

The stereochemistry of compounds **6**, **8**, and **10** was confirmed by NOE experiments. The structure of the  $\beta$ -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.<sup>9</sup> Some  $\beta$ -functionalized lithioalkanes have been reported,<sup>10</sup> but the trans compounds undergo  $\beta$ -elimination reactions except in a few cases in which a halogen is present in the  $\alpha$ -position.<sup>11</sup>

The vinylic iodine present in compound **5** can undergo an exchange reaction with another organolithium reagent yielding the  $\beta$ -functionalized 1,1-dilithio-1-alkene. The consecutive treatment of a solution of **5a** with methylolithium<sup>12</sup> and conventional electrophiles affords the disubstitution products **16-20** (Scheme II).

The THF solutions of **15** are stable at  $-70^\circ\text{C}$ , 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,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, and MS) are in accordance with the proposed structures.<sup>13</sup> The derivatives carrying an isopropoxy group are easily hydrolyzed to the corresponding carbonyl systems.<sup>14</sup>

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  $\beta$ -tricarbonyl compound **20**.

These results show the possibility of the preparation of  $\beta$ -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;  $\text{MeSSMe}$ , 624-92-0;  $\text{MeCHO}$ , 75-07-0;  $\text{Me}_2\text{NCHO}$ , 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.

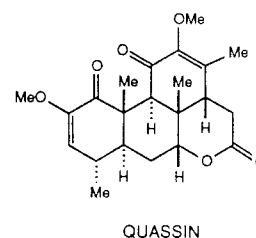
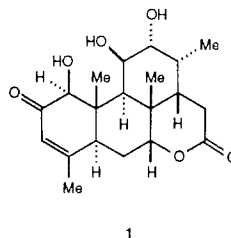
## Total Synthesis of a Highly Oxygenated Quassinoid, ( $\pm$ )-Klaineaneone

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



This structural fragment is essential for the rich array of pharmacological properties associated with quassinoids.<sup>3</sup> Since the report describing the successful completion of the total synthesis of quassin in 1980,<sup>4</sup> 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.<sup>5</sup> The lack of success to date has been in large part due to problems associated with elaboration of the ring A functionality.<sup>6</sup> Reported herein is the first total synthesis of a highly oxygenated quassinoid, ( $\pm$ )-klaineaneone (**1**),<sup>7</sup> possessing the  $1\beta$ -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 previously<sup>4</sup> 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  $172.5-174.0^\circ\text{C}$ , via the corresponding  $\Delta^{11,12}$  enol silyl ether via a two-step process involving reaction of the lithium enolate of **2** [ $\text{LDA}$ , THF,  $-78^\circ\text{C}$  (15 min)  $\rightarrow 0^\circ\text{C}$  (1 h)  $\rightarrow -78^\circ\text{C}$ ] with 3.0 equiv of trimethylchlorosilane [ $-78^\circ\text{C}$  (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  $-78^\circ\text{C}$  with 10 equiv of lithium metal in the presence of 0.9 equiv of *tert*-butyl alcohol. The resulting lithium enolate was trapped [ $0^\circ\text{C}$  (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  $102.0-102.5^\circ\text{C}$ , in 80% overall

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

(2) For an excellent review on quassinoids, see: Polonsky, J. *Fortschr. Chem. Org. Naturst.* **1985**, *47*, 22.

(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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(6) For synthetic methods addressing the problems associated with the construction of the  $1\beta$ -hydroxy-2-oxo- $\Delta^{3,4}$  olefin functionality present in ring A of quassinoids, see: McKittrick, B. A.; Ganem, B. *J. Org. Chem.* **1985**, *50*, 5897. Spohn, R.; Grieco, P. A.; Nargund, R. P. *Tetrahedron Lett.* **1987**, *28*, 2491.

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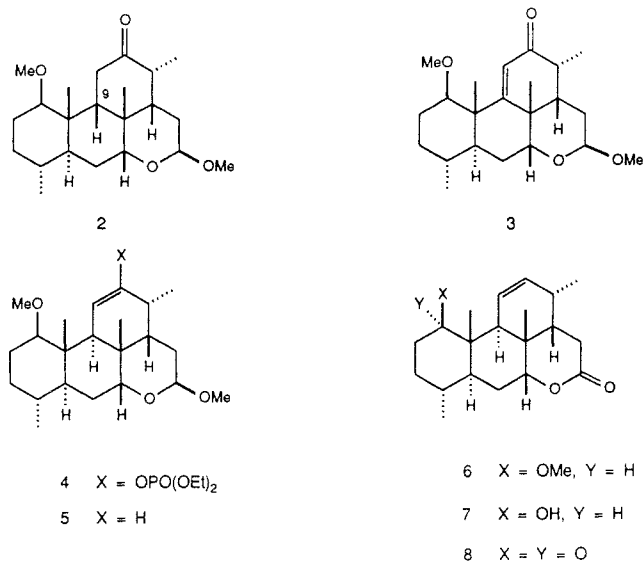
(10) See, for example: Huang, S. J.; Lessar, M. V. *J. Org. Chem.* **1970**, *35*, 1204-1206. Duhamel, L.; Poirier, J.-M. *J. Am. Chem. Soc.* **1977**, *99*, 8356-8357. Wollemberg, R. H.; Albizzati, K. F.; Peries, R. *J. Am. Chem. Soc.* **1977**, *99*, 7365-7367. Ficini, J.; Falou, S.; Touzin, A.-M.; d'Angelo, J. *Tetrahedron Lett.* **1977**, 3589-3592. Lau, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595-1598. Kowalski, C. J.; O'Dowd, M. L.; Burke, M. C.; Fields, K. W. *J. Am. Chem. Soc.* **1980**, *102*, 5411-5412. Barluenga, J.; Fernández, J. R.; Yus, M. *J. Chem. Soc., Chem. Commun.* **1985**, 203-204.

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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,  $\pm 0.23$ ; H,  $\pm 0.16$ ).

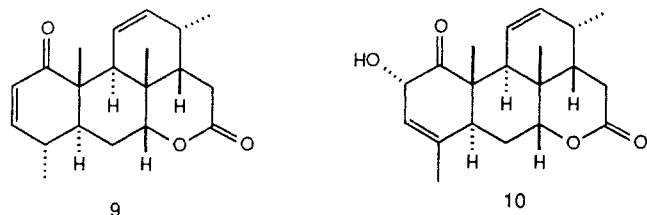
(14) Enol ether (1 equiv) in acetonitrile and 4 equiv of  $\text{HBF}_4$  (35% aqueous solution) were stirred at room temperature for 4 h.



yield. Reductive elimination [Li (100 equiv), EtNH<sub>2</sub>, *t*-BuOH (1.0 equiv), THF] of the phosphate group proceeded smoothly affording tetracyclic olefin **5** in 92% yield.

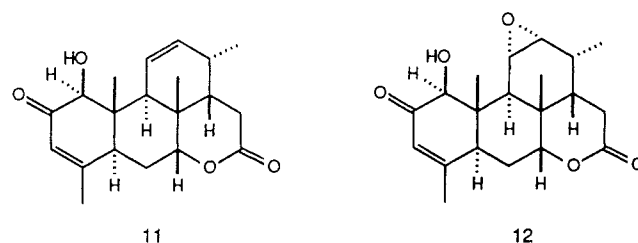
Prior to elaboration of the ring A functionality, the protected lactol in **5** was converted in 77% overall yield into the tetracyclic lactone **6**, mp 174–176 °C, via a two-step sequence (1. 5% HCl, THF, 5 h; 2. Jones oxidation, 0 °C, 30 min). Cleavage of the methyl ether in compound **6** required prolonged exposure (70 h) of **6** to boron trifluoride etherate/ethanedithiol (1.0:1.7) containing a catalytic amount of concentrated hydrochloric acid in order to realize a 70% yield of crystalline tetracyclic alcohol **7**, mp 167.5–169.0 °C. Oxidation [PCC (3.0 equiv), NaOAc (2.5 equiv), CH<sub>2</sub>Cl<sub>2</sub>, 0 °C (30 min) → room temperature (30 min)] of **7** provided in 99% yield ketone **8**, mp 180.5–181.0 °C.

The required ring A functionality was introduced at this stage of the synthesis since all attempts to elaborate ring A in the presence of the C(11), C(12) trans diaxial vicinal diol unit failed. Tetracyclic ketone **8** was converted (82% yield) into enone **9**, mp 206.5–207.5 °C, via a three-step sequence involving enol silyl ether formation [HMDS (7 equiv), Et<sub>3</sub>N (7 equiv), TMSI (5 equiv), ClCH<sub>2</sub>CH<sub>2</sub>Cl, –23 °C → room temperature (3 h)], trapping of the enol silyl ether with phenylselenenyl chloride in tetrahydrofuran at 0 °C (20 min), and oxidation (H<sub>2</sub>O<sub>2</sub>, pyridine, 0 °C, 1.5 h) of the corresponding keto selenide which underwent loss of benzene selenenic acid. Elaboration of the ring A functionality required transformation of enone **9** into the corresponding silyl dienol ether.



Toward this end, enone **9** was treated with 15 equiv of hexamethyldisilazane, 15 equiv of triethylamine, and 10 equiv of trimethylsilyl iodide in 1,2-dichloroethane initially at –23 °C and then at ambient temperature for 13 h. Peracid oxidation<sup>8</sup> [MCPBA (1.2 equiv), NaHCO<sub>3</sub> (1.5 equiv), CH<sub>2</sub>Cl<sub>2</sub>, –23 °C, 45 min] of the corresponding silyl dienol ether followed by treatment with 3.0 equiv of a 1.0 M solution of tetrabutylammonium fluoride in tetrahydrofuran for 1 h at –23 °C provided, in 50% overall yield from **9**, tetracyclic α-hydroxy ketone **10**. Base-catalyzed tautomerism of **10** into **11**, mp 227–230 °C, was realized in 75% yield by treatment of a 0.02 M solution of **10** in methanol with 1.2 equiv of finely powdered potassium carbonate. Epoxidation [MCPBA, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C (35 min) → room tem-

perature (2.5 h)] of tetracyclic olefin **11** gave rise to crystalline



epoxide **12**, mp 217.5–219.5 °C, as the sole product in 80% yield. Acid-catalyzed opening of epoxide **12** with 23% perchloric acid in tetrahydrofuran–methylene chloride, 15:1, at ambient temperature (36 h) produced in 76% yield synthetic (±)-klaineaneone (**1**), mp 234–239 °C, identical with an authentic sample by 500-MHz <sup>1</sup>H NMR, IR, and silica gel TLC analysis in several solvent systems.<sup>9</sup> Completion of the synthesis of **1** confirms the structural assignment put forth by Polonsky and Zylber<sup>7</sup> for klaineaneone nearly 25 years ago. Since that time, the structure of **1** has rested upon limited spectroscopic data and its conversion into quassin. The synthesis of racemic klaineaneone is noteworthy in that (a) the transformation of tetracyclic ketone **2** into **1** requires no protecting groups, (b) the ring A 1β-hydroxy-2-oxo-Δ<sup>3,4</sup> olefin functionality is surprisingly stable (cf. **12** → **1**) contrary to reports in the literature, and (c) the base-catalyzed tautomerism of α-hydroxy ketone **10** into **11** proceeds with remarkable efficiency despite the opportunity for numerous undesired side products.

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(9) All new crystalline compounds have been fully characterized by IR, <sup>1</sup>H NMR, and combustion analysis.

## Spin Echo NMR of Cobalt Zeolite Catalysts: Control of Particle Size and Structure<sup>†</sup>

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Nuclear magnetic resonance (NMR) spectroscopy has recently become a powerful tool in the study of solid zeolite catalysts via magic angle spinning (MAS) procedures.<sup>1</sup> The ordering of Si<sup>4+</sup> and Al<sup>3+</sup> in zeolite frameworks and the effects of dealumination

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