

## Manganese-Catalyzed Benzene Synthesis by [2+2+2] Coupling of 1,3-Dicarbonyl Compound and Terminal Acetylene

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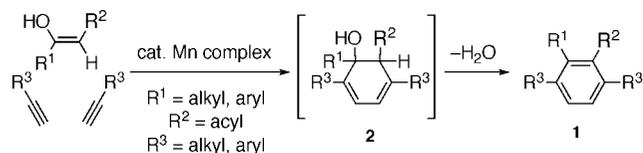
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We report here a new reaction, manganese-catalyzed intermolecular dehydrative [2+2+2] coupling of one mole of a 1,3-dicarbonyl compound and two moles of a terminal acetylene, which produces a benzene derivative in good to excellent yield (Scheme 1). When phenylacetylene derivatives ( $R^3 = \text{aryl}$ ) are employed, the reaction provides a synthetically useful, modular approach to *p*-terphenyl derivatives. The reaction formally resembles the well-known [2+2+2] alkyne trimerization approach to the synthesis of benzene derivatives,<sup>1–3</sup> but differs significantly in that the enol form of the dicarbonyl compound is incorporated into the benzene ring with expulsion of one mole of water. *p*-Terphenyl derivatives are important building blocks for the synthesis of organic materials,<sup>4,5</sup> and their selective synthesis has generally been achieved by group 10 metal-catalyzed cross-coupling of aryl metals and aryl halides. The present reaction provides a new alternative to this conventional methodology.

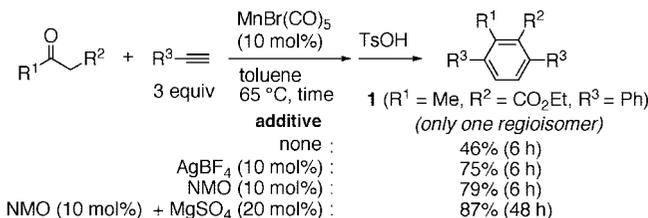
We discovered this reaction serendipitously during our study of the indium-catalyzed reaction of 1,3-dicarbonyl compounds with 1-alkynes.<sup>6</sup> Extensive experimentation was necessary to optimize the reaction conditions, when a mixture of ethyl acetoacetate and 3 equiv of phenylacetylene was heated to 65 °C in toluene in the presence of 10 mol %  $\text{MnBr}(\text{CO})_5$  (Scheme 2). Initially, the reaction formed a mixture of three compounds in low yield: a *p*-terphenyl ester **1**, the corresponding carboxylic acid derivative of **1**, and a cyclohexadienol **2** that is a precursor of **1**. When we increased the reaction time, the amount of acid byproduct increased at the expense of **1**. This observation suggested that water generated during the in situ conversion of **2** to **1** caused acid formation. To assist this conversion as a separate step after cycloaddition, we treated the reaction mixture with a catalytic amount of TsOH to obtain **1**. This procedure increased the yield to 46%. We then examined various other additives, some of which further improved the yield. For instance,  $\text{AgBF}_4$  and *N*-methylmorpholine *N*-oxide (NMO)<sup>7</sup> increased the yield to 75% and 79% yield, respectively, presumably by activation of the catalyst through ligand exchange. Addition of anhydrous  $\text{MgSO}_4$  (20 mol %) further improved the yield to 87%, most likely by trapping water in situ. Other transition metal complexes, such as  $\text{Mo}(\text{CO})_6$ ,  $\text{W}(\text{CO})_6$ ,  $\text{ReBr}(\text{CO})_5$ ,<sup>8</sup>  $\text{FeI}_2(\text{CO})_4$ ,  $[\text{RuCl}_2(\text{CO})_3]_2$ ,  $\text{Co}_2(\text{CO})_8$ ,  $\text{Rh}(\text{acac})(\text{CO})_2$ , and  $\text{IrCl}(\text{CO})(\text{PPh}_3)_2$  were ineffective.

The scope of the reaction was examined and the results are in Table 1. The reaction was found to be sensitive to the steric and electronic effects of the  $R^1$  group. Ethyl acetoacetate reacted with phenylacetylene to afford the *p*-terphenyl product in 87% yield (entry 1), while the benzyl and allyl esters reacted similarly (84% and 81%, respectively, in entries 2 and 3). Substrates bearing a sterically demanding  $R^1$  substituent, cyclohexyl and *tert*-butyl groups, did not afford any product at all (entries 4 and 5). Ethyl benzoylacetate ( $R^1 = \text{Ph}$ ), on the other hand, furnished the expected product in 94% yield (entry 6). An electron-donating substituent (entry 7) afforded the expected product in a somewhat lower yield

### Scheme 1



### Scheme 2



**Table 1.** The Synthesis of **1** from Various 1,3-Dicarbonyl Compounds ( $R^1 = \text{Alkyl, Aryl, or Alkenyl}, R^2 = \text{Ester or Acyl}$ ) and Phenylacetylene<sup>a</sup>

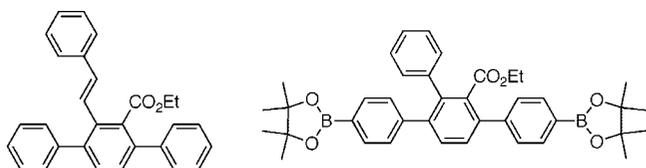
entry	$R^1$	$R^2$	time	yield <sup>b</sup>
1	Me	$\text{CO}_2\text{Et}$	48 h	87%
2	Me	$\text{CO}_2\text{Bn}$	12 h	84%
3	Me	$\text{CO}_2\text{Allyl}$	12 h	81%
4	<i>c</i> -Hex	$\text{CO}_2\text{Et}$	72 h	0%
5	<i>t</i> -Bu	$\text{CO}_2\text{Et}$	72 h	0%
6	Ph	$\text{CO}_2\text{Et}$	18 h	94%
7		$\text{CO}_2\text{Et}$	15 h	75%
8		$\text{CO}_2\text{Et}$	6 h	83%
9	Me	COMe	12 h	98% <sup>c</sup>
10	Ph	COMe	3 h	33% <sup>c,d</sup>

<sup>a</sup> The reaction was carried out using 3 equiv of phenylacetylene in the presence of 10 mol % of  $\text{MnBr}(\text{CO})_5$ , 10 mol % of NMO, and 20 mol % of anhydrous  $\text{MgSO}_4$  in toluene at 65 °C. <sup>b</sup> The yield is based on isolated material. <sup>c</sup> The reaction was carried out without  $\text{MgSO}_4$ . <sup>d</sup> Obtained as a mixture of regioisomers (18%  $R^1 = \text{Ph}, R^2 = \text{COMe}$ ; 15%  $R^1 = \text{Me}, R^2 = \text{COPh}$ ).

(75%). A  $\gamma,\delta$ -unsaturated  $\beta$ -ketoester reacted readily with retention of the conjugated  $R^1$  group giving a highly functionalized stilbene derivative in 83% yield (entry 8, structure in Scheme 3 below).

1,3-Diketones gave mixed results. Pentane-2,4-dione was found to be an excellent substrate and produced the desired benzene derivatives in quantitative yield (entry 9). 1-Phenylbutane-1,3-dione,

## Scheme 3



**Table 2.** The Synthesis of **1** from Ethyl Benzoylacetate ( $R^1 = \text{Ph}$ ,  $R^2 = \text{CO}_2\text{Et}$ ) and Various Terminal Alkynes ( $R^3 = \text{Aryl}$  or  $\text{Alkyl}$ )<sup>a</sup>

entry	$R^3$	time	yield <sup>b</sup>
1		3 h	77%
2		6 h	83%
3		72 h	0%
4		3 h	65%
5		3 h	84%
6		12 h	65%
7	Hex	5 h	94% <sup>c</sup> (major/minor = 73: 27)
8	Bn	3 h	82% <sup>c</sup> (major/minor = 74: 26)

<sup>a</sup> The reaction was carried out using 3 equiv of alkyne in the presence of 10 mol % of  $\text{MnBr}(\text{CO})_5$ , 10 mol % of NMO, and 20 mol % of anhydrous  $\text{MgSO}_4$  in toluene at 65 °C. <sup>b</sup> The yield is based on isolated material. <sup>c</sup> Ratio was determined by <sup>1</sup>H NMR analysis.

whose unsymmetrical structure offers two possible enol structures, gave a nearly 1:1 mixture of two isomeric products in low yield (entry 10). 1,3-Diphenylpropane-1,3-dione did not give the desired [2+2+2] adduct, and instead gave an  $\alpha$ -alkenylated product as in the indium-catalyzed carbometalation reaction.<sup>6</sup> Cyclic 1,3-diketones such as cyclopentane-1,3-dione did not take part in any reaction at all.

Next, the reactions of ethyl benzoylacetate ( $R^1 = \text{Ph}$ ,  $R^2 = \text{COOEt}$ ) with a variety of terminal acetylenes were examined (Table 2). The reaction rate was faster with electron-rich acetylenes than with electron-deficient ones and was sensitive to steric hindrance caused by the acetylene substituent. A variety of monosubstituted acetylenes, but not internal acetylenes, can be used for the reaction. When electron-rich *p*-methoxyphenylacetylene was used, the reaction took place rapidly in 3 h to give the expected product as a single regioisomer in 77% yield (entry 1). The reaction of electron-deficient *p*-trifluoromethylphenylethyne was slow but produced the expected *p*-terphenyl products in 83% yield (entry 2). *o*-Methyl substitution inhibited the reaction (entry 3). 2-Ethynyl-naphthalene afforded the expected products in 65% yield (entry 4), while the reaction of 1-ethynyl-naphthalene was very slow. Functional group tolerance is illustrated by two additional examples. (*p*-Bromophenyl)acetylene participated readily in the reaction and produced the product in high yield (entry 5). A phenylacetylene bearing a pinacolyl boron functionality also gave the expected bis-borinate product in 65% yield (entry 6, structure in Scheme 3 below).

Aliphatic acetylenes took part in the reaction readily, but regioselectivity in the products was low. 1-Octyne and 3-phenylpropyne afforded a 73:27 and 74:26 mixture of regioisomers in 94% and 82% yield, respectively (entries 7 and 8).<sup>9</sup> On the basis of the NMR analysis, the major isomer was assigned as a para isomer, and the minor isomer tentatively as a meta isomer (Supporting Information).

In conclusion, we have developed an efficient method for the synthesis of substituted benzene derivatives using a new manganese-catalyzed dehydrative cycloaddition reaction of 1,3-dicarbonyl compounds and terminal alkynes. This reaction has several synthetically attractive features: the use of naturally abundant and nontoxic manganese metal as a catalyst,<sup>10</sup> an interesting mode of participation of the enol form of a 1,3-dicarbonyl compound in benzene synthesis, good atom economy, good functional tolerance, high regioselectivity of terphenyl formation and diverse structural variation in the product. The structures of the terphenyl products illustrated below suggest that such products will serve as useful starting materials for modular syntheses of larger conjugation arrays useful for materials applications.<sup>11</sup> At present we do not have enough experimental evidence to discuss the reaction mechanism. This will be the subject of further studies.

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**Supporting Information Available:** Detailed experimental procedure and properties of compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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