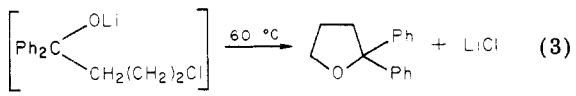
These types of alcohols are intermediates in the preparation of amino alcohols of known pharmacologic activity. Thus, if **6** is allowed to react with piperidine, 1,1-diphenyl-4-piperidylbutanol (an anesthesic) is obtained.[8c] *cis*-2,6-dimethyl-α,α-diphenylpiperidinebutanol (antiarhythmic) may be prepared in a similar way.[9]

Finally, the reaction may be easily extended to produce substituted tetrahydrofurans (eq 3). Thus, the reaction

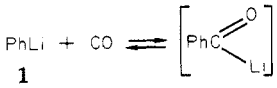


(3)

between **1** and **5** is carried out in the described way, but the reaction mixture is not quenched by water. Instead, the solvent is distilled off by heating at 60 °C. From the residue is obtained **7** in a 45% yield. Presumably, the intramolecular Williamson reaction shown in eq 3 takes place. This one-pot preparation of **7** is shorter than Hamaguchi's[10] and of similar yield (39%).

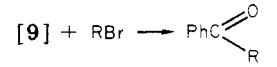
In an effort to establish the extent of the proposed method, the reaction of *o*-anisyllithium (**8**) plus *n*-butyl bromide with CO was also studied. The only reaction product is di-*o*-anisylbutylcarbinol (62% yield), containing some recovered anisole. It had been previously found that the reaction between **8** and CO is incomplete[11] and a different reaction mechanism was proposed.[12]

As mentioned above, the reaction of eq 1 has additional mechanistic relevance. A reasonable mechanism for the formation of **3** involves the intermediacy of *benzoyllithium* (**9**). An alternative pathway is the initial formation of the



(4)

1 9



(5)

10

$$10 + 1 \rightarrow 3 \quad (6)$$

benzophenone dianion (**11**) and its subsequent reaction with **2**. However, **11** does not produce **3** under the described reaction conditions; therefore, it can be reasonably excluded as an intermediate. This result, together with the complete absence of benzophenone among the reaction products, must be considered strong evidence that **9** is a major intermediate in the reaction of **1** with CO.[13]

This new reaction as well as other previously reported carbonylations of lithium amides[14] demonstrates the synthetic potential of the uncatalyzed carbonylation of organolithium reagents and suggests additional ways in which free carbon monoxide might be used in synthesis.[15]

Acknowledgment. We are indebted to the SECYT, CONICET (National Research Council of Argentina), and the Organization of American States for finantial support. UMYMFOR (FCEN-CONICET) is acknowledged for the spectroscopic determinations.

Registry No. 1, 591-51-5; 2 (R = *n*-C_4H_9), 109-65-9; 2 (R = *n*-C_3H_7), 106-94-5; 2 (R = *n*-$C_{12}H_{25}$), 143-15-7; 2 (R = *i*-C_3H_7), 75-26-3; 2 (R = *t*-C_4H_9), 507-19-7; 3 (R = *n*-C_4H_9), 5384-63-4; 3 (R = *n*-C_3H_7, 5331-17-9; 3 (R = *n*-$C_{12}H_{25}$), 79044-19-2; 3 (R = *i*-C_6H_7), 37951-09-0; 3 (R = *t*-C_4H_9), 1657-60-9; 4, 119-53-9; 5, 109-70-6; 6, 59855-97-9; 7, 887-15-0; 8, 31600-86-9; di-*o*-anisylbutylcarbinol, 79044-20-5; 1,1-diphenyl-2-methyl-*n*-propyl isopropyl ether, 79044-21-6; 1,1-diphenyl-2-methyl-*n*-propyl *tert*-butyl ether, 79044-22-7; benzhydryl *tert*-butyl ether, 28567-35-3.

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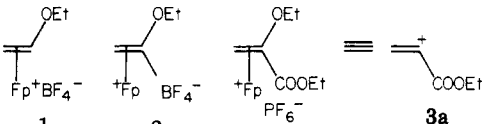
α-Acrylic Ester Cation Equivalent. Application in the Synthesis of α-Methylene γ-Lactones

Summary: The complex cation **3** serves as an α-acrylic ester cation in the conversion of cyclohexanone lithium enolate to the *cis*- and *trans*-α-methylene γ-lactones **10** and **11**.

Sir: We recently described the use of Fp–vinyl ether complexes **1** and **2** (Fp = $C_5H_5Fe(CO)_2$) as vinyl cation equivalents for vinylation[1] and isopropenylation[2] of cyclohexanone enolates. In order to further extend the synthetic utility of such complexes, we have sought to prepare further functionalized members of this class. One such substance (**3**) would, by analogy with the reactions



1 2 3 3a

of **1** and **2**, be expected to behave as an α-acrylic ester cation equivalent (**3a**). We now report the preparation of **3** and its use in the conversion of cyclohexanone to the α-methylene γ-lactones **10** and **11**. The wide occurrence of this functionality among biologically active terpenoid materials has made it an important synthetic objective and led to the development of a number of routes for its construction.[3] However, most of these involve sequences which utilize a preformed γ-lactone as the starting material.[3b]

Complex **3** is readily prepared in two steps from ethyl α-bromopyruvate diethyl ketal.[4] On metalation of this

(7) A total yield of 30% of **6** is obtained by the successive conversion of **5** to the cyano derivative[8a] and to the ethyl γ-chlorobutirate[8b] and its subsequent reaction with PhLi.[8c]

(8) (a) C. F. Allen, "Organic Synthesis", Collect. Vol. I, Wiley, New York, 1941, p 156; (b) C. F. Fehnel, *J. Am. Chem. Soc.*, **74**, 1569 (1952); (c) A. Barrett and S. Wilikinson, British Patent 683 950; *Chem. Abstr.*, **48**, 2112e (1954).

(9) R. W. Fleming, U.S. Patent 4 031 101; *Chem. Abstr.*, **87**, 84839 (1977).

(10) F. Hamaguchi, *Yakugaku Zasshi*, **82**, 1088 (1963); *Chem. Abstr.*, **58**, 4492*f* (1963).

(11) N. S. Nudelman and A. A. Vitale, Proceedings of the XIV Argentine Chemical Symposium, Santa Fe, NM, 1978.

(12) A. A. Vitale, *Diss. Abstr. Int. B*, **41**, 0000 (1981).

(13) Further evidences will be published shortly in *J. Organomet. Chem.*

(14) N. S. Nudelman and D. Pérez, *An. Asoc. Quim. Argent.* **69**, 195 (1981).

(15) N. S. Nudelman, A. A. Vitale, and D. Pérez, *Rev. FCEN* in press.

(1) Chang, T. C. T.; Rosenblum, M.; Samuels, S. B. *J. Am. Chem. Soc.* **1980**, *102*, 5930.

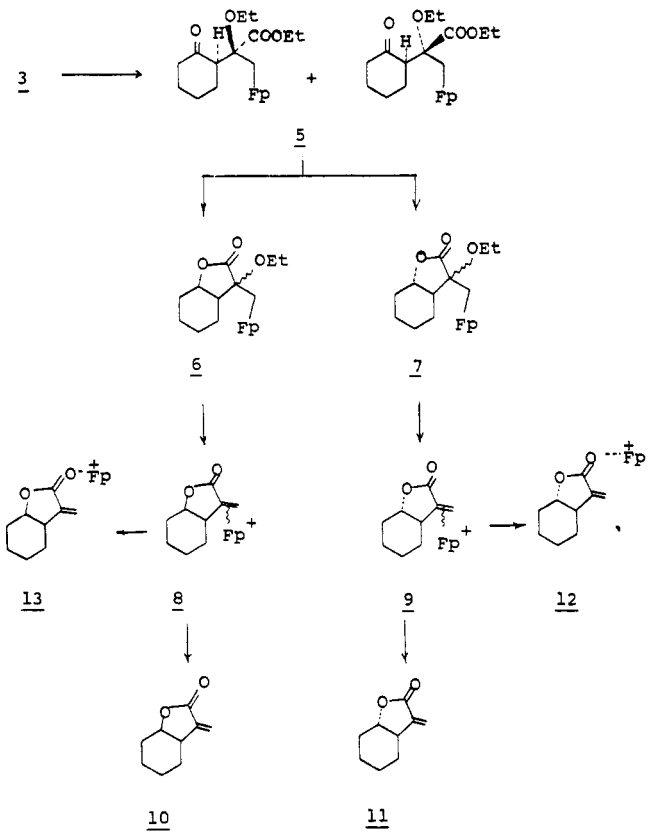
(2) Chang, T. C. T.; Rosenblum, M. *J. Org. Chem.* **1981**, *46*, 4103.

(3) (a) For a review of this see: Grieco, P. A. *Synthesis* **1975**, 67. (b) A number of these methods do not proceed from a preformed γ-lactone, among these are the following: Jones, E. R. H.; Shen, T. Y.; Whiting, H. C. *J. Chem. Soc.* **1950**, 230. Norton, J. R.; Shenton, K. E.; Schwartz, J. *Tetrahedron Lett.* **1975**, 5. Hudrlik, P. F.; Rudnick, I. R.; Korzeniowski, S. H. *J. Am. Chem. Soc.* **1973**, *95*, 6848. Jager, V.; Günther, H. J. *Tetrahedron Lett.* **1977**, 2543. Mariano, J. P.; Floyd, D. M. *J. Am. Chem. Soc.* **1974**, *96*, 7138. Still, W. C.; Schneider, M. J. *Ibid.* **1977**, *99*, 948. Addington, R. M.; Barrett, A. G. M. *J. Chem. Soc., Chem. Commun.* **1978**, 1071.

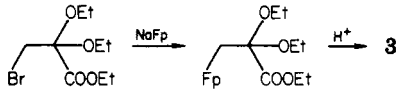
(4) IR (CH_2Cl_2) 1750 cm^{-1}; NMR (CCl_4) δ 4.27 (q, 2, $COOCH_2Me$), 3.56 (m, 4, OCH_2Me), 3.56 (s, 2, CH_2Br), 1.30 (m, CH_3).

0022-3263/81/1946-4626$01.25/0

Scheme I



substance with sodium dicarbonyl(η^5-cyclopentadienyl)-ferrate[5] in THF solution (0 °C, 1 h; 25 °C, 2.5 h) the alkyliron complex **4** is obtained in 63% yield as a red oil:[6a] IR (CH_2Cl_2) 1960, 2010 (C≡O), 1730 cm^{-1} (C=O). This may be transformed, without purification to the cationic π-olefin complex **3** (88%) by treatment of a methylene chloride solution of **4** with 1 equiv of $HPF_6 \cdot Et_2O$ at −78



4

°C. The product, precipitated from solution with ether, collected, and washed with ether, is obtained as a yellow crystalline solid.[6b]

Cyclohexanone lithium enolate, prepared from the silyl enol ether with butyllithium,[7] reacts at −78 °C with suspensions of **3** in THF solution (3 h) to give a 2:1 mixture of diastereomeric adducts **5** in an 81% yield[8] (Scheme I). These may be separated on alumina, but since the chiral quaternary carbon center is removed in the final product, this step is not essential.

Reduction of **5** in THF solution at −78 °C (1.5 h) with L-Selectride gave principally the cis lactone complex **6** as a mixture of diastereomers (mp 84–88 °C) in 93% yield. This was transformed by treatment at −78 °C in CH_2Cl_2 solution with $HPF_6 \cdot Et_2O$ (0.5 h) to the olefin complex **8**. This salt, like the related trans lactone complex **9** is unstable and rapidly rearranges to the carbonyl-complexed cation **13**.[9] In practice it is not necessary to isolate or purify this intermediate since treatment with either sodium iodide in acetone or tetraethylammonium bromide in methylene chloride of either **8** or **13** effects rapid demetalation at room temperature. Thus, treatment of **6** with $HPF_6 \cdot Et_2O$ as described above, followed by demetalation of the product with sodium iodide, gave the *cis*-α-methylene γ-lactone **10** (90%) containing 5% of the trans isomer **11**.[10,11]

The trans lactone can be made the major product of the reaction sequence if the reduction of **5** is effected with sodium borohydride. With this less sterically demanding reagent, the mixture of lactones **6** and **7** (70%) is composed principally of the trans isomer **7**. The spontaneous closure of the intermediate *trans*-oxido ester is surprising in view of the general resistance to closure of such strained systems[12] but may be due to the effect of the large $FpCH_2$ substituent and to geminal substitution on the lactone ring. When the mixture of lactones is converted to the olefin complexes **8** and **9** ($HPF_6 \cdot Et_2O$, CH_2Cl_2, −78 °C, 0.5 h) and then demetalated with Et_4NBr (CH_2Cl_2, 25 °C, 15 min), the product, obtained in 80% yield, was principally the trans isomer **11** (**11**/**10** ratio of 3.3:1).[13]

Further synthetic applications of **3** and related complexes are being examined.

Acknowledgment. This work was supported by a grant from the National Institutes of Health (GM-16395).

Registry No. 3, 79173-01-6; **4**, 79173-02-7; **5** (isomer 1), 79200-27-4; **5** (isomer 2), 79172-74-0; **6** (isomer 1), 79173-03-8; **6** (isomer 2), 79200-28-5; **7**, 79200-29-6; **8**, 79173-05-0; **9**, 79200-31-0; **10**, 16822-06-3; **11**, 3727-53-5; **12**, 79173-07-2; **13**, 79200-33-2; ethyl bromopyruvate diethyl ketal, 79172-42-2; sodium dicarbonyl(η^5-cyclopentadienyl)-ferrate, 12152-20-4; ethyl pyruvate diethyl ketal, 7476-20-2; cyclohexanone silyl enol ether, 6651-36-1.

Supplementary Material Available: Full experimental details (6 pages). Ordering information is given on any current masthead page.

(5) Prepared from $[CpFe(CO)_2]_2$ (obtained from Strem Chemical Co. or by the method of: Eisch, J. J.; King, R. B., Eds. "Organometallic Synthesis"; Academic Press: New York, 1965; Vol. 1, p 114) by reduction with sodium amalgam: Fischer, E. O.; Bötcher, R. *Z. naturforsch.* **1955**, *106*, 600.

(6) (a) This compound may be stored at 0 °C for prolonged periods of time (6 months) without appreciable decomposition. (b) This product is best washed several times in the reaction vessel with ether (−78 °C), and the ether is removed by a cannula. The salt obtained is sufficiently pure for use directly but may be further purified by dissolution in acetone (−30 °C) and reprecipitation with ether. Unlike most other $Fp(olefin)PF_6$ salts, complex **3** cannot be stored even at 0 °C without loss of activity, probably through rearrangement to the isomeric carbonyl coordinated complex.[9] NMR spectrum of **3** (acetone-d_6, −20 °C) δ 5.69 (s, 5, Cp), 5.25 (d, 1, J = 2.5 Hz, =CH), 4.66 (d, 1, J = 2.5 Hz, =CH), 4.21 (q, 2, J = 7 Hz, $COOCH_2$), 3.85 (q, 2, J = 7 Hz, OCH_2), 1.30, 1.27 (2 t, 9, CH_3).

(7) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

(8) The diastereomers **5** were separated on activity IV alumina with 5% ether–Skelly B: IR (CH_2Cl_2) 2000, 1940 (C≡O), 1740, 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) major isomer δ 4.87 (s, Cp), minor isomer 4.78 (s, Cp).

(9) Foxman, B. M.; Klemarczyk, P. T.; Liptrot, R. E.; Rosenblum, M. *J. Organomet. Chem.* **1980**, *187*, 253.

(10) These were identified by comparison with NMR and IR spectral data from the literature. Grieco, P. A. *J. Org. Chem.* **1974**, *39*, 120. Greene, A. E.; Muller, J.-C.; Ourisson, G. *J. Org. Chem.* **1974**, *39*, 186. Marshall, J. A.; Cohen, N. *J. Org. Chem.* **1965**, *30*, 3475.

(11) Reduction of the major keto ester diastereomer **5** with L-Selectride and conversion to lactone gave exclusively the cis lactone **10**, while similar treatment of the minor diastereomer gave a 4:1 ratio of cis to trans lactones.

(12) See for example: Marshall, J. A.; Cohen, N., in ref 10. Patterson, J. W.; McMurry, J. E. *J. Chem. Soc., Chem. Commun.* **1971**, 488. House, H. O.; Babad, H.; Toothill, R. B.; Noltes, A. W. *J. Org. Chem.* **1962**, *27*, 4141.

(13) Reduction of the major keto ester diastereomer **5** with sodium borohydride and subsequent transformation to lactone gave only the trans lactone **11**, while similar treatment of the minor diastereomer gave a 7:3 mixture of cis and trans isomers.

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