Scandium(III) trifluoromethanesulfonate-catalysed reductive Friedel–Crafts benzylation of aromatic compounds using arenecarbaldehydes and propane-1,3-diol

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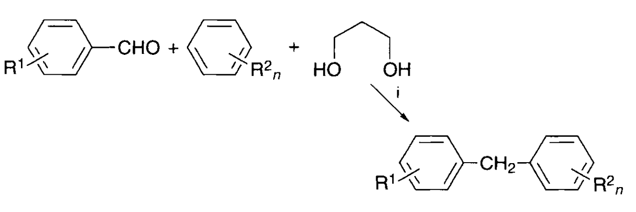
Scandium(III) trifluoromethanesulfonate catalyses the Friedel–Crafts benzylation of aromatic compounds with arenecarbaldehydes and propane-1,3-diol to produce, through a clean redox process, diarylmethanes in high to excellent yields.

Numerous Friedel–Crafts alkylations using various alkyl halides, alcohols, alkenes or ethers as the alkylating agents have been developed and widely used in organic synthesis including industrial production.[1] In contrast, less attention has been focused on the acid-catalysed condensation of aromatic compounds with arenecarbaldehydes because of the formation of many products,[2] even though the prototype of this reaction was recognized in 1886.[3] Further, this type of reaction is generally performed with a large excess of an acid catalyst such as $AlCl_3$ or CF_3SO_3H.[4] Recently, gallium dichloride was reported to promote the reductive Friedel–Crafts reaction of both aliphatic and aromatic carbonyl compounds,[5] but here again the use of an excess of gallium dichloride was essential. Thus, the catalytic Friedel–Crafts-type alkylation reaction using arenecarbaldehydes has yet to be explored.[6]

During the course of our investigation of the Friedel–Crafts alkylation using scandium(III) trifluoromethanesulfonate [$Sc(OTf)_3$],[7] we found that an arenecarbaldehyde, upon treatment with propane-1,3-diol and a catalytic amount of $Sc(OTf)_3$, cleanly underwent a novel reductive Friedel–Crafts benzylation with an aromatic compound (Scheme 1).

First, we examined the efficacy of various alcohols in the reaction of benzene with benzaldehyde in the presence of $Sc(OTf)_3$ as catalyst.† After screening various alcohols, we concluded that propane-1,3-diol was the co-reagent of choice to accomplish the Friedel–Crafts benzylation and diphenylmethane was obtained in 70% yield without any troublesome side reactions.‡ In contrast, no reaction took place in the absence of propane-1,3-diol. A typical experimental procedure is given below. To a benzene suspension of anhydrous $Sc(OTf)_3$ (10 mol%) were added propane-1,3-diol (1.1 mol) and benzaldehyde (1.0 mol) successively at room temp. The mixture was allowed to react at 125 °C (bath temperature) for 10 h, then poured into water, extracted three times with diethyl ether and then the organic layer was dried over $MgSO_4$. GC–MS analysis showed the formation of diphenylmethane. The yield of the products was estimated to be 70% with naphthalene as an internal standard.



Scheme 1 *Reagents and conditions*: i, $Sc(OTf)_3$ (10 mol%), 125 °C

These results prompted us to survey the scope of the reaction. Representative results are summarized in Table 1. The aromatic compound, except in the case of anisole, was utilized not only as the substrate but also as the reaction medium. With benzaldehyde as the benzylation reagent, the Friedel–Crafts products were produced in yields ranging from 37 to 97% (runs 1 and 3–5). The yields of the alkylation products were generally improved by the use of a methyl-substituted arene such as toluene or xylene. However, the reaction using anisole resulted in a lower yield, probably due to further side reactions. The side reactions were suppressed to some extent by the use of 1,2-dichloroethane as the solvent. It is noteworthy that when the reaction was carried out at ambient temperature the corresponding acetal was produced (run 2) instead of the Friedel–Crafts product.[8] The acetal appears to be a crucial intermediate in the present benzylation reaction, since the reaction of 2-aryl-1,3-dioxane with the arene under the same reaction conditions provides diarylmethane in yields consistent with those of the one-pot reaction.

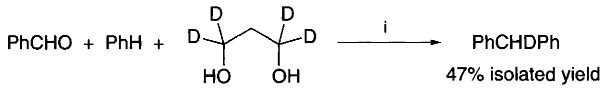
When the protocol was applied to the reaction of 4-methyl-, 4-phenyl- or 4-chloro-benzaldehyde with benzene, toluene or xylene, high to quantitative yields of the corresponding diarylmethane were obtained in every case (runs 6–12). Similarly, naphthalene-1-carbaldehyde reacted with toluene to afford a regioisomeric mixture of 1-naphthylmethylated toluene in 68% yield (run 13). The regioselectivity of the benzylation of substituted arenes showed an *ortho–para* preference, which conforms with typical electrophilic aromatic substitutions.[9]

To gain further insight into the reaction mechanism, we heated a benzene solution of a mixture of benzaldehyde, 2,4-dimethylpentane-2,4-diol and $Sc(OTf)_3$ catalyst at 125 °C

Table 1 $Sc(OTf)_3$-Catalysed Friedel–Crafts reactions of aromatics with aromatic aldehydes

Run	Aldehyde	Aromatic	*t*/h	Yield (%)[a]	Ratio of *o* : *m* : *p*[b]
1	PhCHO	C_6H_6	10	70	—
2[c]	PhCHO	C_6H_6	48	0	—
3	PhCHO	PhMe	10	97	42 : 7 : 51
4	PhCHO	*p*-Xylene	10	96	—
5	PhCHO	PhOMe	10	37	49 : trace : 51
6	4-MeC_6H_4CHO	C_6H_6	8.5	64	—
7	4-MeC_6H_4CHO	PhMe	6	Quant.	34 : 4 : 62
8	4-MeC_6H_4CHO	*p*-Xylene	8	73	—
9	4-PhC_6H_4CHO	PhMe	16	Quant.	34 : 5 : 61
10	4-ClC_6H_4CHO	C_6H_6	17.5	91	—
11	4-ClC_6H_4CHO	PhMe	16	89	41 : 9 : 50
12	4-ClC_6H_4CHO	*p*-Xylene	17	Quant.	—
13	1-Naphtyl-CHO	PhMe	12	68	25 : 5 : 70

[a] GLC yield. [b] The isomer distributions were determined by using GLC analysis or from the ^{13}C NMR spectra. [c] The reaction was carried out at room temp. The product was 2-phenyl-1,3-dioxane (quantitative yield). [d] The reaction was carried out with 5.0 equiv. of anisole in 1,2-dichloroethane.



Scheme 2 *Reagents and conditions*: i, Sc(OTf)$_3$ (10 mol%), 125 °C, 20 h

and found that a complex mixture of products resulted. Thus, we conclude that the hydrogen atoms on C-1 and C-3 of propane-1,3-diol play a significant role in the reduction. To clarify the origin of the hydride, we repeated the reaction using [1,1,3,3-^{2}H$_4$]propane-1,3-diol (Scheme 2) and were pleased to observe that deuterium was incorporated into the benzylic carbon of over 95% of the diphenylmethane. Therefore, the diol was concluded to act as the hydride source in this reaction.

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Footnotes

[†] No other lanthanide(III) trifluoromethanesulfonates, *e.g.* Y(OTf)$_3$, Nd(OTf)$_3$, Sm(OTf)$_3$ or Yb(OTf)$_3$, catalysed the reaction of toluene with benzaldehyde. However CF$_3$SO$_3$H (TFSA) and SnCl$_4$ were found to be effective. The TFSA-catalysed reductive Friedel–Crafts reaction will be reported in due course.

[‡] Use of methanol, propan-2-ol, ethane-1,2-diol, butane-2,3-diol, pentane-2,4-diol or butane-1,4-diol instead of propane-1,3-diol under the same reaction conditions reduced the yield considerably or did not give any trace of diphenylmethane.

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