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COMMUNICATIONS

Published on Web 05/23/2006

Highly Efficient Atom Transfer Radical Addition Reactions with a Ru^{III} Complex as a Catalyst Precursor

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Ruthenium complexes are among the most active catalysts for atom transfer radical addition (ATRA) reactions of halogenated compounds to olefins.[1,2] Despite their high activity, the catalysts still show a severe disadvantage from a practical point of view: they display low catalyst stability. Consequently, high catalyst loadings are needed, and low turnover numbers (TONs) are achieved. This is particularly evident for addition reactions with substrates, which show a low intrinsic reactivity such as $CHCl_3$ or 1-decene. In this case, the maximum TONs generally do not exceed 300.[3] In the following we describe a new catalytic procedure, which allows ATRA reactions with unprecedented TONs of up to 44 000 under mild conditions.

Ruthenium-catalyzed ATRA reactions are assumed to proceed in three steps.[1] For the addition of CCl_4 to olefins, for example, a Ru^{II} complex first abstracts a chloro atom from CCl_4 to give a $Ru^{III}-Cl$ complex and a $\bullet CCl_3$ radical. The latter adds to the olefin, which then combines with the $Ru^{III}-Cl$ complex to give the 1:1 addition product and the regenerated Ru^{II} catalyst. It had been reported that an increased CCl_4 concentration leads to a faster catalyst deactivation[2i] and that the reaction of a Ru^{II} catalyst with CCl_4 in the absence of olefin produces C_2Cl_6.[2a,4] These observations suggest that the combination of two $\bullet CCl_3$ radicals to give C_2Cl_6 is a likely side reaction during ATRA. The formation of C_2Cl_6 would lead to an accumulation of $Ru^{III}-Cl$ complexes and to a decrease in catalytic rate. We therefore examined the possibility of increasing the lifetime of the catalyst by addition of a reagent that could regenerate the Ru^{II} complex. The standard radical initiator azobis(isobutyronitrile) (AIBN) appeared to be a suitable candidate because it provides a source of radicals, which could regenerate the Ru^{II} catalyst by abstraction of a chloro atom from $Ru^{III}-Cl$. To test this hypothesis, we have investigated the addition of CCl_4 to styrene with $[Cp^*RuCl(PPh_3)_2]$ (**1**), an ATRA catalyst reported by Noels and Demonceau,[2i,j] in the absence and in the presence of AIBN. To manifest differences in catalyst lifetime, a substrate/catalyst ratio of 20 000:1 was employed.

Despite the fact that complex **1** is known to be a highly active catalyst for intermolecular ATRA reactions, a conversion of only 3% was observed after 24 h (Table 1, entry 1). This can be explained by the low catalyst/CCl_4 ratio employed in our reaction, which leads to a rapid deactivation of the catalyst. In the presence of 5.0 mol % AIBN, however, a complete conversion was observed with the main product (yield: 83%) being the desired mono adduct (entry 2). The difference between the yield and the conversion can be attributed to the formation of oligomers, which are common side products during ATRA.[1,2] The presence of the Ru catalyst was crucial for the success of the reaction as evidenced by a control reaction without complex **1**, which resulted in the exclusive formation of polymers (entry 3).

The dramatic increase in yield observed for the **1**/AIBN system suggested that the radical initiator was able to efficiently regenerate the Ru^{II} catalyst (see Supporting Information). This prompted us to investigate the possibility of using directly an oxidatively stable Ru^{III} complex instead of the very sensitive[5] complex **1**. We thus performed an ATRA reaction of CCl_4 and styrene with the Ru^{III} complex $[Cp^*RuCl_2(PPh_3)]$ (**2**), which can easily be obtained by addition of PPh_3 to the commercially available $[Cp^*RuCl_2]_2$.[6] Using again only 0.005 mol % Ru, we were able to obtain the mono adduct in 85% yield after 24 h (entry 4). This confirmed that a reverse ATRA[7] process with a Ru^{III}/radical initiator combination is indeed possible. Furthermore, it corroborates the hypothesis[2i] that a complex with only one PPh_3 ligand is the active catalyst in Cp*Ru-catalyzed ATRA reactions. Lowering the AIBN concentration from 5.0 to 1.0 mol % resulted in a slower reaction without reducing the amount of oligomers formed (entry 5). The utilization of an access of CCl_4 with respect to the substrate turned out to be advantageous: when the CCl_4/styrene ratio was lowered from 4.0 (entry 4) to 1.5 (entry 6), an increased amount of side products was observed.

Table 1. ATRA of CCl_4 to Styrene Catalyzed by Complex $[Cp^*RuCl(PPh_3)_2]$ (**1**) or $[Cp^*RuCl_2(PPh_3)]$ (**2**)[a]

entry	catalyst	AIBN [mol %]	$[CCl_4]$/[styrene] ratio	conv. [%]	yield [%]
1	**1**	–	4.0	3	3
2	**1**	5.0	4.0	100	83
3	–	5.0	4.0	50	0
4	**2**	5.0	4.0	100	85
5	**2**	1.0	4.0	73	54
6	**2**	5.0	1.5	100	71

[a] All reactions were performed in toluene at 60 °C with [styrene]/[Ru] = 20 000:1 and [styrene] = 1.38 M using 1,4-dioxane (140 mM) as the internal standard. The conversion is based on the consumption of the olefin, and the yield is based on the formation of product as determined after 24 h by ^1H NMR spectroscopy.

To test the scope of the new catalytic procedure with the Ru^{III} complex **2**, we have investigated the ATRA of various polychlorinated compounds and of *p*-tosyl chloride to olefins (Table 2). The AIBN concentration was fixed to 5.0 mol % with respect to the olefin and the substrate/catalyst ratio was varied according to the reactivity of the respective starting material. For styrene (entry 1), we were able to obtain the CCl_4 adduct in 88 yield after 24 h (TON = 13 200). The reactions with the less reactive α-methylstyrene (entry 2) were slower but provided the monoadduct in a very clean reaction (TON = 9800). The results we obtained for 1-decene (entry 3) and 1-hexene (entry 4) were even more impressive. After 24 h at 60 °C, the CCl_4 adduct of 1-decene was formed in 93% yield using an olefin/catalyst ratio of 25 000 (TON = 23 300). For 1-hexene, we were able to obtain the CCl_4 adduct in 89% yield after 48 h using a catalyst concentration of only 2.0×10^{-3} mol % (TON = 44 500). It should be noted that these TONs are not maximized values because the substrate/catalyst ratio was chosen in such a fashion that a synthetically interesting yield was

10.1021/ja0617542 CCC: $33.50

Table 2. ATRA of Polychlorinated Compounds and of *p*-Tosyl Chloride to Olefins Catalyzed by Complex [Cp*RuCl$_2$(PPh$_3$)] (**2**) in the Presence of AIBN[a]

entry	olefin	chloro substrate	[olefin]/[**2**] ratio	yield [%]
1	styrene	CCl_4	15 000	88 (82)[b]
2	α-methylstyrene	CCl_4	10 000	98
3	1-decene	CCl_4	25 000	93 (87)[b]
4	1-hexene	CCl_4	50 000	89[c]
5	styrene	$CHCl_3$	1500	88 (85)[b]
6	*p*-chlorostyrene	$CHCl_3$	1500	88
7	styrene	CCl_3CO_2Et	1000	95
8	styrene	CCl_2HCO_2Et	1000	96
9	methyl methacrylate	CCl_2HCO_2Et	1000	94
10	styrene	*p*-tosyl chloride	1000	98
11	*p*-chlorostyrene	*p*-tosyl chloride	1000	95
12	α-methylstyrene	*p*-tosyl chloride	1000	96
13	methyl methacrylate	*p*-tosyl chloride	500	75

[a] The reactions were performed in toluene (entries 1−4 and 7−13) or CHCl$_3$ (entries 5 and 6) at 60 °C with [olefin] = 1.38 M (entries 1−9) or 0.44 M (entries 10−13). The following substrate ratios were employed: [CCl$_4$]/[olefin] = 4.0, [CXCl$_2$CO$_2$Et]/[olefin] = 3.0, and [TsCl]/[olefin] = 1.2. The yield is based on the formation of product as determined after 24 h by ^{1}H NMR spectroscopy using the internal standards 1,4-bis(trifluoromethyl)-benzene (270 mM; entries 1−9; 100 mM, entries 10−12) or mesitylene (120 mM) (entry 13). The conversion of the olefin was quantitative except for entry 3, for which a value of 94% was obtained. [b] Isolated yields after column chromatography. [d] Determined after a reaction time of 48 h.

obtained in a reasonable amount of time. Nevertheless, they represent—to best of our knowledge—the highest TONs for the addition of CCl$_4$ to olefins reported thus far. A TON of 9000 was obtained for the addition of CCl$_4$ to styrene after an unspecified reaction time with the carborane complex [(9-SEtPh-7,8-C$_2$B$_9$H$_{10}$)-RuH(PPh$_3$)$_2$] (**4**),[2f,g] which requires a multistep synthesis. For the same reaction, the maximum TON reported for the Cp*Ru complex **2** is 1600−1700 (reaction time: >200 h).[2i] The addition of CCl$_4$ to 1-decene catalyzed by complex **4** gave a yield of only 58% after 16 h using a catalyst concentration of 0.33 mol % (TON = 174).

Efficient ATRA reactions with the more difficult chloro substrates CHCl$_3$, CCl$_3$CO$_2$Et, and CCl$_2$HCO$_2$Et were likewise possible. The CHCl$_3$ adducts of the aromatic olefins styrene (entry 5) and *p*-chlorostyrene (entry 6) were both obtained in a yield of 88% after 24 h using an olefin/Ru ratio of 1500 (TON = 1300). To the best of our knowledge, these are again the highest TONs reported thus far. Tri- and dichlorinated ethyl acetate could be added to styrene and methyl methacrylate using an olefin/Ru ratio of 1000:1 (entries 7−9). This compares very favorably to other synthetic procedures. The addition of CCl$_3$CO$_2$Et to styrene, for example, has been reported to proceed with a yield of 57% using 5 mol % of the Grubbs catalyst [RuCl$_2$(PCy$_3$)$_2$(=CHPh)] (TON = 11).[2e] It should be noted that the products are synthetically interesting precursors because they can be cyclized to give lactones.[2e,8]

ATRA reactions with sulfonyl chlorides have been investigated extensively by Kamigata et al.[9] Typically, the reactions are performed at elevated temperatures with 1 mol % of the catalyst [RuCl$_2$(PPh$_3$)$_3$]. We found that when *p*-tosyl chloride was reacted with styrene, *p*-chlorostyrene, α-methylstyrene, or methyl methacrylate at 60 °C in the presence of 0.1 mol % **2** and 5 mol % AIBN, the monoadducts were obtained in good to excellent yields after 24 h (entries 10−13). The products easily undergo dehydrochlorination. Thus, when the addition of *p*-tosyl chloride to styrene was carried out in the presence of NEt$_3$ (1.0 equiv), the corresponding α,*β*-unsaturated sulfone was obtained in 95% yield. An alternative method for the preparation of the latter compound is a Heck-type coupling of *p*-tosyl chloride and styrene, but 4 mol % of a Pd^{II} catalyst are necessary for this transformation.[10]

In summary, we have described a new catalytic procedure for intermolecular ATRA reactions of halocarbons and sulfonyl chlorides to olefins. The method is based on the utilization of the Ru^{III} complex **2** in combination with AIBN as the cocatalyst. AIBN is responsible for the in situ generation and constant regeneration of the active Ru^{II} catalyst. The new procedure has important advantages. First of all, the Ru precatalyst **2** is easily available in a single step from commercially available starting materials. Furthermore, complex **2** is not air sensitive, which facilitates its handling. Most importantly, the combination of **2** with AIBN allows obtaining unprecedented TONs with various chlorinated substrates including ones with low intrinsic reactivity. It seems likely that the combination of complex **2** with AIBN can also be used for intramolecular ATRA reactions. Given the advantages outlined above, we believe that our new procedure or a conceptually related version may find various applications in organic synthesis.

Acknowledgment. This work was supported by the Swiss National Science Foundation and by the EPFL.

Supporting Information Available: Experimental procedures and mechanistic investigations. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA0617542