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SYNTHESIS OF 4-KETO PIMELATES BY PALLADIUM-CATALYZED CARBONYLATIVE SYMMETRICAL COUPLING OF SILOXYCYCLOPROPANES

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Summary: Treatment of 1-alkoxy-1-siloxycyclopropane with a catalytic amount of a palladium/phosphine complex in chloroform under carbon monoxide atmosphere gives 4-keto pimelate.

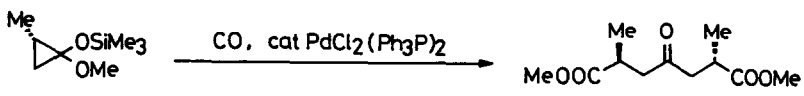
The polyfunctional nature of 4-keto pimelates makes them a useful intermediate for organic synthesis, e.g., for the synthesis of 1,4-cyclohexanedione derivatives.[1] We report here a new preparative route to this class of compounds that involves symmetrical coupling of two molecules of 1-alkoxy-1-siloxycyclopropane (**1**) with the incorporation of one molecule of carbon monoxide. The siloxycyclopropane behaves as a nucleophilic homoenolate,[2] and carbon monoxide as a carbonyl dication in the way schematized in eq 1.

(1)

The experimental procedure is straightforward, involving the heating of siloxycyclopropane **1** in the presence of $PdCl_2(Ph_3P)_2$ under 1 atm of carbon monoxide (Table 1).[3] Although the reaction in benzene needed a stoichiometric amount of the Pd(II) complex, that in chloroform needed only a catalytic amount (5 mol%). Apparently, chloroform acts as an re-oxidant of the Pd(0) species generated during the reaction.

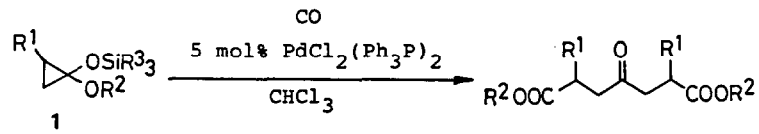
A variety of substituted 1-alkoxy-1-siloxycyclopropanes took part in this coupling reaction (Table 1). Both trimethylsiloxy- and tert-butyldimethylsiloxycyclopropanes were suitable for the reaction. The reaction of 2-substituted cyclopropanes occurred with exclusive cleavage of the less substituted C-C bond directed to the siloxy group (cf. entries 5 and 6).

Coupling of racemic 2-substituted cyclopropanes gave a mixture of dl- and meso-products (GLC) without appreciable selectivity. On the other hand, chiral 2-methyl cyclopropane **2**[4] gave 2,6-dimethylpimelate **3** as a single isomer, indicating that the reaction proceeded without racemization of the chiral center (eq 2). The position of



2 3 (2)

Table 1. 4-Keto Pimelates from Siloxycyclopropanes[a]



entry	R^1	R^2	SiR^3_3	%yield[b]
1	H	Et	$SiMe_3$	65
2	H	Et	Si^tBuMe_2	59
3	H	^{i}Pr	$SiMe_3$	79
4	H	Hex	$SiMe_3$	63
5	Me	Et	$SiMe_3$	60[c]
6	Hex	Et	Si^tBuMe_3	69[c]

[a]See footnote 3 for the experimental procedure. [b]Isolated yield. [c]The structural assignment rests on the analogy to that of the chiral pimelate **3**.

the methyl group in **3** was determined by the long-range selective proton noise decoupling experiment on 50 MHz ^{13}C NMR.[5] The 2- (and 6-) methyl carbon was found to be weakly coupled to the ester carbonyl but not to the ketone carbonyl carbon, supporting the 2,6-dimethyl structure of **3**.

Several lines of evidence suggest that the reaction involves the initial formation of a palladium homoenolate by the cleavage of the cyclopropane ring with a $PdCl_2$/CO complex.[6] The mechanistic details are under active investigation.

Finally we note that, among other procedures reported for the preparation of 4-keto pimelates,[1] the present one has a merit of distinctive operational simplicity, as well as of the capability to produce an optically active derivative.

References and Notes

1. (a) Emerson, W. S.; Longley Jr. R. T. Org. Synth. Coll. Vol, **1963**, 4, 302. McMurry, J. E.; Melton, J.; Padgett, H. J. Org. Cem., **1974**, 39, 259. Hong, P.; Mise, T.; Yamazaki, H. Chem. Lett. **1982**, 361. (b) See also Ryu, I.; Ryang, M.; Rhee, I.; Omura, H.; Murai, S.; Sonoda, N. Synth. Commun. **1984**, 14, 1175.
2. For our previous work in this field, see: ref. 4; Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. J. Am. Chem. Soc. in press.
3. Experimental procedure: A mixture of 1-isopropoxy-1-trimethylsiloxycyclopropane (377 mg, 2.0 mmol) and $PdCl_2(Ph_3P)_2$ (35 mg, 0.05 mmol) in 4 ml of chloroform was heated at 60 °C under carbon monoxide (1 atm). After 16 h, additional 35 mg of the catalyst was added and heating was continued for additional 16 h. Chromatographic purification on silica gel (15% EtOAc in hexane) gave diisopropyl 4-keto pimelate (201 mg, 79%). The formation of isopropyl propionate was the only side reaction noted.
4. Nakamura, E.; Sekiya, K.; Kuwajima, I. Tetrahedron Lett., **1987**, 28, 337.
5. Cf. Nakanishi, K. Ed. Chodendo FT-NMR; Kodansha: Tokyo, 1986.
6. The reaction of **1** (R^1 = H) with 1 equiv of $PdCl_2(Ph_3P)_2$ under nitrogen gave a mixture of alkyl acrylate and propionate suggesting the formation of an unstable palladium homoenolate by the action of Pd(II) on the cyclopropane ring: Unpublished result by T. Fujimura.

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