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A NOVEL SYNTHESIS OF SUBSTITUTED PHENYLPYRUVIC ACID BY DOUBLE CARBONYLATION USING COBALT PYRIDINE-2-CARBOXYLATE CATALYST

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Abstract Synthesis of a substituted phenylpyruvic acid was carried out at 60℃ and 3.0MPa using cobalt pyridine-2-carboxylate as a catalyst for the double carbonylation of benzyl chloride.

The double carbonylation of aryl halides provides a very useful synthetic method for α-keto acid, which is an important intermidiate for the preparation of α-amino acid, α-hydroxy acid, and some other heterocyclic compounds.

Although a number of catalysts such as cobalt and palladium complex have been reported[1,2,3], these catalysts and procedures often exhibit some disadvantage such as low overall yields and /or complicated synthetic procedures.

In a continuation of our investigations on the application of cobalt pyridine-2-carboxylate [$Co(Pyca)_2 \cdot 4H_2O$] as a catalyst in oxidative carbonylation of methanol to dimethyl carbonate[4], the carbonylation of benzyl chloride using this catalyst is carried out. This catalyst is insensitive to oxygen and water, and very easy to handle. Surprisingly, we not only get the product phenylacetic acid, but also a novel substituted phenylpyruvic acid ($C_{16}H_{14}O_3$): α-benzyl phenylpyruvic acid [1]. To the best of our knowledge, both of the catalyst used and the product [1] in this reaction are new.

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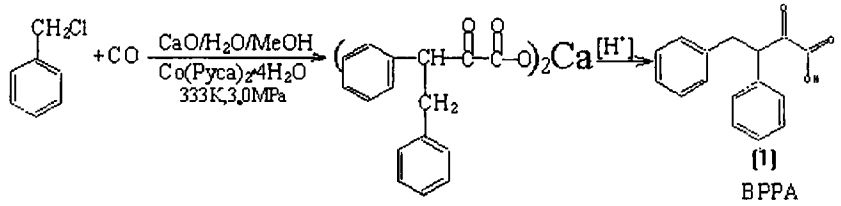


Scheme 1

The catalytic activity of the cobalt pyridine carboxylate for the double carbonylation is given in the Table 1.

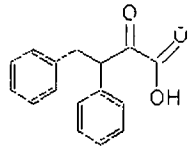
TABLE 1
Catalytic Activity on the Double Carbonylation

No	$PhCH_2Cl$/CaO mmol/mmol	CaO /mmol	T /K	P /MPa	Yield(%) BPPA	Yield(%) PAA	Selectivity of BPPA(%)	Conversion of $PhCH_2Cl$(%)
1	1.33	50	333	3.0	40.2	11.0	78.5	51.2
2	1.33	63	333	3.0	39.6	10.5	79.0	50.1
3	1.33	75	333	3.0	39.1	10.3	79.1	49.4
4	1.33	100	333	3.0	41.4	9.95	80.6	51.4
5	1.33	50	298	0.1	0	0	–	–

Reaction conditions: catalyst 5.5mmol, CH_3OH 80ml, H_2O 25ml, reaction time 10h, BPPA: α -benzyl phenylpyruvic acid [1], PAA: phenylacetic acid.

Because the benzyl group in the reaction is very active, it is possible that the benzyl group may react with other groups or intermediate to produce a benzyl substituted product.

The previous papers had dealt with this reaction system using $Co_2(CO)_8$ or $PdCl_2$ catalysts[1,2,3], it was found that the main products were the phenylacetic acid, phenylpyruvic acid and small amount of esters. Only when o-$CH_3C_6H_4CH_2Br$ was used as the substrate, there was 34% substituted keto acid compared with 30% substituted phenylacetic acid in the products.[1] In our test we found 40% substituted keto acid [1] compared with 10% phenylacetic acid when cobalt pyridine carboxylate was used as the catalyst. The general data of this compound, MS, IR, NMR are given in the experiment part of this paper.



[1]

From the structure of the compound[1], we can find that there is one chiral carbon -CH- in the molecule, which may be very useful in the further synthesis of other complicated molecule.

Experimental: Typical procedure

IR spectra were recorded with an Impact-420(Nicolet) spectrophotometer, ^{1}HNMR were obtained on a Varian XL 200 spectrometer in deuterodimethyl sulfoxide with tetramethylsilane as the internal standard. ^{13}CNMR were obtained on a ARX-500 spectrometer in deuteriochloroform with tetramethylsilane as the internal standard. Mass spectra were recorded with a HP 5890 GC-MS. Microanalyses were performed by using a CHN-analyser Model 600 from LECO. All reagents used were CP and CO purity is over 99.8%.

Synthesis of $Co(Pyca)_2 \cdot 4H_2O$: The catalyst $Co(Pyca)_2 \cdot 4H_2O$ were preparaed following the known procedures[4]. The product was characterized by XRD, IR and TG/DSC.

Synthesis of the title acid: The double carbonylation was performed by using a 500ml stainless steel autoclave with a magnetic stirrer. In a typical experiment, the autoclave was charged with the catalyst 2.0g, CH_3OH 80ml, benzyl chloride 12.7g, CaO 4.2g, and purged 3 times with CO at room temperature. The autoclave is charged with CO and heated to reaction condition. After stirring for 10h, the autoclave was slowly cooled to room temperature, and depressurized. The product mixture was removed from the autoclave and first washed with water, and then ether. After filtration, the α -keto-acid calcium salt with gray color was placed in a 250ml flask. The mother liquid was diluted by water and distilled at reduced pressure to remove benzyl chloride and other organic by-products, then regulated pH=2.0 using HCl, finally the mother liquid was extracted by ether. The organic phase was dehydrated by $MgSO_4$. After filtration of $MgSO_4$, the phenylacetic acid could be obtained by distilling ether.

The calcium salt was acidified with 50ml H_2O/ 40ml HCl/ 40ml ether in the flask. The organic phase was extracted 3 times with ether.

After distillation of ether, the crude product was obtained. Then the crude product was completely dissolved in excess chloroform at 30℃. After evaporating a part of chloroform, a little of crystal was observed and the recrystallized product(white needle crystal) could be obtained after 12 hours at 5℃. The product was afforded to the examination by NMR, IR, MS, and microanalysis.

Melting point: 87-89℃

$C_{16}H_{14}O_3$: C:75.43%(calc. 75.59) H: 5.58%(calc:5.51%)

MS (m/e): 254(M+), 93%; 236, 27%; 209, 33%;
181(C_6H_5-CH-$C_6H_5CH_2$-). 100%; 91($C_6H_5CH_2$); 91%

^{13}C NMR: (125MHZ, $CDCl_3$; δ ppm ,$CDCl_3$=77.0 ppm)
38.0, 53.4, 125-129; 134.2, 138.0, 159.2, 193.2

^{1}HNMR: (200MHZ, DMSO, δ ppm/TMS), 2.90~3.02(q.1H), 3.29~3.40 (q.1H), 4.73~4.81(t.1H), 7.04~7.44(m.10H)

IR (cm^{-1}): 1451, 1493, 1607, 1706, 1728, 2813, 2937, 3028, 3453, 3555

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References

1. Alper H. and Abbayes H., *J. Organometal Chem.*, **1977**, 134, C11-C14.
2. Ozawa F., Soyama H. and Yanagihara H., *J.Am.Chem.Soc.*, **1985**, 107(11), 3235.
3. Foa M. and Francalanci F., *J. Mol.Catal.*, **1987**, 41(1), 89.
4. Li Guang-Xing, Wang Jun-Yi, Mei Fu-Ming, *Petrochemical Technology (Ch)*, **1999**, 7, 144.

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