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Actinide-Catalyzed Intermolecular Addition of Alcohols to Carbodiimides

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ABSTRACT: The unprecedented actinide-catalyzed addition of alcohols to carbodiimides is presented. This represents a rare example of thorium-catalyzed transformations of an alcoholic substrate, and the first example of uranium complexes showing catalytic reactivity with alcohols. Using the uranium and thorium-amides $U[N(SiMe_3)_2]_3$ and $[(Me_3Si)_2N]_2An[\kappa^2-(N,C)-CH_2Si(CH_3)_2N(SiMe_3)]$ ($An = Th$ or U), alcohol additions to unsaturated carbon-nitrogen bonds are achieved in short reaction times with excellent selectivities and high to excellent yields. Computational studies, supported by experimental thermodynamic data, suggest plausible models of the profile of the reaction which allow the system to overcome the high barrier of scission of the actinide-oxygen bond. Accompanied by experimentally determined kinetic parameters, a plausible mechanism is proposed for the catalytic cycle.

The chemistry of the actinides has drawn considerable attention in recent years and given rise to impressive structures and reactivities.^{1–13} As the development of organoactinides to these ends has advanced, so too have their application in demanding stoichiometric and catalytic chemical transformations such as hydroaminations,^{14–19} hydrosilylations,^{20–22} oligomerizations,^{23–25} polymerizations of dienes,²⁶ esters, and epoxides,^{27–32} and a host of small-molecule activations.^{33–38} However, some of the most challenging transformations for actinides are those involving oxygenated substrates. To date, a very limited number of works exist which present the catalytic reaction of oxygen-containing substrates, the first of which being the demonstration of a thorium-mediated catalytic Tishchenko reaction,³⁹ with another recent example of (imidazolin-2-iminato)thorium catalyzed aldehyde dimerization,⁴⁰ yet the most impressive of such reactions since has been an intramolecular hydroalkoxylation,⁴¹ which was long thought to be inaccessible due to the formation of an intractable actinide-oxo species.⁴² This work challenged the conventional wisdom of the rules of actinide catalysis, however it is of note that even the remarkable intramolecular hydroalkoxylation was confined to a limited substrate scope and only for organothorium complexes.

Most recently, we have reported interesting actinide-catalyzed reactions mediated by actinide-amides, including terminal alkyne cyclotrimerizations,⁴³ and the addition of various E-H nucleophiles into heterocumulenes.^{44,45} These studies revealed distinctive modes of bonding for actinide chemistry which facilitate the observed reactivity. The potential of this catalysis is exemplified in the observed reactivity of actinide-amide complexes (**1–3**) (Figure 1) as adept catalysts for demanding chemical transformations.

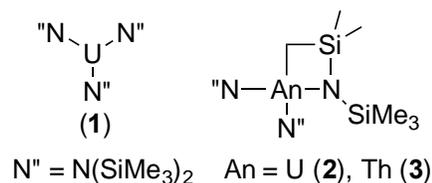
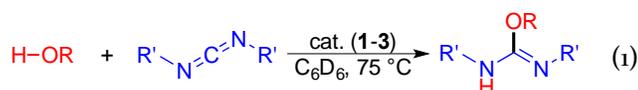


Figure 1. Amido-actinide complexes used in the catalytic addition of alcohols to carbodiimides.

The catalytic investigation of these complexes have allowed for a systematic study of the difference between a U^{III} and U^{IV} precatalysts, and the reactivity difference between analogous U^{IV} and Th^{IV} complexes. We predicted that opening the metal coordination sphere around these actinide centers would aid in facilitating challenging chemical transformations; these expectations were based on previous research which has shown that increasing coordinative unsaturation yields higher reactivity and selectivity for actinide-metallocene complexes.^{46,47}

The success in performing the aforementioned reactions using the actinide complexes (**1–3**) raised a significant conceptual question as to whether actinide complexes possess the ability to perform the catalytic transformation of alcohols. This is a particularly challenging notion when considering the significant bond strengths of the actinide-oxygen bonds and the difficulty in cleaving such species ($Th-O = 208.0$, $U-O = 181.0$ kcal mol^{-1}).⁴⁸ The most sensible approach to achieve this was determined to be the insertion of carbodiimides into various alcohols according to the following reaction (Equation 1); this process has been shown to be efficiently catalyzed by transition metal complexes, most notably those of copper,^{49–53} however

no such reaction has been seen to be mediated by group 4 or early actinide systems.



To our pleasure, it was seen that the addition of several alcohols into diisopropylcarbodiimide (DIC) and 1,3-di-*p*-tolylcarbodiimide (DTC) was efficiently catalyzed by complexes **1-3** in benzene-*d*₆ to generate the corresponding isoureas (Table 1). While organocopper reagents are most widely used to form isoureas, the investigation of this product class remains limited, surprising especially considering the utility of isoureas as valuable biologically active molecules and versatile synthons for combinatorial total synthesis.⁵⁴⁻⁵⁶

Table 1. Product scope of actinide-mediated intermolecular alcohol addition to carbodiimides.^a

Entry	Catalyst	ROH	R'N=C=NR'	Time (h)	Conv (%) ^b
1	2		ⁱ Pr	24	42
2	3		ⁱ Pr	24	85
3	1	MeOH	<i>p</i> -tolyl	3	>99
4	2		<i>p</i> -tolyl	3	>99
5	3		<i>p</i> -tolyl	3	>99
6	1		ⁱ Pr	12	83
7	2		ⁱ Pr	24	76
8	3	EtOH	ⁱ Pr	12	83
9	1		<i>p</i> -tolyl	3	90
10	2		<i>p</i> -tolyl	3	93
11	3		<i>p</i> -tolyl	3	93
12	1		ⁱ Pr	24	28
13	2		ⁱ Pr	24	83
14	3	ⁱ PrOH	ⁱ Pr	24	77
15	1		<i>p</i> -tolyl	6	83
16	2		<i>p</i> -tolyl	3	93
17	3		<i>p</i> -tolyl	3	93
18	2		ⁱ Pr	24	17
19	1	^t BuOH	<i>p</i> -tolyl	12	88
20	2		<i>p</i> -tolyl	12	97
21	3		<i>p</i> -tolyl	12	88
22	1		<i>p</i> -tolyl	6	95
23	2	PhOH ^[c]	<i>p</i> -tolyl	3	94
24	3		<i>p</i> -tolyl	9	77

^aReaction conditions: ~1.5 μmol catalyst (1 mol%), 600 μL C₆D₆, 75 °C. ^bDetermined by ¹H NMR of the crude reaction mixture. [c] Reaction of phenol with DIC was the only reaction shown to proceed without the need of catalyst.

Performing the reactions in THF-*d*₈ and methylcyclohexane-*d*₁₄ revealed inhibited catalytic activity, or complete deactivation of the catalytic cycle, respectively. Blank reactions showed that of the substrate combinations attempted, only the reaction of

1,3-di-*p*-tolylcarbodiimide and *tert*-butanol occurred without the need of catalyst.

A clear trend in the activity of insertion is observed when comparing the nucleophilicity of the carbodiimide used, evident by the decreased reactivity of the more nucleophilic DIC. Conversely, 1,3-di-*p*-tolylcarbodiimide, a more electrophilic substrate, reacts much more rapidly, suggesting of a weaker, more labile An-N bond formed after insertion. In addition, the acidity and steric encumbrance of the alcohol used is a crucial factor in determining the efficiency of the catalytic system. For example, the percent conversion is seen to markedly drop using the thorium complex (**3**) when increasing the steric encumbrance from methanol to *iso*-propanol (Table 1, entries 2, 8, and 14), with no catalytic turnover observed for *tert*-butanol. In the reaction of DTC, the thorium complex shows the best catalytic activity in the addition of aliphatic alcohols (Table 1, entries 5, 11, 17, and 21), however in the reaction with phenol, the uranium complexes (**1** and **2**) proved superior. These results illustrate the delicate interplay between the electronic nature of the metal, the coordination sphere created around the catalyst, and the stereoelectronic nature of the substrate of the reaction.

This transformation, occurring outside of the known capabilities of actinide catalysis, stands in need of thorough mechanistic investigation. Knowing that some Brønsted acids are capable of mediating insertions into carbodiimides, it was first necessary to confirm that no such reaction was taking place; performing this reaction in the presence a proton trap (2,6-di-*tert*-butyl-4-methylpyridine) did not show any inhibition of the product formation. With Brønsted acid-mediated insertion excluded, attention was diverted to experimentally deriving the active catalytic cycle. Kinetic studies revealed first-order behavior in catalyst and carbodiimide, with inverse first-order kinetics in alcohol. The latter of these findings demonstrates a rapid pre-equilibrium of alcohol coordination, wherein the larger excess of alcohol saturates the metal center and excludes nitrogen coordination by the carbodiimide substrate, inhibiting the catalytic turnover.

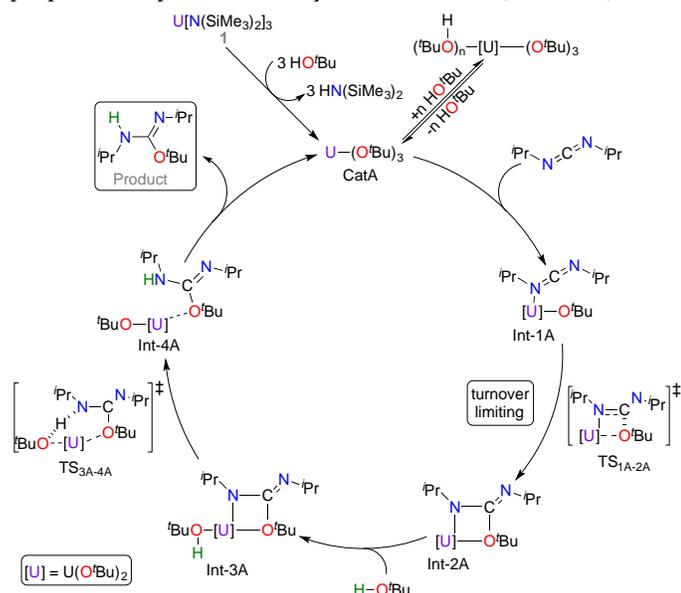
Kinetic isotope studies using deuterated ethanol and *tert*-butanol showed KIE values of 0.99 and 0.98, respectively, showing that protonolysis by alcohol is not turnover limiting. These data supply us with the kinetic rate law presented in Equation 2 (see Scheme 1 for variables in equation):

$$\frac{\partial P}{\partial T} = \frac{k_1[\text{DIC}][\mathbf{1}]}{1 + K_{eq}[\text{ROH}]} \quad (2)$$

(a thorough analysis of the kinetic equation can be found in the Supporting Information).

Thermodynamic parameters were experimentally calculated from Eyring analysis using each of the three precatalyst complexes. As a model system, the Eyring plot of the addition of *tert*-butanol to DIC mediated by uranium complex **2** was investigated (see Supporting Information), revealing a moderate enthalpic activation barrier ($\Delta H^\ddagger = 12.1 \text{ kcal mol}^{-1}$), and a highly negative entropy of activation ($\Delta S^\ddagger = -39.0 \text{ e.u.}$), the latter of

which is evocative of a highly ordered transition state, suggesting that a migratory insertion is likely in agreement with the characteristic catalytic behavior of the actinides. These kinetic and thermodynamic parameters provide sufficient data for the proposal of a plausible catalytic mechanism. (Scheme 1).



Scheme 1. Proposed reaction mechanism of actinide-mediated intermolecular alcohol addition to carbodiimides.

The activation of precatalyst **1** is achieved by protonolysis of the amides by alcohol substrate to yield the uranium-alkoxide (Cat_A); while the exact identity of this species is unknown, ¹H NMR analysis revealed complete displacement of the amides, indicated by the loss of alcohol proton signals and appearance of the N-H signal of HN(SiMe₃)₂. The formation of Cat_A has also been verified using theoretical approaches (see ESI) and the sequential protonolysis of the amides are computed to be both thermodynamically and kinetically favorable. When the metallacycles (**2** and **3**) are used, the first equivalent of alcohol cleaves the An-C bond, followed by displacement of the remaining amides. The catalytic cycle for each of the three complexes is then proposed to follow a similar mechanism wherein the active actinide-alkoxide complex undergoes coordination by the nitrogen atom of the carbodiimide (Int-1A), followed by migratory insertion of the C=N bond to form actinide-isourea as the turnover limiting step (Int-2A). Coordination by an additional equivalent of alcohol (Int-3A) followed by protonolysis regenerates Cat_A and liberates the desired isourea product. The lack of any dimerization or amidine product further supports this mechanism and excludes the likelihood of a Lewis acid mediated process.

In order to further support both the observed reactivity and proposed mechanism, DFT calculations were carried out. The reaction profiles were determined *in silico* for each catalyst for the reaction of DIC with either *tert*-butanol or ethanol. The nature of the resting state of Cat_A was first investigated, and the formation of dimers are found to be thermodynamically favored over the monomers for both uranium(III) and ura-

nium(IV). In the uranium(IV)-mediated addition of *tert*-butanol (Figure 2), the disruption of the dimer costs 8.0 kcal mol⁻¹ while the subsequent coordination of DIC is found to be exothermic, liberating -3.9 kcal mol⁻¹ (making an overall step slightly endothermic by 4.1 kcal mol⁻¹); the migratory insertion is calculated as the rate-determining step of the reaction, requiring 12.7 kcal mol⁻¹ from the DIC adduct and in excellent agreement with the experimentally found 12.1 kcal/mol. Interestingly, in the case of uranium(III), the disruption of the dimer costs 27.6 kcal mol⁻¹, making the overall reaction difficult in line with the experiment. The complete catalytic cycle is accompanied by a release of 18.0 kcal mol⁻¹, and reveals the synergistic effects between nitrogen and oxygen coordination to the actinide center making this reaction possible.

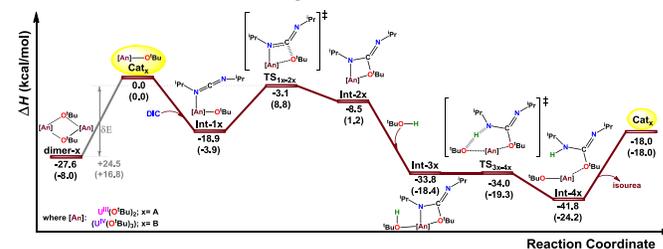


Figure 2. Plausible reaction profile of *t*BuOH addition to DIC mediated by complex **1**. Values in parenthesis refer to complex **2**.

These results demonstrate an alternative approach to the preparation of new isourea products, but more importantly presents a novel reactivity for actinide-mediated catalysis. The intermolecular addition of an alcohol substrate has only a single predecessor for thorium catalysis which was limited to intramolecular reactions, however no example prior to this work exists for uranium-catalyzed conversion of alcohols. The findings herein reopen a long avoided field of actinide catalysis and provide a useful tool in the development of catalytic strategies to facilitate challenging chemical transformations complementary to classical organic and/or late-transition metal chemistry.

ASSOCIATED CONTENT

Supporting Information. Experimental details, characterization data, reaction order plots, Eyring plots, discussion of kinetic rate law, and DFT computation details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) Mills, D. P.; Cooper, O. J.; Tuna, F.; McInnes, E. J. L.; Davies, E. S.; McMaster, J.; Moro, F.; Lewis, W.; Blake, A. J.; Liddle, S. T. *J. Am. Chem. Soc.* **2012**, *134*, 10047.
- (2) Matson, E. M.; Crestani, M. G.; Fanwick, P. E.; Bart, S. C. *Dalton Trans.* **2012**, 41, 7952.
- (3) Cooper, O. J.; Mills, D. P.; McMaster, J.; Tuna, F.; McInnes, E. J. L.; Lewis, W.; Blake, A. J.; Liddle, S. T. *Chem. - Eur. J.* **2013**, *19*, 7071.
- (4) Schnaars, D. D.; Gaunt, A. J.; Hayton, T. W.; Jones, M. B.; Kirker, I.; Kaltsoyannis, N.; May, I.; Reilly, S. D.; Scott, B. L.; Wu, G. *Inorg. Chem.* **2012**, *51*, 8557.
- (5) Diaconescu, P. L.; Cummins, C. C. *Inorg. Chem.* **2012**, *51*, 2902.
- (6) Vidjayacoumar, B.; Ilango, S.; Ray, M. J.; Chu, T.; Kolpin, K. B.; Andreychuk, N. R.; Cruz, C. A.; Emslie, D. J. H.; Jenkins, H. A.; Britten, J. F. *Dalton Trans.* **2012**, 41, 8175.
- (7) Lam, O. P.; Franke, S. M.; Nakai, H.; Heinemann, F. W.; Hieringer, W.; Meyer, K. *Inorg. Chem.* **2012**, *51*, 6190.
- (8) Lewis, A. J.; Nakamaru-Ogiso, E.; Kikkawa, J. M.; Carroll, P. J.; Schelter, E. J. *Chem. Commun.* **2012**, 48, 4977.
- (9) Monreal, M. J.; Wright, R. J.; Morris, D. E.; Scott, B. L.; Golden, J. T.; Power, P. P.; Kiplinger, J. L. *Organometallics* **2013**, *32*, 1423.
- (10) Arnold, P. L.; Jones, G. M.; Odoh, S. O.; Schreckenbach, G.; Magnani, N.; Love, J. B. *Nat. Chem.* **2012**, *4*, 221.
- (11) King, D. M.; Tuna, F.; McInnes, E. J. L.; McMaster, J.; Lewis, W.; Blake, A. J.; Liddle, S. T. *Nat. Chem.* **2013**, *5*, 482.
- (12) Evans, W. J.; Miller, K. A.; Kozimor, S. A.; Ziller, J. W.; DiPasquale, A. G.; Rheingold, A. L. *Organometallics* **2007**, *26*, 3568.
- (13) Evans, W. J.; Walensky, J. R.; Ziller, J. W. *Organometallics* **2009**, *29*, 101.
- (14) Eisen, M. S.; Straub, T.; Haskel, A. *J. Alloys Compd.* **1998**, 271-273, 116.
- (15) Haskel, A.; Straub, T.; Eisen, M. S. *Organometallics* **1996**, *15*, 3773.
- (16) Hayes, C. E.; Platel, R. H.; Schafer, L. L.; Leznoff, D. B. *Organometallics* **2012**, *31*, 6732.
- (17) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 4253.
- (18) Stubbert, B. D.; Stern, C. L.; Marks, T. J. *Organometallics* **2003**, *22*, 4836.
- (19) Straub, T.; Haskel, A.; Neyroud, T. G.; Kapon, M.; Botoshansky, M.; Eisen, M. S. *Organometallics* **2001**, *20*, 5017.
- (20) Dash, A. K.; Wang, J. Q.; Eisen, M. S. *Organometallics* **1999**, *18*, 4724.
- (21) Dash, A. K.; Wang, J. Q.; Wang, J.; Gourevich, I.; Eisen, M. S. *J. Nucl. Sci. Technol.* **2002**, *39*, 386.
- (22) Dash, A. K.; Wang, J. X.; Berthet, J. C.; Ephritikhine, M.; Eisen, M. S. *J. Organomet. Chem.* **2000**, *604*, 83.
- (23) Straub, T.; Haskel, A.; Eisen, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 6364.
- (24) Haskel, A.; Straub, T.; Dash, A. K.; Eisen, M. S. *J. Am. Chem. Soc.* **1999**, *121*, 3014.
- (25) Wang, J. Q.; Dash, A. K.; Berthet, J. C.; Ephritikhine, M.; Eisen, M. S. *Organometallics* **1999**, *18*, 2407.
- (26) Mansell, S. M.; Bonnet, F.; Visseaux, M.; Arnold, P. L. *Dalton Trans.* **2013**, 42, 9033.
- (27) Karmel, I. S. R.; Botoshansky, M.; Tamm, M.; Eisen, M. S. *Inorg. Chem.* **2014**, *53*, 694.
- (28) Hayes, C. E.; Sarazin, Y.; Katz, M. J.; Carpentier, J. F.; Leznoff, D. B. *Organometallics* **2013**, *32*, 1183.
- (29) Barnea, E.; Moradove, D.; Berthet, J. C.; Ephritikhine, M.; Eisen, M. S. *Organometallics* **2006**, *25*, 320.
- (30) Fang, J.; Walshe, A.; Maron, L.; Baker, R. J. *Inorg. Chem.* **2012**, *51*, 9132.
- (31) Walshe, A.; Fang, J.; Maron, L.; Baker, R. J. *Inorg. Chem.* **2013**, *52*, 9077.
- (32) Karmel, I. S. R.; Elkin, T.; Fridman, N.; Eisen, M. S. *Dalton Trans.* **2014**, 43, 11376.
- (33) Lam, O. P.; Franke, S. M.; Heinemann, F. W.; Meyer, K. *J. Am. Chem. Soc.* **2012**, *134*, 16877.
- (34) Schmidt, A. C.; Nizovtsev, A. V.; Scheurer, A.; Heinemann, F. W.; Meyer, K. *Chem. Commun.* **2012**, 48, 8634.
- (35) Mougel, V.; Camp, C.; Pécaut, J.; Copéret, C.; Maron, L.; Kefalidis, C. E.; Mazzanti, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 12280.
- (36) Mansell, S. M.; Farnaby, J. H.; Germeroth, A. I.; Arnold, P. L. *Organometallics* **2013**, *32*, 4214.
- (37) Arnold, P. L.; Mansell, S. M.; Maron, L.; McKay, D. *Nat. Chem.* **2012**, *4*, 668.
- (38) Arnold, P. L.; Turner, Z. R.; Bellabarba, R. M.; Tooze, R. P. *Chem. Sci.* **2011**, *2*, 77.
- (39) Andrea, T.; Barnea, E.; Eisen, M. S. *J. Am. Chem. Soc.* **2008**, *130*, 2454.
- (40) Karmel, I. S. R.; Fridman, N.; Tamm, M.; Eisen, M. S. *J. Am. Chem. Soc.* **2014**, *136*, 17180.
- (41) Wobser, S. D.; Marks, T. J. *Organometallics* **2013**, *32*, 2517.
- (42) Lin, Z.; Marks, T. J. *J. Am. Chem. Soc.* **1987**, *109*, 7979.
- (43) Batrice, R. J.; McKinven, J.; Arnold, P. L.; Eisen, M. S. *Organometallics* **2015**, *34*, 4039.
- (44) Batrice, R. J.; Eisen, M. S. *Chem. Sci.* **2016**, *7*, 939.
- (45) Karmel, I. S. R.; Tamm, M.; Eisen, M. S. *Angewandte Chemie* **2015**, *54*, 12422.
- (46) Dash, A. K.; Gourevich, I.; Wang, J. Q.; Wang, J.; Kapon, M.; Eisen, M. S. *Organometallics* **2001**, *20*, 5084.
- (47) Wang, J.; Gurevich, Y.; Botoshansky, M.; Eisen, M. S. *Organometallics* **2008**, *27*, 4494.
- (48) *CRC Handbook of Chemistry and Physics*; 96th ed. ed.; CRC Press: Boca Raton, FL, 2015-2016.
- (49) Däbritz, E. *Angewandte Chemie International Edition in English* **1966**, *5*, 470.
- (50) Duffy, M. G.; Grayson, D. H. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1555.
- (51) Wang, M. F.; Golding, B. T.; Potter, G. A. *Synth. Commun.* **2000**, *30*, 4197.
- (52) Abdigali, A. B.; Shtrykova, V. V. *Russ. Chem. Rev.* **1995**, *64*, 929.
- (53) Mathias, L. J. *Org. Prep. Proced. Int.* **1980**, *12*, 309.
- (54) Finke, P. E.; Ashe, B. M.; Knight, W. B.; Maycock, A. L.; Navia, M. A.; Shah, S. K.; Thompson, K. R.; Underwood, D. J.; Weston, H. J. *Med. Chem.* **1990**, *33*, 2522.
- (55) García-Moreno, M. I.; Díaz-Pérez, P.; Ortiz Mellet, C.; García Fernández, J. M. *J. Org. Chem.* **2003**, *68*, 8890.
- (56) LaMarche, M. J.; Leeds, J. A.; Amaral, K.; Brewer, J. T.; Bushell, S. M.; Dewhurst, J. M.; Dzik-Fox, J.; Gangl, E.; Goldovitz, J.; Jain, A.; Mullin, S.; Neckermann, G.; Osborne, C.; Palestrant, D.; Patane, M. A.; Rann, E. M.; Sachdeva, M.; Shao, J.; Tiamfook, S.; Whitehead, L.; Yu, D. *J. Med. Chem.* **2011**, *54*, 8099.

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