UC Santa Barbara

UC Santa Barbara Previously Published Works

Title

Tandem Reaction Progress Analysis as a Means for Dissecting Catalytic Reactions: Application to the Aza-Piancatelli Rearrangement

Permalink

<https://escholarship.org/uc/item/892067f4>

Journal

ACS Catalysis, 5(8)

ISSN

2155-5435

Authors

Chung, R
Yu, D
Thai, VT
et al.

Publication Date

2015-08-07

DOI

10.1021/acscatal.5b01087

Peer reviewed

Tandem Reaction Progress Analysis as a Means for Dissecting Catalytic Reactions: Application to the Aza-Piancatelli Rearrangement

Ryan Chung,[†] Diana Yu,[†] Van T. Thai,[†] Alyssa F. Jones,[†] Gesine K. Veits,[‡] Javier Read de Alaniz,[‡] and Jason E. Hein^{*,†}

[†]Department of Chemistry and Chemical Biology, University of California, Merced, Merced, California 95343, United States

[‡]Department of Chemistry and Biochemistry, University of California, Santa Barbara, Santa Barbara, California 93106, United States

S Supporting Information

ABSTRACT: Continuing developments in the elucidation techniques of complex catalytic processes is of foremost importance to modern synthetic chemistry, and the identification of efficient synthetic techniques relies on precise, reliable, and adaptable methods to dissect the mechanism of a given transformation. Currently, methods of reaction development are grounded upon the systematic modification of specific variables—such as temperature, time, concentration, etc.—to account for and control the dynamic series of coupled equilibria within a catalytic environment. On the other hand, tandem reaction analytical methods that involve the concomitant use of different instruments to probe a reaction can provide time-resolved information regarding active chemical species and facilitate the interrogation and optimization of the system. Herein, we report our study applying tandem in situ ReactIR and HPLC-MS monitoring to the dysprosium(III) triflate-catalyzed aza-Piancatelli rearrangement of 2-furylcarbinols, a reaction that grants access to *trans*-4,5-disubstituted cyclopentenones—common motifs in important biologically relevant and natural compounds. With a prototype automated sampling apparatus, information was obtained about the intrinsic chemoselectivity of the reaction, and previously unseen intermediates were observed, allowing for a more detailed reaction mechanism to be substantiated. The advantages of applying this type of tandem measurement to study these types of systems are also discussed.

KEYWORDS: aza-Piancatelli rearrangement, tandem reaction progress analysis, automated sampling, transient intermediate tracking, reaction mechanisms, homogeneous catalysis, cascade rearrangement

INTRODUCTION

The discovery, study, and elucidation of catalytic processes are essential for the creation of new synthetic transformations, synthesis of natural products, manufacture of value-added commodity materials, and obtainment of mechanistic insight on chemical transformations.^{1,2} Additionally, the identification and design of highly efficient catalytic methods to supplant wasteful processes is of paramount importance to achieve global chemical sustainability.^{3–5} However, progress in these realms is, in part, restricted by our current approach to studying catalytic reactions. Typically, reaction development focuses solely on product yield or selectivity as a function of very specific independent variables—such as temperature, time, concentration, and so forth. By systematically modifying these parameters, the underlying goal is to account for and control the complex and dynamic series of coupled equilibria within a catalytic environment. This traditional methodology is performed in lieu of continually monitoring changes in the chemical species present over time, a tactic that would also give critical insight. If we are granted this type of information, we can readily locate specific regimes of these variables that are

especially conducive to the desired transformation and quantify catalytic efficiency as a function of these regimes.

An alternative strategy employs in situ analytical tools to furnish time-resolved information pertaining to all observable species present within the reaction, giving ready access to kinetic parameters relating reactants, intermediates, byproducts, catalyst reservoirs, and products. Admittedly, acquiring accurate time-course measurements for a complex mixture presents a significant challenge. Although a variety of “operando” spectroscopic techniques such as FT-IR, Raman scattering, NMR, UV/vis, EPR, EXAFS, and ESI-MS are capable of providing information on reactions under synthetically relevant conditions at very fast sampling rates, they also depend on sufficient separation between the signals of different analytes.^{6–11} Thus, their effectiveness can only be determined on a case-by-case basis. A complementary and/or supplementary approach involves the removal and quenching of time aliquots for off-line analysis by chromatographic techniques, which also gives an excellent means of analysis. However, successful

Received: February 18, 2015

Published: June 22, 2015

In this study, parallel in situ monitoring was applied to the dysprosium(III) triflate-catalyzed aza-Piancatelli rearrangement. This reaction transforms 2-furylcarbinols into *trans*-4,5-disubstituted cyclopentenones (Scheme 1), which are common

The reaction scheme illustrates the synthesis of compound 6 from 1-phenylethanol (1). The process begins with the treatment of 1 with Lewis acid, leading to the formation of an oxonium ion intermediate (2). This intermediate then reacts with aniline (ArNH₂) to form a zwitterionic adduct (3). Subsequent rearrangement and loss of a proton (-H⁺) yields the bicyclic intermediate 5. Finally, 5 undergoes a 4π electrocyclic ring closure (conr.) to form the bicyclic enone 6.

These limitations are rooted in the lack of detailed mechanistic investigation with regard to reactive species generated during the cascade reaction. To date, theoretical and experimental work has mainly focused on validating the proposed 4π conrotatory electrocyclization.^{16–20} We chose to investigate this reaction further because a series of highly reactive chemical species are involved in the rearrangement, providing a perfect platform for study.

■ RESULTS AND DISCUSSION

Description of Sampling Apparatus. In this article, we report the detailed kinetic behavior of the catalytic pathway with data acquired using a prototype apparatus capable of rapid parallel reaction analysis (for a detailed description, see SI. Refer to Figure 1 for schematic). The instrument consists of a

Figure 1. Illustration depicting prototype sampling apparatus used to collect tandem reaction progress data.

Mettler-Toledo ReactIR 15 equipped with a DiComp (diamond) probe connected by an AgX (silver halide) fiber

Scheme 2. Previously Proposed Catalytic Cycle Highlighting the Disconnect between the Rate- and Selectivity-Determining Events

and inserted through a PTFE-lined septum fitted on the reaction vial. The instrument was configured to monitor the reaction continuously, recording from 2000–800 cm^{-1} . Simultaneously, a PEEK capillary (1/32 in. outer diameter, 0.15 mm inner diameter) was threaded into the vial and attached to a Gilson 815 rheodyne valve, which in turn was coupled to a Gilson 215 automated liquid handling robot and programmable syringe pump. The timing and synchronization of the liquid sampling technology was governed by a programmable syringe pump that removed the timed aliquot, triggered the actuation of the rheodyne, and activated the subsequent sample dilution and quenching into the waiting LC vials. These samples were manually transferred to the HPLC-MS for analysis either as they were prepared or upon completion of the sampling period.

Applying automation in this fashion obviates the need for an internal standard, which in some cases can be detrimental to the system under study. Together, this configuration delivers accurate, time-resolved information for the concentrations of starting materials, intermediates, and products. With regard to sensitivity and range, it is anticipated that the ReactIR is the limiting technique due to the difficulty differentiating between compounds with similar or overlapping frequencies or intermediates present in very low concentrations. The use of HPLC-MS, on the other hand, allows for an incredible dynamic range depending on dilution factor in both sample collection and chromatography and allows for the viability of ReactIR information to be assessed under chosen reaction conditions. Ultimately, it is the net sum of the two analytical tools that furnishes highly accurate and reliable information.

Furthermore, it can be envisioned that this type of modular analytical set up can be adapted to allow reaction progress analysis for difficult systems that operate at high temperatures and/or pressures. This setup could potentially also allow kinetic analysis to be easily acquired from reactions containing multiple phases, such as reactions with heterogeneous catalysts or systems with immiscible liquid/liquid or solid/liquid components. The ability to address these kinds of reactions highlights the advantage of this technique over more conventional in situ monitoring approaches, such as NMR, which cannot easily be adapted to monitor such processes.

In this particular study, the Dy(III)-catalyzed rearrangement operates at elevated temperature and requires the introduction of catalyst into the system while it is too hot to appropriately capture the initial reaction behavior. This complicated analysis by NMR with the instrumentation at our disposal. In addition, separate studies aimed at elucidating the structure and binding of the dysprosium triflate Lewis acid though ^1H NMR failed due to significant problems locking and shimming these samples in our NMR instrument. We attribute this issue to the particularly high magnetic susceptibility of dysprosium salts.^{25,26} Together these two problems made reaction progress analysis by NMR untenable.

Dissecting the Reaction of *N,O*-Dibenzylhydroxylamine. Our most recent work utilized the sampling apparatus to monitor the rearrangement of 2-furyl(phenyl)carbinol (**7**) with *N,O*-dibenzylhydroxylamine (**8**) in place of the typical arylamine (Scheme 3). Although more nucleophilic (Lewis basic) alkylamines, such as *N*-benzylamine, were not competent nucleophilic partners, *N,O*-dibenzylhydroxylamine did allow the reaction to proceed to completion to give cyclopentenone **9a** in good yield (see SI for Experimental). This choice of nucleophile was made because of its increased synthetic

Scheme 3. Reaction of 2-Furyl(phenyl)carbinol and *N,O*-Dibenzylhydroxylamine Yields Cyclopentenone **9a** and *exo*-Substituted Furan **9b**

potential; reduction of the N–O bond reveals a free secondary amine that can be used for subsequent synthetic transformations. This, of course, is not feasible with the previously developed system.

Reaction progress curves for the aza-Piancatelli rearrangement were obtained using our apparatus are depicted in Figure 2. This figure immediately shows that there is excellent

Figure 2. Reaction progress data from both HPLC-MS and ReactIR instruments show good agreement for aza-Piancatelli rearrangement with *N,O*-dibenzylhydroxylamine.

agreement between the independent measurements and highlights the advantage of utilizing tandem reaction monitoring. Applying the techniques in concert allows each to compensate for a weakness in the other. This configuration does not suffer from common complications that plague either ReactIR or HPLC-MS sampling alone. The high data rate of the ReactIR allows subtle features of the reaction progress trend, such as the abrupt change in product formation at 20 min, to be recorded. In contrast, while the sample rate of the HPLC-MS is slower by comparison, it captures the formation and consumption of an unexpected intermediate **9b** that is less discernible by ReactIR.

Isolation and characterization of this species revealed that the transient intermediate was the result of nucleophilic addition of the *N,O*-dibenzylhydroxylamine at the 5' position of oxocarbenium **10**, generating *exo*-substituted product **9b** (Scheme 4). Curiously, similar products have rarely been observed with arylamine nucleophiles, suggesting that either the hydroxylamine shows a greater propensity for *exo*-substitution or that **9b** is particularly stable relative to its arylamine equivalent and is formed reversibly in the course of the rearrangement. Information as to the cause of this new intermediate can be extracted by examining the trends in concentration, which indicate that the rate of formation of

Scheme 4. Scheme Showing the Reversible Formation of the *N,O*-Dibenzylhydroxylamine *exo*-Substituted Product

cyclopentenone **9a** appears to have two distinct domains: Initially, a fast zero-order period occurs (0–20 min) and is followed by a slower, first-order regime. In particular, the rate of appearance of product **9a** after 20 min is associated with the loss of intermediate **9b**, suggesting that the formation of the *exo*-substituted species is reversible.

Further evidence for the greater stability of **9b** relative to furylcarbinol **7** was obtained by resubjecting the isolated intermediate to experimental conditions (Scheme 5). Heating a

Scheme 5. Resubjecting Intermediate **9b** to Reaction Conditions Yields the Rearrangement Product **9a**

solution of **9b** (0.1 M) in the presence of catalyst led to efficient conversion to cyclopentenone **9a**, albeit at a slower rate than that observed for furylcarbinol **7** (Figure 3).

Competition Reactions. To test the versatility of our analytical method and to further dissect the reaction, we next carried out a series of competition experiments where both aniline and hydroxylamine nucleophiles were present (Scheme 6). The first experiment was conducted using furylcarbinol (**7**, 0.10 M), *N,O*-dibenzylhydroxylamine (**8**, 0.05 M), and aniline

Figure 3. Comparison of reaction progress curves of rearrangement product **9a** formation starting from carbinol **7** and *N,O*-dibenzylhydroxylamine **8** (hollow markers) and isolated *exo*-substituted furan **9b** (solid markers).

Scheme 6. Competition Reaction between 2-Furyl(phenyl)carbinol, *N,O*-Dibenzylhydroxylamine, and Aniline

(**12**, 0.05 M). In this system, the ReactIR was able to track formation of rearrangement products **9a** and **13** as an aggregate sum over time because the key distinguishing IR features could not be resolved between the two species. Despite this, the information gathered does provide an accurate trend of the total conversion to the cyclopentenone products as a function of time and the reaction trends from the IR and HPLC are in excellent agreement.²⁶ Examining the HPLC data (Figure 4)

Figure 4. Aniline **10** in competition with *N,O*-dibenzylhydroxylamine **8** for rearrangement with furylcarbinol **7** shows a significant chemoselectivity the aniline cyclopentenone **13**.

reveals one of the more striking features of this reaction—namely, that the competition reaction appears to be divided into three regimes of product selectivity that change as a function of conversion.

Initially, cyclopentenones **9a** and **13** and furan **9b** are formed, each displaying a zero-order rate dependence. During the first phase (0–35 min), addition of aniline to the oxocarbenium is much faster than hydroxylamine; the rate of formation of **13** is 12 times faster than that of either **9a** or **9b**. After the aniline is consumed (phase 2, at ~35 min), the rate of hydroxylamine addition to give both **9a** and **9b** jumps to approximately twice that of the previous domain. Finally, at ~45 min (phase 3), **9b** is consumed under a relatively slow first-order decay with concomitant formation of **9a**. The decrease in the concentration of **13** after 40 min is attributed to the formation of Friedel–Crafts alkylation product between the newly formed, highly electron-rich aryl ring of **13** and free oxocarbenium.²⁷

Although complicated, each of these salient kinetic behaviors can be accounted for by our proposed catalytic mechanism (Scheme 7). The behavior in the second and third phase can be

Scheme 7. Competing Pathways Present in the Catalytic System

rationalized by considering both the productive and unproductive nucleophilic addition of hydroxylamine, as we have seen in our previous experiments (Figure 2 and 3). The model also accounts for the nearly exclusive preference for **13** in the first regime, which results from a difference in the relative nucleophilicity of aniline compared with *N,O*-dibenzylhydroxylamine. This agrees with our previous study where in a competition reaction the rearrangement products resulting from more electron-rich anilines were formed quickest. Finally, the sudden change in the rate of formation of hydroxylamine products **9a** and **9b** once aniline is exhausted reflects the liberation of free catalyst from the off-cycle reservoir, which promotes rearrangement with *N,O*-dibenzylhydroxylamine.

The high degree of chemoselectivity seen in the early phase of the competition reaction between aniline and hydroxylamine illuminates a very synthetically useful feature—that anilines can be coupled to furylcarbinols in preference to hydroxylamines. This phenomenon can be demonstrated clearly by performing a reaction where addition of the aniline nucleophile is delayed (Figure 5). A reaction under the same catalyst loading was performed with furylcarbinol **7** (0.10 M) and hydroxylamine **8** (0.15 M) and was allowed to proceed for ~30 min. At this point, aniline **12** (0.05 M) was introduced neatly by syringe. As a result, the reaction with the hydroxylamine is completely arrested, leading to exclusive formation of the aniline product.

Figure 5. Late addition of aniline changes the course of the operational reaction between 2-furyl(phenyl)carbinol, *N,O*-dibenzylhydroxylamine to favor cyclopentenone **13**.

Aside from its interesting mechanistic implications, the results from the experiment demonstrate a key advantage to studying catalytic systems using tandem reaction progress analysis. This single reaction allows us to extract practical information relating to the relative nucleophilicity of two dissimilar nitrogen nucleophiles. Moreover, it clearly reveals the exquisite chemoselectivity for aniline over hydroxylamine, which would have been overlooked if we had attempted to predict this value using rate data from individual reactions. Furthermore, it allows the chemoselectivity to be easily measured as a function of time. Together, HPLC and IR record identical reaction progress trends with respect to starting material consumption and total product formation (**9a** and **13**; see SI, Figure S7), and individual selectivity is immediately discernible from the HPLC (Figure 5).

Kinetic Simulations. Finally, our method of tandem reaction progress analysis using automated sampling technology facilitates examination of the catalytic system using kinetic simulation (see SI for more details), allowing us to further validate our proposed mechanism and obtain estimated relative values of the relevant kinetic constants. This is due to the fact that this sampling technique provides concentration measurements for multiple species throughout the reaction course, which is corroborated with ReactIR information.

Pertaining to our study, the kinetic model was constructed using the competitive equilibria from the proposed mechanism (Scheme 7). Fifteen independent optimizations from randomly selected starting values converged to give rate constants and simulated reaction progress curves, which were in good agreement with the measured values. Although each constant individually from each of the 15 trials showed significant variation, the relative values illustrate four critical points.

First, the simulation predicts, regardless of the nucleophile, that the ionization to form the oxocarbenium intermediate is the key rate-limiting step in the overall productive pathway. It is important to recall that the observed rate of reaction is modulated by the concentration of unbound $\text{Dy}(\text{OTf})_3$. Having a relatively slow ionization of the carbinol results in a very low concentration of free oxocarbenium during the reaction, thus accounting for the relatively low level of undesired Friedel–Crafts alkylation products when $\text{Dy}(\text{OTf})_3$ is used as the promoting Lewis acid.

Second, the model indicates that both hydroxylamine and aniline bind to dysprosium and contribute to the off-cycle reservoir (Scheme 7, K_1 and K_2 , respectively). However, the coordination to aniline is much stronger than that of *N,O*-dibenzylhydroxylamine (parameter estimation indicates K_1 may

be as large as 5-fold bigger than K_2). The tighter binding of aniline to dysprosium is confirmed on the basis of the immediate decrease in carbinol consumption upon injection of aniline (Figure S).

Third, nucleophilic addition of hydroxylamine kinetically favors the cyclopentenone-producing *N,O*-acetal **11** over the *exo*-addition product **9b** (Scheme 8, $k_3 > k_4$). Both *endo*- and

Scheme 8. Different Possible Pathways Confirmed in This Study^a

^aThe main catalytic cycle and off-cycle reservoir are not shown for clarity.

exo-addition equilibria are largely product-favored (Scheme 7, K_3 and $K_4 \gg 1$). These facts are consistent with intermediate **9b** being a competitively generated and relatively stable complex that must later undergo re-elimination to form the oxocarbenium to give product **9a**.

Finally, our model predicts that decomposition of the reactive oxocarbenium is responsible for lower than 100% product yields, not instability of the products formed under the reaction conditions. This is a very important feature of the chemistry and attests to the mild nature of the Dy(OTf)₃ catalyst.²⁸

CONCLUSIONS

In conclusion, we have reported the development of a prototype automated robotic reaction sampling apparatus that was employed in studying the aza-Piancatelli rearrangement of 2-furyl(phenyl)carbinol and *N,O*-dibenzylhydroxylamine. By tandem ReactIR and HPLC-MS technologies simultaneously, each method served to validate the information obtained from the other, and we were able to obtain critical information about the key chemical species and predominant equilibria present during the course of the rearrangement reaction that either ReactIR or HPLC-MS alone would not have easily furnished.

This study has also identified a previously unreported reaction intermediate and characterized it in the context of the active catalytic pathway. Our data has been used in kinetic simulation to identify relative rate constants for the catalytic network, providing significant credence to our proposed mechanism and the interplay between multiple catalyst reservoirs and reactive intermediates (summarized in Scheme 8).

This study is an excellent demonstration of the power of tandem reaction progress analysis and its ability to dissect catalytic reaction mechanisms. Although this particular work utilizes tandem ReactIR and HPLC-MS, it lays the groundwork for application of multiple tandem analytical technologies to provide ready access to time-resolved reaction progress and kinetic analysis in order to aid in the development of new catalytic transformations.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b01087.

Description of the prototype sampling apparatus, experimental methods, ReactIR and HPLC-MS reaction progress curves, kinetic simulation parameters, and NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: jhein2@ucmerced.edu.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by UCM and the National Science Foundation (DMR-1359406). Additional support was provided by the National Science Foundation (to J.R., CAREER Award CHE-1057180) and a UCM summer fellowship (to V.T.).

REFERENCES

- (1) Allen, A. E.; MacMillan, D. W. C. *Chem. Sci.* **2012**, 3, 633–658.
- (2) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, 107, 5606–5655.
- (3) Sankar, M.; Dimitratos, N.; Miedziak, P. J.; Wells, P. P.; Kiely, C. J.; Hutchings, G. J. *Chem. Soc. Rev.* **2012**, 41, 8099–8139.
- (4) Centi, G.; Perathoner, S. *Catal. Today* **2009**, 148, 191–205.
- (5) Bulushev, D. A.; Ross, J. R. H. *Catal. Today* **2011**, 171, 1–13.
- (6) Bañares, M. A. *Adv. Mater.* **2011**, 23, 5293–5301.
- (7) Diebolt, O.; van Leeuwen, P. W. N. M.; Kamer, P. C. J. *ACS Catal.* **2012**, 2, 2357–2370.
- (8) Schmid, M. B.; Zeitler, K.; Gschwind, R. M. *Angew. Chem., Int. Ed.* **2010**, 49, 4997–5003.
- (9) Marquez, C. A.; Fabbretti, F.; Metzger, J. O. *Angew. Chem., Int. Ed.* **2007**, 46, 6915–6917.
- (10) Vikse, K. L.; Ahmadi, Z.; Manning, C. C.; Harrington, D. A.; McIndoe, J. S. *Angew. Chem., Int. Ed.* **2011**, 50, 8304–8306.
- (11) Frenkel, A. I. *Chem. Soc. Rev.* **2012**, 41, 8163–8178.
- (12) Piancatelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett.* **1976**, 17, 3555–3558.
- (13) Piancatelli, G.; D'Auria, M.; D'Onofrio, F. *Synthesis* **1994**, 1994, 867–889.
- (14) Piancatelli, G.; Scettri, A. *Tetrahedron Lett.* **1977**, 18, 1131–1134.
- (15) Henschke, J. P.; Liu, Y.; Huang, X.; Chen, Y.; Meng, D.; Xia, L.; Wei, X.; Xie, A.; Li, D.; Huang, Q.; Sun, T.; Wang, J.; Gu, X.; Huang, X.; Wang, L.; Xiao, J.; Qiu, S. *Org. Process Res. Dev.* **2012**, 16, 1905–1916.
- (16) Piancatelli, G.; Scettri, A.; David, G.; D'auria, M. *Tetrahedron* **1978**, 34, 2775–2778.
- (17) D'Auria, M. *Heterocycles* **2000**, 52, 185–194.
- (18) Nieto Faza, O.; Silva López, C.; Álvarez, R.; de Lera, Á. R. *Chem. - Eur. J.* **2004**, 10, 4324–4333.
- (19) Davis, R. L.; Tantillo, D. J. *Curr. Org. Chem.* **2010**, 14, 1561–1577.
- (20) Yin, B. L.; Lai, J. Q.; Zhang, Z. R.; Jiang, H.-F. *Adv. Synth. Catal.* **2011**, 353, 1961–1965.
- (21) Veits, G. K.; Wenz, D. R.; Read de Alaniz, J. *Angew. Chem., Int. Ed.* **2010**, 49, 9484–9487.
- (22) Palmer, L. I.; Read de Alaniz, J. *Angew. Chem., Int. Ed.* **2011**, 50, 7167–7170.
- (23) Yu, D.; Thai, V. T.; Palmer, L. I.; Veits, G. K.; Cook, J. E.; Read de Alaniz, J.; Hein, J. E. *J. Org. Chem.* **2013**, 78, 12784–12789.

- (24) Veits, G. K.; Wenz, D. R.; Palmer, L. I.; St. Amant, A. H.; Hein, J. E.; Read de Alaniz, J. *Org. Biomol. Chem.*, accepted.
- (25) Herz, R.; Kronmüller, H. *Phys. Status Solidi A* **1979**, *54*, 217–223.
- (26) Saeed, M.; Wendland, M. F.; Yu, K. K.; Higgins, C. B. *J. Am. Coll. Cardiol.* **1992**, *20*, 1634–1641.
- (27) Refer to [SI](#) for graph showing concordance between HPLC- and ReactIR-derived concentration data.
- (28) This was confirmed by isolating product **13** and resubjecting it to reaction conditions with furylcarbinol **7**. The isolated products were identified as Friedel–Crafts alkylation products.
- (29) Veits, G. K.; Read de Alaniz, J. *Tetrahedron* **2012**, *68*, 2015–2026 and references therein .