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# A CONVENIENT METHOD FOR THE CONVERSION OF *trans* to *cis*-CINNAMIC ACIDS

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*Summary*: *trans*-Cinnamic acids react in sequence with bromine, base, and carbon monoxide [palladium(0) and phase transfer catalysis] to give *cis*-acids in reasonable yields.

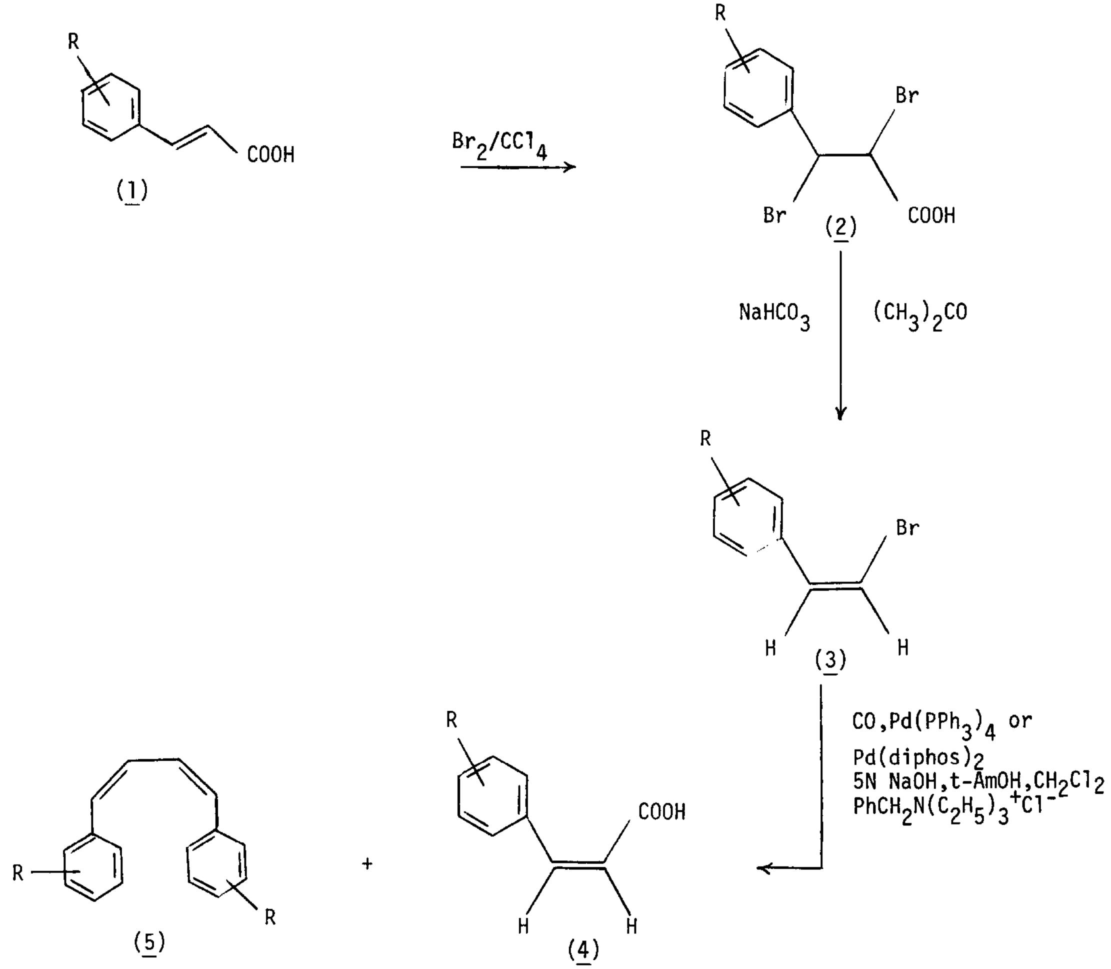
The conversion of *trans* to *cis*-cinnamic acids has attracted attention over many years. For example, irradiation of *trans* (or *cis*)-cinnamic acid for 2.5 - 120 hr. affords an equilibrium mixture from which the *cis*-isomer can be obtained in 10-40% yields[1,2]. Another approach involves esterification of the E-acid followed by bromination, base-induced elimination to the arylpropiolic acid and subsequent hydrogenation affording the Z-cinnamic acid in 28-31% overall yield from the ester (the yield from the acid was not reported)[3]. Other unattractive routes involving ester substrates include the use of derivatives of phenylpropiolic acid[4a] and phenylalanine (i.e., diazo esters)[4b].

The use of vinylic bromides as intermediates has also been examined. Bromination of the *trans*-cinnamic acid followed by treatment with sodium bicarbonate in acetone gave the *cis*-bromostyrene. Grignard formation from the latter, followed by conventional carbonation and protonation afforded cinnamic acid in a 2:1 cis/trans ratio. Lithiation of *cis*-bromostyrene and subsequent carbonation and work-up gave a 4:1 mixture of *trans*-cinnamic acid and phenylpropiolic acid[5].

Phase transfer catalysis is an excellent means of effecting metal catalyzed processes under gentle conditions[6,7]. For instance, benzylic halides are carbonylated to acids, at room temperature and atmospheric pressure in the presence of cobalt carbonyl[6,7] or tetrakis(triphenylphosphine)palladium[8], sodium hydroxide, methylene chloride, and a phase transfer agent. We now wish to report that *cis*-bromostyrenes (**3**), obtained from *trans*-cinnamic acids (**1**) as illustrated in Scheme 1, can be carbonylated to *cis*-acids (**4**) using palladium (0) and phase transfer catalysis conditions.

Bromination of a variety of *trans*-acids, **1**[R=H, p-Cl, p-$CH_3$, p-$CF_3$, m-Br, o-$CH_3$] in carbon tetrachloride gave the dibromoacids (**2**) in 90-97% yields (Table 1). The *cis*-bromides (**3**) were formed in 86-91% yield by exposure of **2** to bicarbonate ion in acetone[9]. When **3** was reacted with carbon monoxide, 5N sodium hydroxide, t-amyl alcohol as the organic phase (and some methylene chloride to solubilize $Pd(PPh_3)_4$), benzyltriethylammonium chloride as the phase transfer catalyst and tetrakis(triphenylphosphine)palladium(0) as the metal catalyst [25-40 / 1 mole ratio of **3** /$Pd(PPh_3)_4$], the pure *cis*-cinnamic acids (**4**) were obtained in 35-56%

Scheme 1



yields (not optimized). By-products of some of these reactions were the cis,cis-1,4-diaryl-1,3-butadienes (5)and very small amounts of the t-amyl ester of 4 were also sometimes isolated.

Note that, in contrast to benzylic halides[8], the nature of the palladium(0) catalyst does not change the reaction course as bis[bis(1,2-diphenylphosphino)ethane]palladium(0) [$Pd(diphos)_2$] behaved in the same manner as tetrakis(triphenylphosphine)palladium(0)[for 3, R=p=Cl]. A phase transfer agent is required for these reactions, since the yield of 4 is much lower in the absence of the quarternary ammonium salt. No reaction occurs in the absence of the palladium catalyst.

TABLE 1

Product yields[a]

| 1,R= | 2, % | 3, % | 4, %[b] | Overall yield, % | M.p., °C | lit. m.p. °C | Other products |
|---|---|---|---|---|---|---|---|
| H | 93 | 89 | 56 | 47 | 66-67 | 68[1] | 5, trace |
| p-Cl[c] | 94 | 91 | 47 | 41 | 114-115 | 111-111.5[2] | 5, 16.6% |
| m-Br | 91 | 89 | 35 | 28 | 75.5-77.0 | 75-77[2] | 5, 17.1% |
| p-$CH_3$ | 97 | 87 | 49 | 41 | 73-75 | 77.5-79.0[1] | 5, 8.4% |
| p-$CF_3$ | 90 | 91 | 48 | 40 | 53.0-53.5[d] | - | 5, 21.4% |
| o-$CH_3$ | 94 | 86 | 54 | 44 | 91-92 | 89-90[4] | - |
| p-$CH_3O$ | 90 | -[e] | | | | | |

[a] Yields are of pure materials. [b] Using $Pd(PPh_3)_4$ as the catalyst. [c] Yield of 4, R=p-Cl, was 51% using $Pd(diphos)_2$ as the catalyst. [d] New compound. Anal. calcd. for $C_{10}H_7F_3O_2$: C, 55.56; H, 3.26. Found: C, 55.95; H, 3.16. [e] Only the trans-isomer of 3, R=p-$CH_3O$ was formed.

The reaction is apparently insensitive to substituent effects since essentially the same yields of 4 were realized using 3, R=p-$CF_3$, or 3, R=p-$CH_3$ as reactants. The use of the less polar solvent, 4-methyl-2-pentanone, as the organic phase give superior yields of 4. However, the reaction is not useful, since a mixture of cis and trans acids are produced (e.g., 3, R=H afforded cinnamic acid in 79% yield, with the cis/trans ratio being 62:38). Isomeric mixtures of acids, in high yield, were also isolated when benzene was employed as the organic phase.

The overall yield for the described conversion of trans to pure cis-cinnamic acids are reasonable (28-47%). In addition, this reaction sequence is simple both in execution and work-up. The palladium catalyzed reaction is regiospecific, in terms of the formation of either 4 or 5 [i.e., no geometric isomers].

The following general procedure was used: a mixture of 5N sodium hydroxide [15 ml.] and benzyltriethylammonium chloride [0.5-0.6 mmol] was stirred for 30 minutes under nitrogen. The palladium(0) catalyst [0.09-0.12 mmol] in t-amyl alcohol (15 ml.) containing methylene chloride (4-6 ml.), was added and the reaction atmosphere was changed to carbon monoxide. After stirring for 3.5-4.0 hours, 3 [2.75-3.75 mmol] in t-amyl alcohol (5 ml.) was added dropwise and then the mixture was vigorously stirred overnight (CO atmosphere). The phases were separated, the aqueous phase was extracted with ether (2 x 15 ml.), and the organic phase was washed with water (20 ml.). The combined aqueous phases were cooled, acidified (c. HCl), extracted with ether (4 x 50 ml.), and the ether extracts were dried ($MgSO_4$) and concentrated. Analytically pure acid (4) was then obtained by thin-layer chromatography.

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