and Et_3N (9.41 g, 0.093 mol) were mixed together in CH_2Cl_2 (50 mL). The solution was cooled to 0 °C, and a solution of pivaloyl chloride (11.2 g, 0.093 mol) dissolved in CH_2Cl_2 (10 mL) was slowly added. On completion of the addition, the solution was stirred for $^1/_2$ h and then poured into water (200 mL). The organic layer was washed with water (3 × 100 mL) and dried over Na_2SO_4. Evaporation of the solvent afforded a crude white solid, which after two recrystallizations from hot methylene chloride-/hexane (12/80 mL) afforded *N*-pivaloyl-*o*-toluidine as a white crystalline solid: yield 88%; mp 109–110 °C (lit.[11] mp 109–111 °C). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.36; H, 8.96; N, 7.32. Found: C, 75.62; H, 8.92; N, 7.24.

***N*-Pivaloyl-*o*-benzylaniline (2).** The same procedure as above was used. Recrystallization of the crude product from hot hexane (200 mL) afforded *N*-pivaloyl-*o*-benzylaniline as a white crystalline solid: yield 90%; mp 83 °C (lit.[11] mp 78–80.5 °C). Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 81.14; H, 8.06; N, 5.19.

Titration of Organolithium Reagent. A 25-mL round-bottom flask fitted with a septum and containing a magnetic stirring bar was evacuated and flushed with argon or nitrogen. Approximately 250–380 mg (0.9–2.0 mmol) of the reagent 1 or 2 was charged into the flask. Anhydrous THF (5–10 mL) was added, and a white sheet of paper was placed behind the flask. The organolithium solution was added from a 1-mL Hamilton gas-tight syringe. The solution was rapidly stirred under argon. Triplicate analyses were performed in all cases.

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Registry No. 1, 61495-04-3; 2, 85864-33-1; BuLi, 109-72-8; *s*-BuLi, 598-30-1; *t*-BuLi, 594-19-4; MeLi, 917-54-4; PhLi, 591-51-5; *o*-toluidine, 95-53-4; pivaloyl chloride, 3282-30-2; *N*-pivaloyl-*o*-benzylaniline, 28059-64-5.

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Selective Synthesis and Hydrolysis of Dimethyl *cis,cis*-3-Halomuconates

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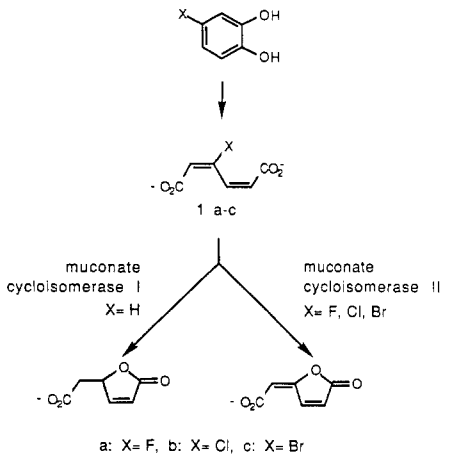
The microbial degradation of halogenated aromatic acids has received increased attention recently in light of its importance in the detoxification of environmental pollutants.[2] A key step in the degradation of 4-halocatechols is the lactonization and dehalogenation of the 3-halomuconates catalyzed by muconate cycloisomerase II (Scheme I).[3] A number of important questions concerning the chemical mechanism of this conversion have remained unresolved due to the lack of an unambiguous chemical synthesis of these substrates. Thus, we here report the synthesis of the dimethyl *cis,cis*-3-halomuconates[4] and their hydrolysis.

Scheme I



In reference to the three known isomers of unsubstituted muconic acid,[5,6] it has been established that only the cis,cis isomer is a substrate for muconate cycloisomerase I (Scheme I).[7] By analogy, it is generally accepted that only the cis,cis isomers of the 3-halomuconates **1a–c** are biologically active.[8,9] Detailed characterization of the geometry of the biological substrates, however, has been impaired by their instability in acidic media toward C-4, C-5 double bond isomerization and lactonization.[8,9]

The classical synthesis of *cis,cis*-muconic acid involves the oxidation of phenol[5,10] or catechol[11] with peracetic acid. This method has been applied to the synthesis of 3-chloromuconate,[9] yielding an unidentified mixture of isomers. In our hands the Fe(III)-catalyzed oxidation of 4-chlorocatechol with peracetic acid[11] produced only the cis,trans isomer **6b**. Several other reported methods for the synthesis of *cis,cis*-muconic acid or its derivatives[12] have not produced satisfactory results when applied to the synthesis of the title compounds.

Alkyl-substituted 1,2-benzoquinones are known to undergo oxidation with lead tetraacetate in the presence of methanol to give the alkyl-substituted dimethyl *cis,cis*-muconates.[13,14] We were able to obtain the title com-

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(4) To simplify the discussion of the various isomers we use the trivial nomenclature, where the cis,cis or cis,trans prefix refers to the orientation of the hexadienedioate carbon skeleton. The systematic name of these compounds is (2*E*,4*Z*)-dimethyl 3-halo-2,4-hexadienedioate.
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