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SYNTHESIS OF β,γ-UNSATURATED CARBOXYLIC ACID DERIVATIVES BY THE NOVEL $Ni(CO)_4$-INDUCED RING-OPENING CARBONYLATION REACTION OF 1,1-DIBROMO-2-CHLOROCYCLOPROPANES

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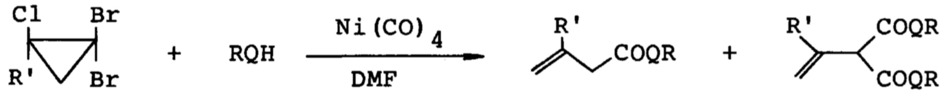
1,1-Dibromo-2-chlorocyclopropanes underwent the $Ni(CO)_4$-induced ring-opening carbonylation reaction with alcohol or amine giving the β,γ-unsaturated carboxylic acid and dicarboxylic acid derivatives. Use of N,N-dimethyltrimethylsilylamine as an initial nucleophile in the presence of benzaldehyde led to a dienecarboxamide presumably via codensation of the nickel enolate intermediate.

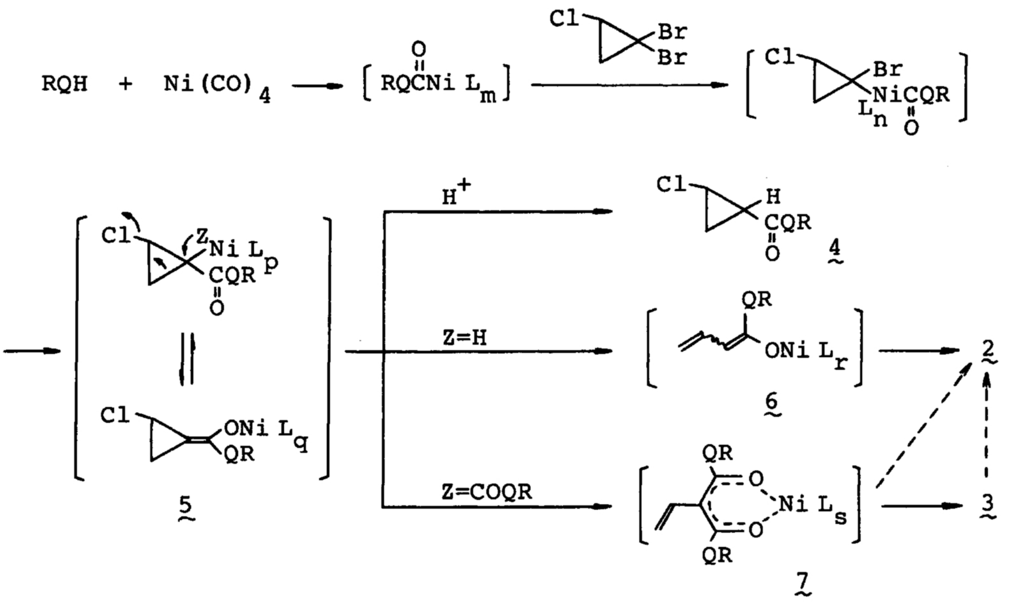
The $Ni(CO)_4$-induced carbonylation reactions of gem-dibromocyclopropanes permit gem-functionalization leading to a variety of cyclopropanecarboxylic acid derivatives.[1,2] This unique transformation is considered to depend on the intermediacy of nickel enolate compounds. We describe herein a novel ring-opening carbonylation reaction, which is effective for a synthesis of β,γ-unsaturated carboxylic acid derivatives.



1 Q=O, NH, S **2** **3**

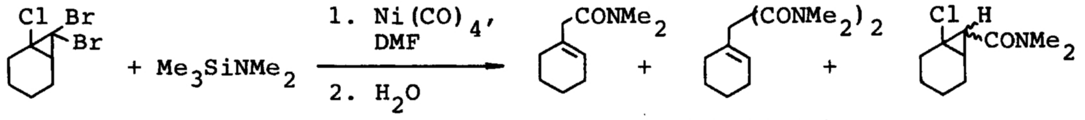
Treatment of the 1,1-dibromo-2-chlorocyclopropane **1**[3] with 1-propanol in the presence of $Ni(CO)_4$ in DMF at 70 °C gave the β,γ-unsaturated ester **2** (Q=O) and the corresponding diester **3** (Q=O) as major products. No α,β-unsaturated isomer was detected. The 2-chlorocyclopropanecarboxylate **4** (Q=O) derived by normal reductive carbonylation was produced in a small amount. Some results including the preparation of β,γ-unsaturated carboxamides and carbothiolate are listed in Table 1.

Without the addition of alcohol, the carbonylation reaction did not occur and **1** was recovered. This finding excludes the possibility that $Ni(CO)_4$ attacks **1** at the first step. One of the plausible reaction paths is outlined in the following scheme. The nickel enolate complex **5** (Q=O) might intervene as reported previously.[2] Further displacement with the alkoxycarbonyl group (Z=COOR) results in the formation of **7**. Decarboxylation of **3** or **7** is assumed to lead to the β,γ-unsaturated ester **2** since a longer reaction time increased the **2a**/**3a** ratio (Table 1). Another route to **2** is explained by hydride[4] transfer which gives the nickel enolate intermediate **6**.

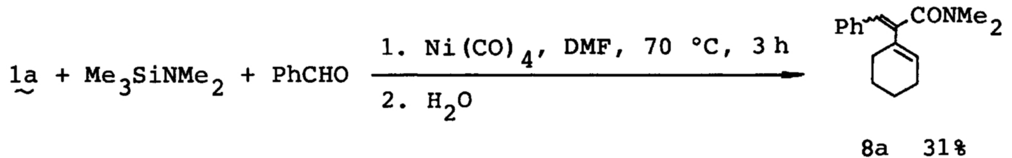


The present method provides a versatile synthetic procedure for β,γ-unsaturated carboxylic acid derivatives from vinyl chlorides[3)] based on carbonylation with one-carbon homologation. Its utility was also demonstrated by preparing a precursor of the key intermediate, 7-hydroxy-3-octenoic acid, for the pyrenophorin synthesis[5,6)] as shown by the bottom example of Table 1; the β,γ-unsaturated ester 2d was produced exclusively.[7)] The corresponding diester and cyclopropanecarboxylate were not formed, this being in sharp contrast to the results mentioned above.

With N,N-dimethyltrimethylsilylamine as an initial nucleophile,[2)] 1a underwent the similar ring-opening carbonylation reaction. This outcome contributes another C-C bond formation between a nickel enolate intermediate and an electrophile. The $Ni(CO)_4$-induced reaction[8)] of 1a with the silylamine and benzaldehyde was carried out leading to the dienecarboxamide 8a.[9)] It remains uncertain which of the enolate 6[10)] or 7[11)] participates in the condensation reaction. This method achieves the introduction of two functional groups into a cyclopropane with ring cleavage only by mixing the silylamine, 1, $Ni(CO)_4$, and benzaldehyde together in one flask.

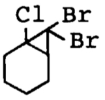
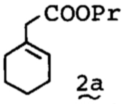
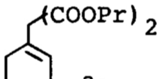
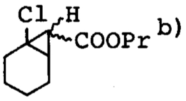
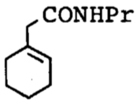
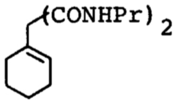
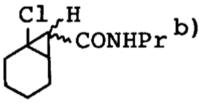
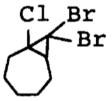
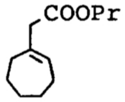
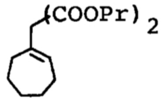
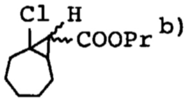
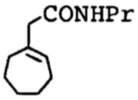
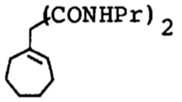
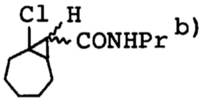
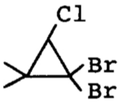
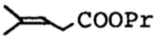
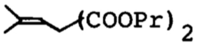
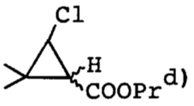
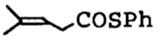
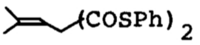
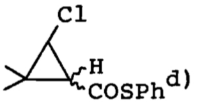
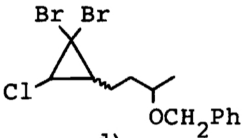


1a 55% (36:51:13)



8a 31%

Table 1. Preparation of Carboxylic Acid Derivatives by the Ni(CO)$_4$-Induced Carbonylation Reaction of 1$^{a)}$

1	RQH, equiv.		Isolated yield/ % (ratio)		
 1a	PrOH		 2a	 3a	 b)
	1	31	(61:29:10)		
	2.2$^{c)}$	46	(35:61:4)		
	2.2	57	(49:45:6)		
1a	PrNH$_2$				 b)
	2.2	62	(37:39:24)		
 1b	PrOH				 b)
	2.2	80	(43:40:17)		
1b	PrNH$_2$				 b)
	2.2	74	(43:38:19)		
 1c	PrOH				 d)
	2.2	33	(52:48:1)		
	— e)	— f)			
1c	PhSH				 d)
	2.2	19	(58:1:42)		
 1d$^{d)}$	PrOH		 2d$^{d,g)}$		
	2.2	45			

a) Reaction temperature, 70 °C; time, 6 h. Ni(CO)$_4$, 7 equiv. b) An endo and exo mixture. c) Reaction time, 3 h. d) A cis and trans mixture. e) 1-Propanol was not added. f) The starting compound 1c was recovered. g) The other products were not isolated.

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References

1) T. Hirao, Y. Harano, Y. Yamana, Y. Ohshiro, and T. Agawa, Tetrahedron Lett., **24**, 1255 (1983).

2) T. Hirao, S. Nagata, Y. Yamana, and T. Agawa, Tetrahedron Lett., in press.

3) The 1,1-dibromo-2-chlorocyclopropanes **1** were easily obtained by the addition of dibromocarbene to the corresponding vinyl chlorides.

4) P. W. Jolly, "Comprehensive Organometallic Chemistry," ed by G. Wilkinson, Pergamon Press (1982), Vol. 6, p. 37.

5) R. S. Mali, M. Pohmakotr, B. Weidmann, and D. Seebach, Liebigs Ann. Chem., **1981**, 2272.

6) Another synthetic route to pyrenophorin via 7-hydroxy-cis-3-octenoic acid was explored by use of reductive deconjugation with diethyl phosphonate as a key reaction; T. Hirao, Y. Fujihara, K. Kurokawa, Y. Ohshiro, and T. Agawa, to be published.

7) The starting 1,1-dibromo-2-chlorocyclopropane **1d** was prepared in the following way. 1,3-Dichloropropene was treated with the anion of ethyl acetoacetate, followed by decarboxylation in DMSO in the presence of LiCl. Thus obtained 6-chloro-5-hexen-2-one was reduced to the corresponding alcohol with $NaBH_4$. After protecting the hydroxyl group, addition of dibromocarbene gave **1d**.

8) To a mixture of **1a** (1.0 mmol), N,N-dimethyltrimethylsilylamine (3.0 mmol), and benzaldehyde (3.0 mmol) in DMF (2.4 mL) was added $Ni(CO)_4$ (3.0 mmol) at room temperature. The resultant solution was stirred at 70 °C for 3 h. After removal of 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 column chromatographed to give N,N-dimethyl-2-(1-cyclohexenyl)cinnamamide (**8a**) in 31% yield.

9) The geometry of the benzylidene moiety was not determined yet although only one isomer was produced.

10) E. Yoshisato and S. Tsutsumi, J. Chem. Soc., Chem. Commun., **1968**, 33; I. Rhee, I. Ryu, H. Omura, S. Murai, and N. Sonoda, Chem. Lett., **1979**, 1435.

11) J. H. Nelson, P. N. Howells, G. C. DeLullo, and G. L. Landen, J. Org. Chem., **45**, 1246 (1980). Decarboxylation of the adduct might lead to **8a**.

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