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Registry No. Fe(TPP)O₂, 88083-22-1; O₂, 7782-44-7; OFe(TPP), 84152-32-9; ¹⁸O, 14797-71-8.

Synthesis of 2-Functionalized 1,1-Diiodo-1-alkenes. Generation and Reactions of 1-Iodo-1-lithio-1-alkenes and 1,1-Dilithio-1-alkenes

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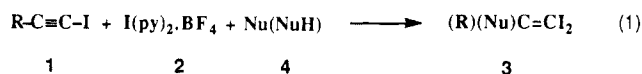
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In recent years, 1,1-dilithio-1-alkenes have been the center of interest.^{1,2} A few compounds of this class have been prepared,^{1,3} but in all the cases the 1,1-dilithioalkenes were unfunctionalized. We report here the first preparation of a β -functionalized 1,1-dilithio-1-alkene and its precursor, a 1-iodo-1-lithio-1-alkene, by treatment of a 1,1-diiodo-1-alkene with organolithium compounds as well as some synthetic applications of these lithioalkenes. A general method for the synthesis of previously undescribed 2-substituted 1,1-diiodo-1-alkenes are also shown.

Examples of 1,1-diiodo-1-alkenes containing a function in 2-position are unknown,⁴ but they could be appropriate antecedents for functionalized 1,1-dilithio-1-alkenes. This fact prompted us to study the reactivity of 1-iodoacetylenes **1**⁵ toward bis(pyridine)iodine(I) tetrafluoroborate **2**,⁶ since this reagent adds I⁺Nu⁻ to internal acetylenes⁷ and thus would lead to a general entry to 1,1-diiodo-1-alkenes **3**.

When the iodinating reagent **2** is allowed to react with 1-iodoacetylenes **1** and a wide variety of nucleophiles **4**, 2-substituted 1,1-diiodo-1-alkenes **3** are produced in good to very good yields (see eq 1 and Table I).



1a, R = Ph; **1b**, R = *n*-C₄H₉

The reaction conditions are similar to the additions earlier mentioned.⁷ These processes are clean, and, after the usual workup procedures, compounds **3** are obtained in more than 90% purity.

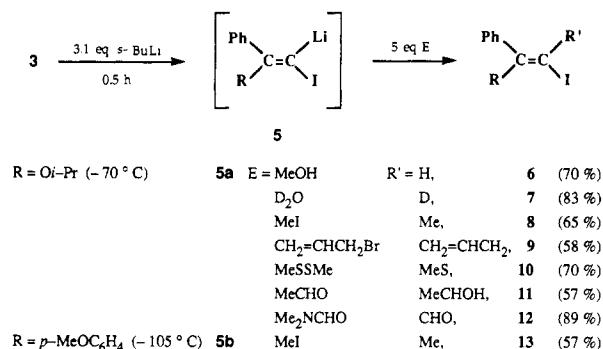
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Table I. Synthesis of Compounds **3**

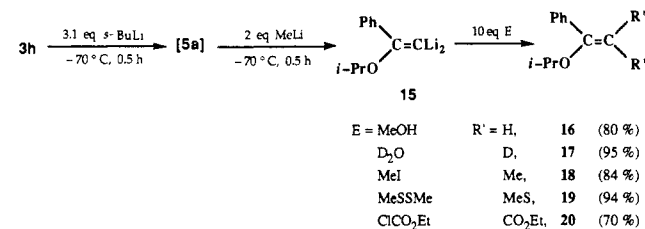
1	nucleophile	solvent	time ^a (h)	3	yield ^b (%)
a	ClSiMe ₃	CH ₂ Cl ₂	3	a ^c	65
a	Br ⁻	MeCN/H ₂ O	60	b	64
b	I ⁻	MeOH	14	c	70
a	NCS ⁻	dioxane/H ₂ O	60	d	75
a	pyridine	CH ₂ Cl ₂	20	e	57
b	CH ₃ COOH	CH ₃ COOH/CH ₂ Cl ₂ (2:1)	14	f	63
a	HCOOH	85% HCOOH/CH ₂ Cl ₂ (2:1)	14	g	85
a	<i>i</i> -PrOH	<i>i</i> -PrOH/CH ₂ Cl ₂ (2:1)	4	h	80
a	anisole	CH ₂ Cl ₂	22	i ^d	50 ^e
a	PhSH	CH ₂ Cl ₂	15	j	80

^a At room temperature except for the synthesis of **3a** and **3i** (-50 °C). ^b Yields of isolated products, relative to starting **2** and not optimized. ^c Structural formula (Ph)(Cl)C=Cl₂. ^d Structural formula (Ph)(*p*-CH₃OC₆H₄)C=Cl₂. ^e The crude reaction mixture contains 20% of *p*-iodoanisole.

Scheme I



Scheme II

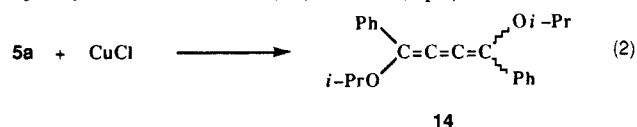


The synthetic potential of these new 2-functionalized 1,1-diiodo-1-alkenes by transformation of each iodine atoms is noteworthy. In this paper we describe the conversion of aromatic 1,1-diiodo-1-alkenes **3** to 1-iodo-1-alkenes and 1,1-dilithio-1-alkenes.

When compound **3** bearing an isopropoxy (**3h**) or a *p*-methoxyphenyl (**3i**) group in the 2-position is treated in THF with an excess of *sec*-butyllithium, a solution of the organolithium system **5** is obtained. The reaction of **5** with different electrophiles gives the corresponding monosubstituted products **6-13** (Scheme I).

The solution of **5a** is stable at -20 °C. Above this temperature it slowly begins to decompose, yielding the product **6** corresponding to abstraction of a solvent proton. At room temperature treatment of **5a** with an excess of iodomethane gives a complex mixture of **8**, **6**, and 1-isopropoxy-2-phenylacetylene (analyzed by ¹³C NMR).

A solution of **5a** in the presence of cuprous chloride (3 eqs) at -60 °C is quantitatively transformed in 1,4-diisopropoxy-1,4-diphenyl-1,2,3-butatriene (**14**)⁸ in 2 h (eq 2).



(8) Compound **14** is a stable yellow solid (mp 105-107 °C, MeOH) corresponding to a single diastereoisomer but at 60 °C in methanol is converted in a *cis-trans* mixture (1:1). Its spectral data (IR, ¹H and ¹³C NMR, and MS) and the acidic hydrolysis to *trans*-1,4-diphenyl-2-buten-1,4-dione are in accordance with the proposed 1,2,3-butatrienic structure.

The stereochemistry of compounds **6**, **8**, and **10** was confirmed by NOE experiments. The structure of the β -functionalized compound **5** is not well defined due to its carbenoid nature, but its chemical behavior suggests a trans relationship for the lithium and the isopropoxy groups. Recently, we have prepared and characterized examples of 2-functionalized lithioalkanes which are rare and unstable species.⁹ Some β -functionalized lithioalkanes have been reported,¹⁰ but the trans compounds undergo β -elimination reactions except in a few cases in which a halogen is present in the α -position.¹¹

The vinylic iodine present in compound **5** can undergo an exchange reaction with another organolithium reagent yielding the β -functionalized 1,1-dilithio-1-alkene. The consecutive treatment of a solution of **5a** with methylolithium¹² and conventional electrophiles affords the disubstitution products **16–20** (Scheme II).

The THF solutions of **15** are stable at -70°C , and they give the same results shown in Scheme II upon treatment with electrophiles after 10 h at this temperature.

The yields and purities of compounds **3**, **6–13**, and **16–20** were determined by GC, and the spectral data (IR, ^1H NMR, ^{13}C NMR, and MS) are in accordance with the proposed structures.¹³ The derivatives carrying an isopropoxy group are easily hydrolyzed to the corresponding carbonyl systems.¹⁴

Among all the products derived from lithioalkenes **5** and **15** we can emphasize the synthetic interest of the unconjugated diene **9**, the tetrasubstituted alkene **10**, the 1,2,3-trifunctionalized compounds **11** and **12** (with very different functional groups), the masked functionalized ketene **19** and the β -tricarbonyl compound **20**.

These results show the possibility of the preparation of β -functionalized 1-iodo-1-lithio-1-alkenes and 1,1-dilithio-1-alkenes and their use as synthons of the type $\text{RR}'\text{C}=\text{C}<$ or $\text{RCOCH}<$ after hydrolysis.

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Registry No. **1a**, 932-88-7; **1b**, 1119-67-1; **2**, 15656-28-7; **3a**, 115117-72-1; **3b**, 115117-47-0; **3c**, 115117-48-1; **3d**, 115117-49-2; **3e**, 115117-73-2; **3f**, 115117-50-5; **3g**, 115117-51-6; **3h**, 115117-52-7; **3i**, 115117-53-8; **3j**, 115117-54-9; **5a**, 115117-55-0; **5b**, 115117-56-1; **6**, 115117-57-2; **7**, 115117-58-3; **8**, 115117-59-4; **9**, 115117-60-7; **10**, 115117-61-8; **11**, 115117-62-9; **12**, 115117-63-0; **13**, 109000-22-8; **14**, 115117-64-1; (*Z*)-**14**, 115117-70-9; (*E*)-**14**, 115117-71-0; **15**, 115117-65-2; **16**, 42237-98-9; **17**, 115117-66-3; **18**, 115117-67-4; **19**, 115117-68-5; **20**, 115117-69-6; MeSSMe , 624-92-0; MeCHO , 75-07-0; Me_2NCHO , 68-12-2; *p*-iodoanisole, 696-62-8; *trans*-1,4-diphenyl-2-buten-1,4-dione, 959-28-4.

Supplementary Material Available: Experimental procedures for a typical preparation of **3** and the formation of **5** and **15** and their reactions with electrophiles (2 pages). Ordering information is given on any current masthead page.

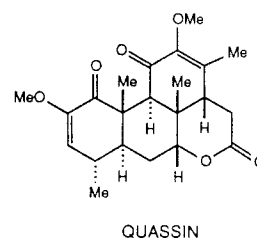
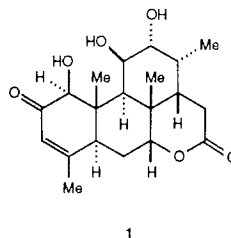
Total Synthesis of a Highly Oxygenated Quassinoid, ($\pm$)-Klaineaneone

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A characteristic feature common to many naturally occurring quassinoids is the presence in ring A of a 1β -hydroxy-2-oxo- $\Delta^{3,4}$ olefin unit bearing a methyl group at C(4) [cf. klaineaneone (**1**)].²



This structural fragment is essential for the rich array of pharmacological properties associated with quassinoids.³ Since the report describing the successful completion of the total synthesis of quassin in 1980,⁴ there has not been a single published account detailing a total synthesis of a complex quassinoid. This is particularly surprising in view of the numerous synthetic groups worldwide who have been working on this problem for more than 15 years.⁵ The lack of success to date has been in large part due to problems associated with elaboration of the ring A functionality.⁶ Reported herein is the first total synthesis of a highly oxygenated quassinoid, ($\pm$)-klaineaneone (**1**),⁷ possessing the 1β -hydroxy-2-oxo- $\Delta^{3,4}$ olefin functionality in ring A. It is of interest to note that of the ten stereocenters present in klaineaneone, nine are contiguous.

The preparation of **1** commences with tetracyclic ketone **2** prepared previously⁴ in connection with our synthesis of ($\pm$)-quassin. While compound **2** possesses all the carbon atoms needed for the construction of **1**, the configuration of C(9), which was established by a Diels–Alder strategy, requires inversion of configuration. Thus ketone **2** was transformed (92% yield) into enone **3**, mp $172.5\text{--}174.0^\circ\text{C}$, via the corresponding $\Delta^{11,12}$ enol silyl ether via a two-step process involving reaction of the lithium enolate of **2** [LDA , THF , -78°C (15 min) $\rightarrow 0^\circ\text{C}$ (1 h) $\rightarrow -78^\circ\text{C}$] with 3.0 equiv of trimethylchlorosilane [-78°C (30 min) $\rightarrow 0^\circ\text{C}$ (30 min)] and subsequent exposure (45 $^\circ\text{C}$, 48 h) of the $\Delta^{11,12}$ enol silyl ether in acetonitrile to 1.3 equiv of palladium acetate and 4.0 equiv of sodium carbonate. Enone **3** was subjected to Birch reduction in liquid ammonia at -78°C with 10 equiv of lithium metal in the presence of 0.9 equiv of *tert*-butyl alcohol. The resulting lithium enolate was trapped [0°C (30 min) $\rightarrow$ room temperature (3 h)] with 3.0 equiv of diethyl phosphorochloridate in tetrahydrofuran-*N,N,N',N'*-tetramethylethylenediamine (2:1) giving rise to enol phosphate **4**, mp $102.0\text{--}102.5^\circ\text{C}$, in 80% overall

(1) Procter and Gamble Predoctoral Fellow, 1987–1988.

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(3) Quassinoids possess a wide spectrum of biological properties including in vivo antileukemic, antiviral, antimalarial, antifedant, amoebicidal, and insecticidal activity (Polonsky, J. "Chemistry and Biological Activity of the Quassinoids" In *The Chemistry and Chemical Taxonomy of the Rutales*; Waterman, P. G., Grundon, M. F., Eds.; Academic Press: New York, 1983; p 247. Lidert, Z.; Wing, K.; Polonsky, J.; Imakura, Y.; Okano, M.; Tani, S.; Lin, Y.-M.; Kiyokawa, H.; Lee, K.-H. *J. Nat. Prod.* **1987**, *50*, 442).

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(12) Different organolithium compounds were tried, but the best results were obtained with methylolithium.

(13) All the new compounds present satisfactory microanalyses (C, ± 0.23 ; H, ± 0.16).

(14) Enol ether (1 equiv) in acetonitrile and 4 equiv of HBF_4 (35% aqueous solution) were stirred at room temperature for 4 h.