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SELECTIVE SYNTHESIS OF γ,δ-UNSATURATED CARBOXYLIC ACID DERIVATIVES BY THE $Ni(CO)_4$-INDUCED RING-OPENING CARBONYLATION REACTION

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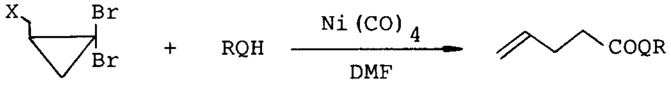
Summary: gem-Dibromocyclopropanes bearing the chloromethyl or mesyloxymethyl substituent at the vicinal position underwent the $Ni(CO)_4$-induced ring-opening carbonylation reaction with alcohol or amines leading to the γ,δ-unsaturated carboxylic acid derivatives selectively via nickel enolate intermediates. Successful utilization of N,N-dimethyltrimethylsilylamine as an initial nucleophile resulted in condensation with benzaldehyde giving 2-allylcinnamamides.

Regioselective C-C bond formation in allylic substitution is difficult in spite of its high potential utility in organic synthesis.[1] We report herein a useful procedure for the regioselective introduction of an alkoxycarbonyl group to allylic chlorides or alcohols with one-carbon homologation. The $Ni(CO)_4$-induced reactions of gem-dibromocyclopropanes have provided a versatile method for gem-functionalization, which allows reduction or introduction of an electrophile accompanied by carbonylation at the geminal position of cyclopropanes.[2,3] The novel nickel enolate species are considered to be present as key intermediates. Based on these observations, a unique ring-opening carbonylation reaction is now disclosed to lead to a selective synthesis of γ,δ-unsaturated carboxylic acid derivatives.

Treatment of the 1-chloromethyl-2,2-dibromocyclopropanes 1 with $Ni(CO)_4$ and 1-propanol in DMF afforded the γ,δ-unsaturated esters 3 exclusively.[4] Neither the β,γ-unsaturated ester nor the α,β-isomer was not formed. Use of amine gave



1 (X=Cl)
2 (X=OMs)

Q=O, NH, NR'

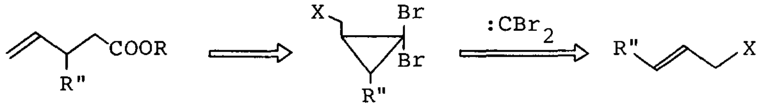
3

the corresponding γ,δ-unsaturated amide. Some results are listed in Table I.

In related studies, the same ring-opening carbonylation reaction was realized when the methanesulfonates 2 were employed (Table I). The methanesulfonates 2 were derived from 2,2-dibromocyclopropanemethanols, which are subjected to intramolecular reductive carbonylation with $Ni(CO)_4$ into the corresponding bicyclic lactones.[2]

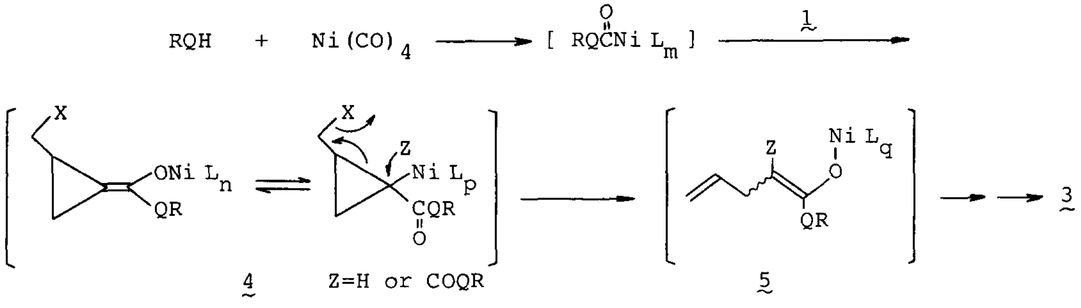
Since 1 and 2 are easily obtained by the addition of dibromocarbene to allylic chlorides and alcohols, respectively,[5] the present process is formally regarded as the S_N2' reaction of allylic compounds with the ester enolate anion (Scheme I).

Scheme I



The selective ring cleavage is based on the presence of the chloromethyl or mesyloxymethyl substituent at the vicinal position of gem-dibromocyclopropanes. One of the plausible reaction paths is depicted in Scheme II. The similar nickel enolate 4 (Q=O) as described in the reactions of gem-dibromocyclopropanes[3] might be involved as a key intermediate. The displacement with another alkoxycarbonyl group or hydride[6] is considered to induce ring cleavage with removal of the chloro or mesyloxy group to give the nickel enolate intermediate 5. Protonation and decarboxylation[7] (in the case of Z=COOR) of 5 lead to the requisite compound 3 selectively. Starting from 2b, propyl 4-methyl-2,4-

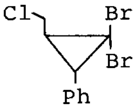
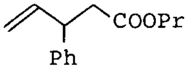
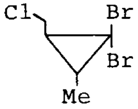
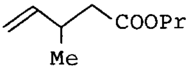
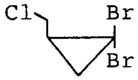
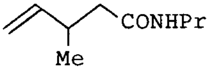
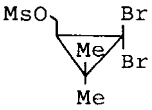
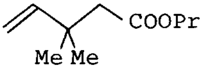
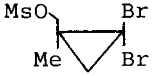
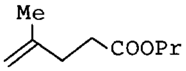
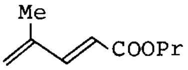
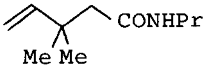
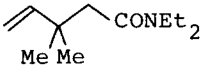
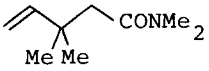
Scheme II



pentadienoate was produced together with the γ,δ-unsaturated ester. The former product might be derived by a β-elimination reaction of the nickel enolate 5b.

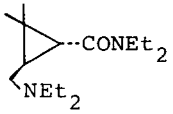
The reaction of 2 with sec-amine did not give the desired amide 3 exclusively. The selective transformation and improvement of yield were performed by using N,N-dimethyltrimethylsilylamine as an initial nucleophile (Table I). This finding makes it possible to introduce an electrophile instead of proton. The presence of benzaldehyde in the $Ni(CO)_4$-induced reaction of 1 with the

Table I. Synthesis of γ,δ-Unsaturated Carboxylic Acid Derivatives[a)]

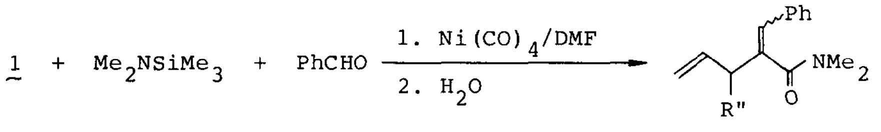
1 or 2		RQH[b)]	$Ni(CO)_4$, equiv	3	Isolated Yields, %
	1a	PrOH	6		73
	1b	PrOH	6		63
	1c	PrOH	6		61
1b		$PrNH_2$	3		30
	2a	PrOH	6		80
	2b	PrOH	6		20
					10
2a		$PrNH_2$	3		34
2a		Et_2NH	3		15[c)]
2a		Me_2NSiMe_3	3		46

a) Reaction conditions: 70 °C, 3 h.

b) RQH (2.2 equiv) was used.

c)  (15%) was obtained as a byproduct.

silylamine led to a one-pot synthesis of the 2-allylcinnamamide 6[8] although yields were not so high. The formation of 6 is explained by condensation of the nucleophilic[9i-k] enolate 5 with benzaldehyde. This four-component construction is formally interpreted as the allylic substitution and subsequent condensation with the enolate dianion.



6 R"=Ph, 30%
Me, 28%

These results are also evaluated to disclose a new method for the generation of nickel enolates and their synthetic reactions because only few studies on transition metal enolates have been reported.[9]

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References and Notes

1. For example, B. M. Trost and M. Lautens, J. Am. Chem. Soc., 105, 3343 (1983), and references cited therein.
2. T. Hirao, Y. Harano, Y. Yamana, Y. Ohshiro, and T. Agawa, Tetrahedron Lett., 24, 1255 (1983).
3. T. Hirao, S. Nagata, Y. Yamana, and T. Agawa, Tetrahedron Lett., in press.
4. A typical procedure is as follows. The gem-dibromocyclopropane 1a (1.0 mmol) was treated with 1-propanol (3.0 mmol) and Ni(CO)$_4$ (3.0 mmol) in DMF (2.4 mL) at 70 °C for 6 h under nitrogen. After removing excess Ni(CO)$_4$ under the reduced pressure, the mixture was diluted with ether and filtered on celite 545. The ethereal solution was concentrated and flash chromatographed to produce propyl 3-phenyl-4-pentenoate in 73% yield.
5. 1: W. E. Keller, "Compendium of Phase-Transfer Reactions and Related Synthetic Methods", Fluka AG, 1979. 2: Treatment of 2,2-dibromocyclopropanemethanols (prepared from allylic alcohols) with methanesulfonyl chloride and triethylamine in ether gave 2 in high yields; K. Kleveland, L. Skattebøl, and L. K. Sydnes, Acta Chem. Scad., B, 31, 463 (1977).
6. P. W. Jolly, "Comprehensive Organometallic Chemistry", ed. by G. Wilkinson, Pergamon Press (1982), Vol. 6, p 37.
7. A similar kind of decarboxylation is proposed in the reaction of 1-chloro-2,2-dibromocyclopropanes; T. Hirao, S. Nagata, and T. Agawa, Chem. Lett. in press.
8. The reaction was carried out by mixing 1 (1.0 mmol), N,N-dimethyltrimethylsilylamine (3.0 mmol), PhCHO (3.0 mmol), and Ni(CO)$_4$ (3.0 mmol) in DMF (2.4 mL) at 70 °C for 3 h under nitrogen. The geometry of the benzylidene moiety has not been determined although only one isomer was produced.
9. a) T. Mukaiyama, K. Banno, and K. Narasaka, ibid., 96, 7503 (1974). b) E. A. Jeffery and A. Meisters, J. Organometal. Chem., 82, 315 (1974). c) Y. Ito, T. Hirao, and T. Saegusa, J. Org. Chem., 43, 1011 (1978). d) Y. Ito, H. Aoyama, T. Hirao, and T. Saegusa, J. Am. Chem. Soc., 101, 494 (1979). e) Y. Yamamoto and K. Maruyama, ibid., 104, 2323 (1982). f) T. Hirao, N. Yamada, Y. Ohshiro, and T. Agawa, Chem. Lett., 1982, 1997. g) T. Hirao, Y. Fujihara, S. Tsuno, Y. Ohshiro, and T. Agawa, ibid., 1984, 367. h) J. J. Doney, R. G. Bergman, and C. H. Heathcock, J. Am. Chem. Soc., 107, 3724 (1985). i) E. Yoshisato and S. Tsutsumi, J. Chem. Soc., Chem. Commun., 1968, 33. j) I. Rhee, I. Ryu, H. Omura, S. Murai, and N. Sonoda, Chem. Lett., 1979, 1435. k) J. H. Nelson, P. N. Howells, G. C. DeLullo, and G. L. Landen, J. Org. Chem., 45, 1246 (1980).

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