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Enantioselective Cyanation/Brook Rearrangement/*C*-Acylation Reactions of Acylsilanes Catalyzed by Chiral Metal Alkoxides

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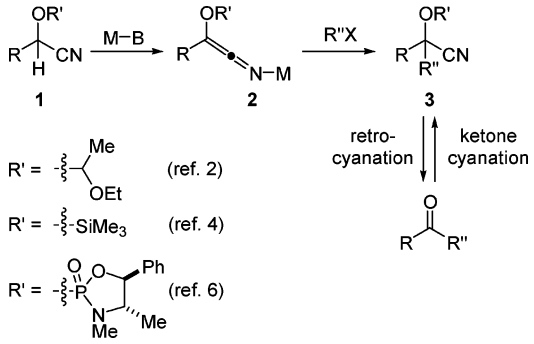
New catalytic enantioselective cyanation/1,2-Brook rearrangement/*C*-acylation reactions of acylsilanes (**4**) with cyanoformate esters (**7**) are described. The products of the reaction are fully substituted malonic acid derivatives (**8**). Catalysts for this transformation were discovered via a directed candidate screen of 96 metal−ligand complexes. Optimization of a (salen)aluminum complex revealed significant remote electronic effects and concentration effects. The scope of the reaction was investigated by using a number of aryl acylsilanes and cyanoformate esters. Chemoselective reduction of the reaction products (**8**) afforded new enantioenriched α-hydroxy-α-aryl-*β*-amino acid derivatives (**32**−**34**) and *β*-lactams (**35** and **36**). This reaction provides a simple method for the construction of new nitrogen-containing enantioenriched chiral building blocks.

Introduction

Protected cyanohydrins (**1**) may be converted to their derived anions **2** through the action of strong base. The utility of these nucleophilic species in the formation of new carbon−carbon bonds is documented.[1] Seminal work from Stork and Maldonado established the feasibility of accessing anion **2** through deprotonation of a suitably protected cyanohydrin with stoichiometric quantities of a strong base such as lithium diisopropylamide (Scheme 1).[2] That work, and subsequent contributions from Hünig and co-workers, showed that intermediate **2** can be intercepted by a variety of electrophiles to yield new ketone products after deprotection and retrocyanation.[3,4] Intermediate **2** serves as an acyl anion equivalent in this context; however, preservation of the newly functionalized cyanocarbinol derivative (**3**) gives rise to chiral compounds that may be regarded formally as products of ketone cyanation.

Little is known about stereocontrolled versions of these reactions (**2** → **3**).[5] Schrader has shown that when **1** bears a chiral ephedrine-based *O*-phosphate auxiliary, alkylation reactions may be achieved with high diastereoselectivity.[6] Cativiela and co-workers developed a diastereoselective methylation of an α-acetoxycyanoacetate derivative controlled by an isoborneol-derived chiral auxiliary to access an analogous product.[7] Catalytic asymmetric reactions proceeding via intermediates resembling **2** are rare.[8]

SCHEME 1. Protected Cyanohydrin Functionalization and Hydrolysis to Ketones



A significant challenge in the development of catalytic reactions involving intermediate **2** is the low acidity of **1**, which necessitates stoichiometric quantities of an amide or alkyllithium base. An alternative method of generating anions of protected cyanohydrins can be realized through the use of acylsilanes (**4**).[9] Nucleophilic addition of a metal cyanide to an acylsilane can initiate a carbon-to-oxygen silyl migration (Brook rearrangement)[10] that generates a carbanion analogous to **2**. Takeda, Reich, and Degl'Innocenti have effectively utilized this in situ method to achieve alkylation, enone acylation, and *β*-elimination reactions of the derived (silyloxy)nitrile anions.[11−14]

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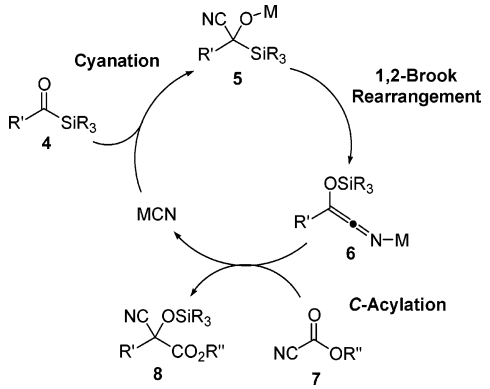
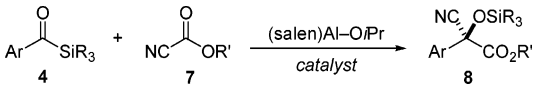
SCHEME 2. Tandem Cyanation/1,2-Brook Rearrangement/*C*-Acylation Reaction of Acylsilanes (4)



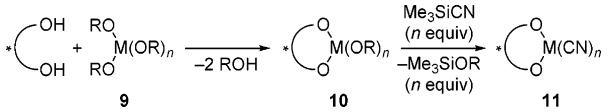
In a previous report we employed a Brook rearrangement strategy in a tandem cyanation/C-acylation reaction between acylsilanes and cyanoformate esters catalyzed by KCN/18-crown-6.[15] The reactions yielded a variety of aryl and alkyl α-cyano-α-silyloxy esters (**8**). To account for the observed products, a catalytic cycle involving acylation of the (silyloxy)nitrile intermediate **6** by a cyanoformate (**7**) was proposed (Scheme 2).[16−19] The reactions are rendered catalytic by virtue of $^-$CN expulsion in the *C*-acylation event. Access to enantiomerically enriched silylcarbinol **8** could provide expeditious syntheses for a number of new nonracemic 3,3-disubstituted *β*-lactams and unnatural α-hydroxy-*β*-amino acids. Previously reported approaches to **8** typically involved the Lewis acid- or Lewis base-promoted additions of silylcyanide reagents to α-ketoesters (R′ = alkyl).[20,21] While enantioselective additions of Me_3SiCN to ketones are common,[22] to the best of our knowledge there are no reported examples of enantioselective α-ketoester cyanation. Additionally, aromatic α-ketoester cyanosilylation will be extremely challenging with sterically undemanding silyl groups (e.g., Me_3SiCN) due to retrocyanation tendencies of the derived products.[15]

As a mechanistic alternative to asymmetric α-ketoester cyanation, we speculated that it might be possible to control the absolute stereochemical course of the acylation reaction (**6** → **8**) through judicious selection of the metal counterion. This report provides a full account of the development of new enantioselective cyanation/1,2-Brook rearrangement/*C*-acylation reactions of acylsilanes

SCHEME 3. Catalytic Enantioselective Cyanation/1,2-Brook Rearrangement/Acylation Reactions



SCHEME 4. Generation of Chiral Metal Cyanide Complexes



mediated by (salen)aluminum alkoxides (Scheme 3).[23] These represent, to the best of our knowledge, the first catalytic asymmetric reactions of protected cyanohydrin anions.

Results

We expected that chiral (cyanide)metal complexes might be conveniently prepared from the two-step sequence depicted in Scheme 4. Exchange between a chiral diol and metal alkoxide should result in loss of 2 equiv of alcohol and formation of a new alkoxide **10**. Upon treatment with the appropriate amount of Me_3SiCN, metal cyanide **11** is the expected product. Cyanation of an acylsilane by complex **11** could, in principle, initiate a 1,2-Brook rearrangement and thereby lead to the desired chiral metal anion intermediate (**6**). Effective chirality transfer from the ligand in the acylation step is essential for high levels of stereoselectivity. Salicylimine (salen) ligands were judged promising candidates for two reasons: (1) ease of structural modification of the diamine backbone and aryl substituents for evaluation of steric and electronic factors; and (2) precedent for the use of (salen)metal complexes as catalysts involving delivery of cyanide.[24−28]

Catalyst Development. With many metal alkoxides and salen ligands available, we presumed that a screen of several different metals and ligands would be the most efficient method for catalyst determination. Eight metal alkoxides ($Al(OiPr)_3$, $Er(OiPr)_3$, $Sm_5O(OiPr)_{13}$, $Ti(OMe)_4$, $Ti(OiPr)_4$, $Y_5O(OiPr)_{13}$, $Yb(OiPr)_3$, $Zr(OiPr)_4$) were employed in conjunction with twelve common chiral ligands (**12**−**23**, Figure 1) to give 96 individual metal complexes to be examined for reactivity and enantioselectivity in the title reaction. Individual complexes were prepared by mixing equimolar amounts of the ligand and metal alkoxide in toluene for 30 min. The solvent along with the alcohol generated was subsequently removed under reduced pressure. A solution of benzoyl triethylsilane (1.0 equiv), benzyl cyanoformate (4.0 equiv), and Me_3SiCN

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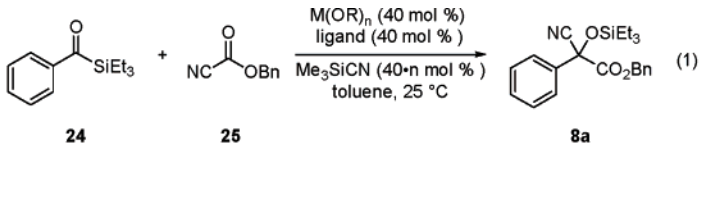
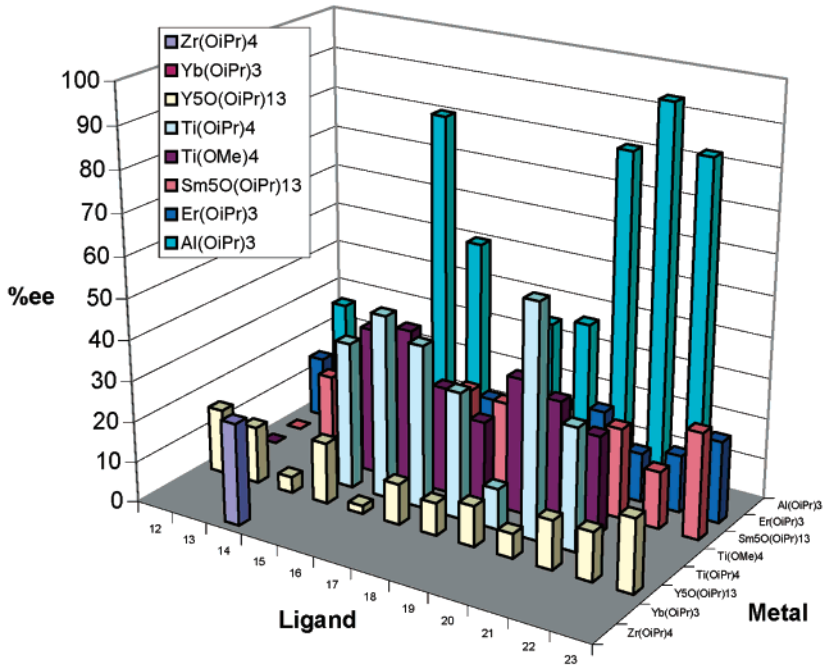




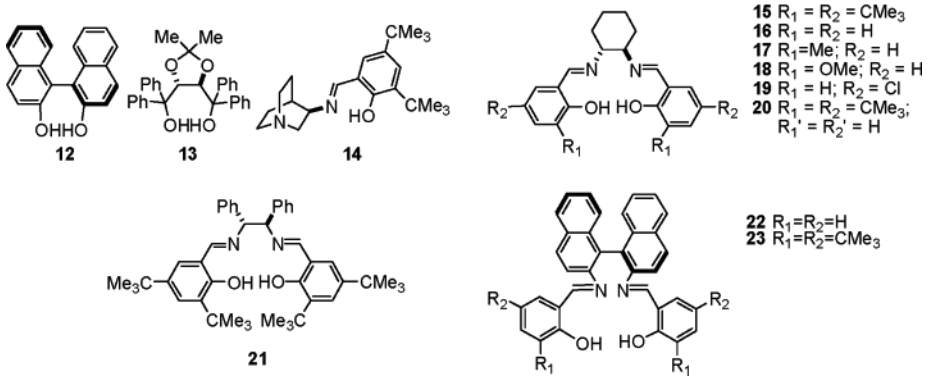


FIGURE 1. Catalyst evaluation for enantioselective cyanation/Brook rearrangement/*C*-acylation of acylsilanes (reagents and conditions: $PhC(O)SiEt_3$ (1.0 equiv, 0.025 M), $NCCO_2Bn$ (4.0 equiv), PhMe for 72 h). Enantioselectivities were determined by CSP−SFC analysis.

(0.8 equiv) in toluene was then added to the preformed (salen)M(OR)$_n$ complex (0.4 equiv) and allowed to react for 72 h.

The results from the catalyst screen are depicted in Figure 1. Lanthanide alkoxide complexes (Er, Sm, Y, Yb) were generally reactive; however, they gave only low levels of enantioselectivity (0−26% ee). Zr(O*i*Pr)$_4$ catalysts were not selective, with the exception of the complex with **14**, which otherwise rendered the Zr series ineffective. Catalysts derived from Ti(O*i*Pr)$_4$ and Ti(OMe)$_4$ gave good reactivity and moderate enantioselectivity with most of the ligands tested (Ti(O*i*Pr)$_4$ and **20** gave 58% ee). Aluminum alkoxides gave the most promising results, displaying good to excellent selectivity (80% ee with **15**, **20**; 92% ee with **21**), albeit with only small amounts of product formation (<5%). Jacobsen has recently reported a highly enantioselective conjugate addition reaction of Me_3SiCN to α,*β*-unsaturated imides catalyzed by in situ generated (salen)Al(CN) complexes.[25] Additionally, it was observed that Al(O*i*Pr)$_3$ alone does not facilitate catalysis, whereas $Y_5O(OiPr)_{13}$, $Sm_5O(OiPr)_{13}$, and Er(O*i*Pr)$_3$ promote the title reaction in as little as 5 mol % without the aid of a supporting ligand. When these points were considered in the context of the catalyst screen, (salen)-Al(O*i*Pr) complexes were selected for further evaluation and optimization.

SCHEME 5. Isopropoxide Exchange with Benzyl Cyanoformate

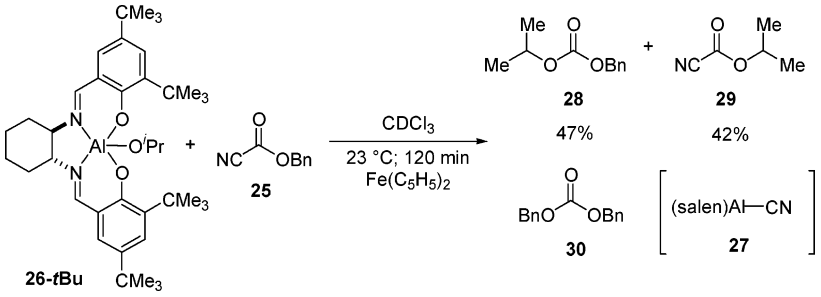
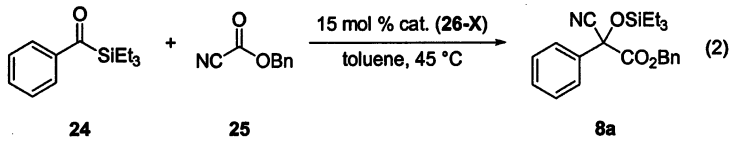
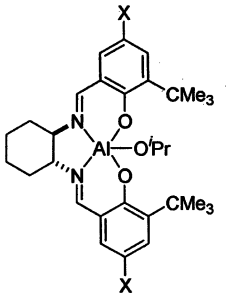
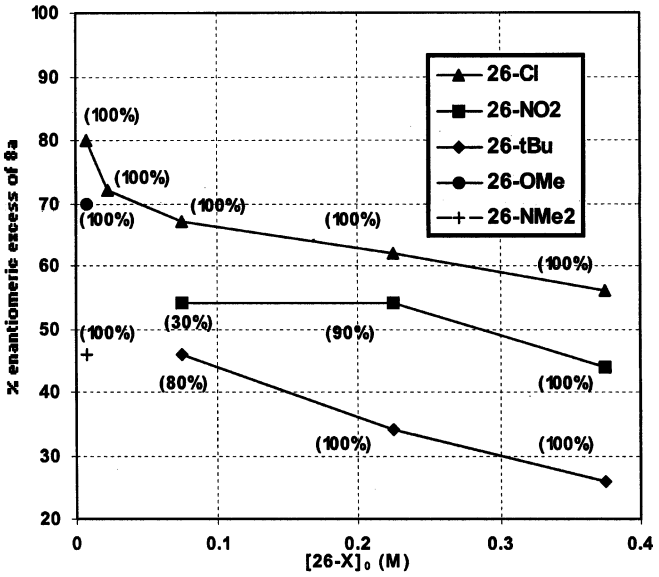


CHART 1. Ligand and Concentration Effects in Enantioselective Cyanation/Brook Rearrangement/ *C*-Acylation Reactions (Eq 2)[a−c]







[a] $PhC(O)SiEt_3$ (1.0 equiv), $NCCO_2Bn$ (2.0 equiv), for 72 h. [b]Enantioselectivities determined by CSP−SFC analysis. [c]Percent conversions shown in parentheses determined by ^1H NMR spectroscopy.

Initial attempts to reproduce the results from the catalyst screen proved problematic. Only trace product formation (<10%) after several days could be attained with use of any of the (salen)aluminum catalysts prepared by the initial screening protocol. Variable amounts of a cyanohydrin byproduct (**1**, R′ = $SiEt_3$) were also obtained. Monitoring the complexation of $Al(OiPr)_3$ with **15** by ^1H NMR spectroscopy revealed that catalyst formation was negligible at 25 °C. Complete complexation between the corresponding salen ligand and $Al(OiPr)_3$ required 3 days at 80 °C in toluene,[29] in contrast with the complexation conditions that were employed in the catalyst screen (25 °C for 30 min). Cyanohydrin formation was attributed to small quantities of adventitious water leeching into the reaction over the long reaction times. To circumvent this problem, the reactions were carried out in sealed tubes. With this protocol, reactivity was significantly enhanced: the complex derived from $Al(OiPr)_3$ and **15** in conjunction with Me_3SiCN (40 mol %) gave 100% conversion and no cyanohydrin formation when employed at 20 mol % of catalyst loading.

The role of and need for Me_3SiCN as a catalyst activator was next examined. We presume that the active catalyst is a (salen)Al(CN) species (**27**), generated initially upon reaction with Me_3SiCN. Gorsi and Mehrotra had shown that titanium and zirconium alkoxides undergo exchange reactions with cyanoacetates to afford mixed (alkoxy)metal(cyanides): $M(OiPr)_4 + n$ NCCOMe $\rightarrow n$ *i*PrOCOMe + $(NC)_nM(OiPr)_{4-n}$.[30] If an analogous reaction were possible between cyanoformates and alu-

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minum alkoxides, the putative catalyst could be accessed and the Me_3SiCN would be superfluous. Indeed, the reaction of benzoyl triethylsilane (**24**) with benzyl cyanoformate (**25**) in the presence of (salen)Al(O*i*Pr) (**26-*t*Bu**, 15 mol %) at 45 °C furnished the desired product **8a** in the absence of an additional cyanide source. Examination of the exchange reaction by ^{1}H NMR spectroscopy supported the proposed mode of activation. The reaction of (salen)Al(O*i*Pr) (**26-*t*Bu**) with an excess of benzyl cyanoformate in $CDCl_3$ at 23 °C for 120 min afforded a mixture of the expected isopropyl benzyl carbonate (**28**; 47% vs internal standard) as well as isopropylcyanoformate (**29**; 42% vs internal standard) and dibenzyl carbonate (**30**; observed, unable to quantify, Scheme 5).[31] It is interesting to note that although isopropylcyanoformate is observed, it does not participate in the acylation step. Formation of **28** implicates a (salen)Al(CN) complex (**27**); however, the ^{1}H NMR resonances of the organometallic product could not be conclusively assigned. Efforts to crystallize complexes from this reaction have been unsuccessful to date.

Although complete conversion with complex **26-*t*Bu** was now possible in the absence of TMSCN, the level of stereoselection was still not consistent with the results from the initial screen.[32] An enantiomeric excess of 80% with trace product formation was observed in the catalyst screen with **26-*t*Bu**; however, when repeated with the optimized conditions, the desired product **8a** could only be obtained in 36% ee, albeit with 100% conversion. Since (salen)metal catalysts often exhibit second-order rate dependence with respect to the catalyst,[33] the impact of catalyst concentration was evaluated. A closer examination of substituent effects on the salen ligand structure was simultaneously undertaken since the electronic properties of salen ligands are known to exert dramatic effects in the epoxidation of simple olefins.[34] Chart 1 depicts the coupled effect of [**26-X**]$_o$ and the para substituent on the ligand. Using the parent **26-*t*Bu** catalyst at 45 °C in toluene ([**26-*t*Bu**]$_o$ = 0.38 M) afforded **8a** in 26% ee. However, diluting to 0.23 M gave an increase in enantiomeric excess (34%). Switching to complex **26-Cl** significantly increased the selectivity (80% ee) and complete conversion at high dilution was still possible (7.5×10^{-3} M). Seeking to improve this selectivity, we investigated the strongly electron-withdrawing **26-NO_2** catalyst, but observed a sharp decrease in enantiomeric ratio (54% ee at 0.075 M compared to 67% ee with **26-Cl** at 0.075 M). Electron-releasing substituents (**26-OMe** and **26-NMe_2**) at high dilution (7.5×10^{-3} M) did not improve on the selectivity achieved with **26-Cl**. These data consistently correlated lower reaction concentrations with enhanced enantioselectivity; however, remote substituent effects unfortunately failed to reveal a general trend. Attempts to further enhance the selectivity observed with **26-Cl** by employing additives such as 2,6-lutidine[35] or triphenylphosphine oxide[36] were not successful. It is also of note that reaction time has no effect on enantioselectivity; employing **26-Cl**, **8a** was formed in nearly identical levels of enantiomeric excess at 4 h (≤20% conversion; 79% ee) and at 72 h (100% conversion; 80% ee).

Reaction Scope. The scope of the enantioselective acylation reaction was investigated using **26-Cl**. Several different acylsilanes bearing a variety of aryl substituents (R′) with either triethylsilyl or *tert*-butyldimethylsilyl groups (SiR_3) were treated with either benzyl or ethyl cyanoformate (R″) in the presence of catalytic amounts of **26-Cl** to give the desired enantioenriched cyano ester product **8** (eq 3). The results of these experiments are summarized in Table 1. Varying the silyl goup (entries 1 and 2) from triethylsilyl to *tert*-butyldimethylsilyl led to a significant reduction in selectivity (79% to 64% ee, respectively). In contrast, variation of the cyanoformate from benzyl to ethyl affected neither yield nor enantioselectivity (cf. entries 1 vs 3 and 7 vs 8). Electron-releasing substituents on the aryl ring of the acylsilane (entries 4 and 6) provided good levels of enantioselectivity (up to 82% ee, entry 6), while electron-poor acylsilanes (entries 5, 7, 8, and 10) underwent coupling with only moderate enantioenrichment (61% to 64% ee). The only exception was 4-FPhC(O)$SiEt_3$ (78% ee, entry 9). Overall, the substrates examined gave moderate to good enantioselectivities with good to excellent yields. An air-stable aluminum oxo complex derived from the *p*-Cl-salen ligand, (Cl-salen)Al(O)Al(salen-Cl),[26] also catalyzes the coupling of acylsilane **24** with cyanoformate **25** to give **8a** with identical selectivity (80% ee) as complex **26-Cl** (entry 1). Alkyl acylsilanes ($MeCOSiMe_3$, *i*$PrCOSiEt_3$) were unreactive under (salen)Al catalysis, in contrast to catalysis by KCN/18-crown-6.[15]

Derivatization and Absolute Stereochemical Assignment. Since the products (**8**) derived from the title reaction are susceptible to $NCSiR_3$ loss to form α-ketoesters, the nitrile functionality must be manipulated at the outset. Reduction of the nitrile by H_2/Raney nickel to the free amine is best suited for ethyl ester products (**8c**, eq 4).[37] This reaction proceeds smoothly at 23 °C to afford **32** in 74% yield. Nitrile reduction of compounds bearing benzyl ester groups requires different conditions. Tertiary nitrile **8a** is reduced in the presence of $NaBH_4$/$CoCl_2 \cdot 6H_2O$ in MeOH at 0 °C to give a 48% isolated yield of the primary amine (**33**).[38] Alternatively, nitrile **8g** can be reduced in the presence of $(BOC)_2O$ to give a *tert*-butoxycarbonyl-protected amine (**34**), a fully protected α-hydroxy-*β*-amino acid that bears a tertiary carbinol center.

Absolute stereochemical assignment of the products (**8**) of eq 3 was achieved via transformation to a known enantiopure *β*-lactam (**36**, Scheme 7).[39] Lactamization of amine **32** required 3.0 equiv of MeMgBr but cleanly afforded the cyclized product **35** in 67% yield. *N*-Methy-

(31) Ferrocene was used as an internal standard

(32) Although ligand **21** provided the most promising levels of enantioselectivity in the initial screen, attempts to optimize reaction efficiency (i.e., conversion) with this ligand were uniformly unsuccessful. This difference in reactivity and the large changes in enantioselectivity within the (salen)Al series are subtleties that to date have eluded explanation.

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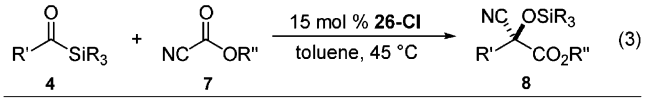
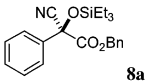
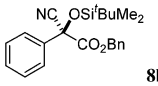
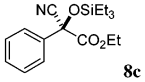
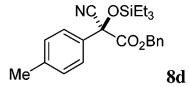
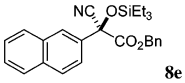
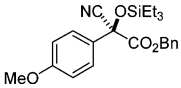
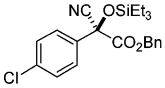
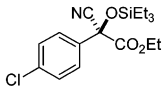
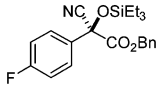
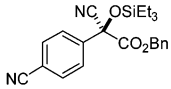
TABLE 1. Catalytic Enantioselective Cyanation/Brook Rearrangement/*C*-Acylation of Acylsilanes (Eq 3)[a]



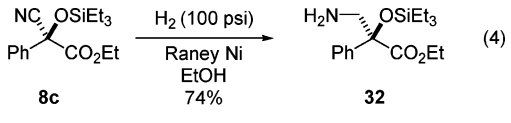
4 **7** **8**

entry	R'	SiR_3	R''	product	% yield[b]	% ee[c]
1	Ph	$SiEt_3$	Bn	 **8a**	83	79[i]
2	Ph	Si^tBuMe_2	Bn	 **8b**	82[d]	64[i]
3	Ph	$SiEt_3$	Et	 **8c**	93[e]	77[g,i]
4	(4-Me)C_6H_4	$SiEt_3$	Bn	 **8d**	79	80[i]
5	2-naphthyl	$SiEt_3$	Bn	 **8e**	90	62[j]
6	(4-OMe)C_6H_4	$SiEt_3$	Bn	 **8f**	84[f]	82[j]
7	(4-Cl)C_6H_4	$SiEt_3$	Bn	 **8g**	87	64[h,j]
8	(4-Cl)C_6H_4	$SiEt_3$	Et	 **8h**	87	61[g,i]
9	(4-F)C_6H_4	$SiEt_3$	Bn	 **8i**	81	78[h,j]
10	(4-CN)C_6H_4	$SiEt_3$	Bn	 **8j**	70	64[j]

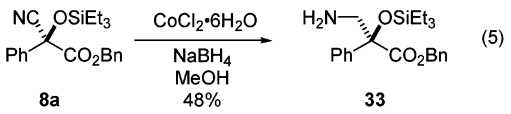
[a] R′C(O)SiR_3 (1.0 equiv), $NCCO_2R''$ (2.0 equiv), C_7H_8 (0.05 M) for 72 h unless otherwise noted. [b] Isolated yield of analytically pure material; average of at least two experiments. [c] Determined by CSP−SFC analysis of the adduct, unless otherwise noted. [d] 20 mol % of catalyst used. [e] [**26-Cl**]$_0$ = 3.75 × 10^{-3} M. [f] [**26-Cl**]$_0$ = 0.015 M. [g] Determined by CSP−SFC analysis after reduction of the nitrile and coupling to (*S*)-mandelic acid. See Supporting Information. [h] Determined by CSP−SFC analysis after reduction of the nitrile and protection as the *N*-BOC carbamate. See Supporting Information. [i] Absolute configuration determined by derivatization to *β*-lactam **36**. [j] Absolute configuration assigned by analogy.

lation of **35** by a NaH/MeI protocol followed by silyl deprotection furnished the known *β*-lactam **36** in 70% yield (2 steps). Optical rotation measurements $[\alpha]^{25}_D$ −54.2 (*c* 0.18, $CHCl_3$; 62% ee) indicated that the *β*-lactam derived from **32** was the (*S*)-enantiomer after comparison to the literature value $[\alpha]^{25}_D$ −99.7 (*c* 0.34, $CHCl_3$; 99% ee).[39] Products **8a**, **8b**, and **8h** were also correlated to the same compound and found to have the same absolute configuration.[40]

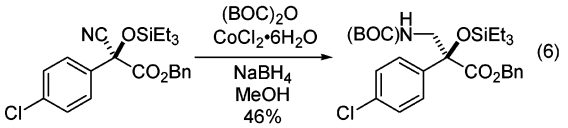
SCHEME 6. Derivatization of Title Reaction Products



8c **32**

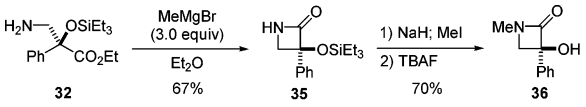


8a **33**



8g **34**

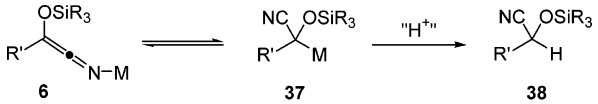
SCHEME 7. Lactamization and Absolute Stereochemistry of 36



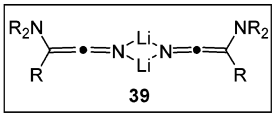
32 **35** **36**

$[\alpha]_D^{25}$ -54.2 (c = 0.18, $CHCl_3$; 62 % ee)
lit. $[\alpha]_D^{25}$ -99.7 (c = 0.34, $CHCl_3$; 99 % ee)

SCHEME 8. Possible (Silyloxy)nitrile Anion Structures



6 **37** **38**



39

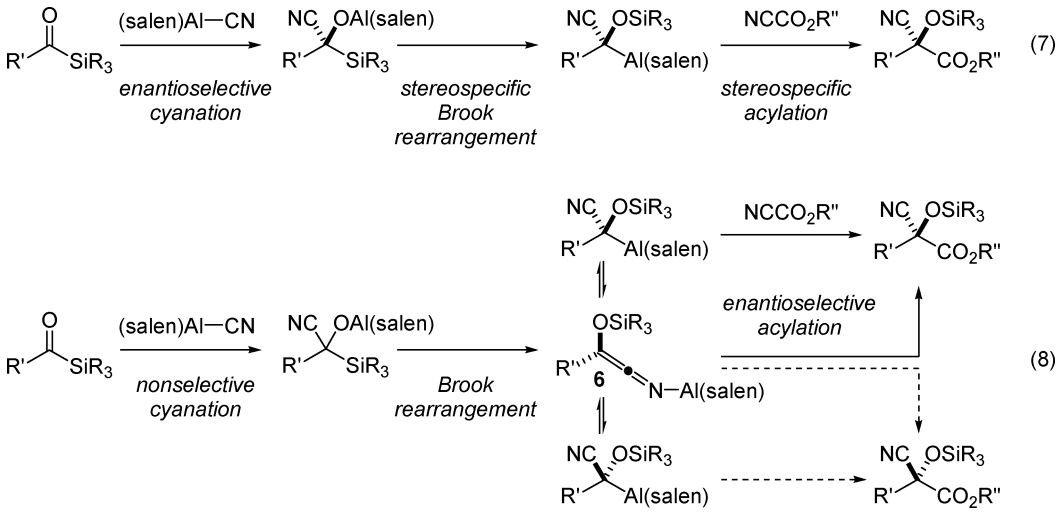
ref. 41

Discussion

The results from the catalyst screen revealed a wide range of potentially useful (ligand)metal(CN) catalysts. From the ^1H NMR experiment in Scheme 5, the presence of isopropyl benzyl carbonate **28** implies the existence of a (salen)Al−CN (**27**) or (salen)Al−NC complex. Although there is no direct spectroscopic evidence for **27**, its existence has also been proposed by Jacobsen.[25] Implicit in the successful catalysis of the cyanation/Brook rearrangement/*C*-acylation sequence are metal complexes that (1) are sufficiently nucleophilic to add to the acylsilane, (2) form M−O bonds that are weak enough to allow the Brook rearrangement to occur, and (3) afford (metallo)silyloxynitriles that are sufficiently reactive to undergo acylation reactions. Circumstantial evidence suggests that all of these criteria are met with (salen)Al−CN complexes. The formation of silylcyanohydrin **38** when water is present suggests the intermediacy of **6** or **37**, perhaps as equilibrating species. Similar (lithio)-

(40) See the Supporting Information for details.

SCHEME 9. Possible Mechanisms for Chirality Transfer



aminonitriles (**39**) have been isolated by Enders and their existence in the solid state provides support for structure **6**.[41] The exact structure of the nucleophile undergoing acylation is not known, however.

Several limiting mechanisms can be advanced for chirality transfer to the nascent stereogenic center. Enantioselective cyanation of acylsilane followed by stereospecific 1,2-Brook rearrangement with retention[42] or inversion[43] could lead to a configurationally defined organoaluminum that undergoes stereospecific acylation with cyanoformate (Scheme 9, eq 7). Alternatively, acylsilanes may undergo nonselective cyanation and/or Brook rearrangement to afford interconverting organoaluminum diastereomers that undergo acylation at different rates (eq 8). The interconversion could take place via the intermediacy of the 1-azaallene-type structure **6**, also a reasonable candidate for enantioselective acylation. We have not been able to observe intermediates in these reactions, but the homology between known, isolated structure **39** and proposed structure **6** should be noted. At this point it is not possible to assess the reversibility of either the cyanation or the 1,2-Brook rearrangement step.

The observed concentration/enantioselectivity effects indicate that the overall mechanism is more complex than Scheme 2 depicts. A possible explanation for the inverse relationship between concentration and selectivity may be competing first- and second-order reaction manifolds whose rates depend on [catalyst]^1 and [catalyst]^2, respectively. At lower concentrations the first-order pathway should become more dominant; however, this would imply that the second-order cycle is less enantioselective. Such a condition would be unique in (salen)-metal catalysis.[33] Alternatively, the observations could be explained by interconverting aggregates in solution that are all catalytically active. The propensity of aluminum cyanide complexes to bridge in the solid state has been noted.[44] The broad resonances in the ^{1}H NMR spectrum for the putative (salen)Al−CN complex do not allow confirmation of aggregation, but may be suggestive. Lower bulk concentrations should increase the relative quantity of the monomer; if it were the most selective complex, the observed enantioselectivity would increase.

Conclusion

A new catalytic enantioselective cyanation/1,2-Brook rearrangement/*C*-acylation reaction of acylsilanes with cyanoformates in the presence of a chiral aluminum complex was developed. This represents the first reported instance of a catalytic asymmetric reaction of a (silyloxy)-nitrile anion. Screening a variety of chiral metal complexes proved key in developing the enantioselective variant of the title reaction. Substrate concentration and remote ligand substituent effects play an important role in both enantioselectivity and reactivity. The scope of the reaction proved general for an array of aryl acylsilanes and cyanoformates, affording moderate to good selectivities in all cases studied. Further manipulation of the reaction products provided a simple means for preparing enantioenriched, fully protected α-hydroxy-*β*-amino acids as well enantioenriched *β*-lactams. This reaction provides access to a new series of chiral building blocks.

Experimental Section

(*R*,*R*)-26-Cl. To a flamed-dried Schlenk tube equipped with a magnetic stir bar was added, in a drybox, 900 mg of (*R*,*R*)-*N*,*N*′-bis(3-*tert*-butyl-5-chlorosalicylidene)-1,2-diaminocyclohexane (1.79 mmol, 1.0 equiv), 365 mg of Al(O*i*Pr)$_3$ (1.79 mmol, 1.0 equiv), and 6 mL of C_7H_8. The tube was sealed and heated to 80 °C and was maintained at that temperature with stirring for 72 h. After 72 h, the yellow-green solution was transferred back to a glovebox and the toluene was removed under reduced pressure. The residual solid was washed with pentane three times and the solid was again dried under reduced pressure to give 910 mg (87%) of pure **26-Cl** as a yellow powder. Analytical data for title compound: ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.27 (s, 1H), 8.05 (s, 1H), 7.33 (d, *J* = 2.8 Hz, 1H), 7.31 (d, *J*

(41) Enders, D.; Kirchhoff, J.; Gerdes, P.; Mannes, D.; Raabe, G.; Runsink, J.; Boche, G.; Marsch, M.; Ahlbrecht, H.; Sommer, H. *Eur. J. Org. Chem.* **1998**, *63*, 3−72.

(42) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392−2398.

(43) Brook, A. G.; Pascoe, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 6224−6227.

(44) Ulh, W.; Schütz, U.; Hiller, W.; Heckel, M. *Z. Anorg. Allg. Chem.* **1995**, *621*, 823−828. The authors thank Professor R. Hancock (UNC−Wilmington) for alerting us to this reference.

= 2.8 Hz, 1H), 7.08 (d, J = 2.8 Hz, 1H), 3.90−3.87 (m, 1H), 3.62 (sept, J = 6.0 Hz, 1H), 3.12−3.11 (m, 1H), 2.56−2.52 (m, 1H), 2.37−2.34 (m, 1H), 2.08−2.05 (m, 2H), 1.50 (s, 18H), 1.47 (s, 18H), 1.45−1.40 (m, 4H), 0.83 (d, J = 6.0 Hz), 0.79 (d, J = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.8, 163.2, 161.4, 144.1, 143.9, 130.6, 130.5, 130.2, 130.1, 120.9, 120.5, 120.1, 119.9, 63.2, 62.9, 62.7, 35.9, 35.8, 29.9, 29.8, 29.7, 29.6, 27.6, 27.5, 27.4, 27.3. A ^{1}H NMR spectrum of **26-Cl** is attached in Appendix B of the Supporting Information.

Representative Procedure for Enantioselective Acylation Reactions. (*S*)-(+)-Benzyl 2-Cyano-2-phenyl-2−triethylsiloxyacetate (8a): A flame-dried Schlenk tube equipped with a magnetic stir bar was charged with aluminum complex **26-Cl** (23.8 mg, 0.04 mmol, 0.15 equiv) under Ar. Benzoyl triethylsilane (60 mg, 0.27 mmol, 1.0 equiv), benzyl cyanoformate (87.8 mg, 0.54 mmol, 2.0 equiv), and C_7H_8 (5.4 mL, 0.05 M) were all added to the Schlenk tube under Ar and the tube was sealed and heated to 45 °C. After 72 h at 45 °C, the crude product was purified by flash chromatography with 95:5 petroleum ether−EtOAc to afford 85.3 mg (83%) of **8a** as a colorless oil in 79% ee as determined by chiral SFC analysis (Chiralpak OD, 0.3% MeOH, 0.5 mL/min, 150 psi, 40 °C, 240 nm, $t_{r-major}$ 37.0 min, $t_{r-minor}$ 41.5 min). Analytical data for title compound: $[\alpha]^{25}_D$ +4.2 (c 1.97, CH_2Cl_2); IR (thin film, cm^{-1}) 3067, 3035, 2958, 2878, 2245, 1766, 1588, 1451, 1241, 1152, 1003, 835; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.61 (m, 2H), 7.38−7.35 (m, 3H), 7.29−7.26 (m, 3H), 7.19−7.17 (m, 2H), 5.17 (s, 2H), 0.93 (t, J = 7.6 Hz, 9H), 0.70 (q, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 134.5, 129.9, 128.9, 128.8, 128.7, 128.2, 125.7, 118.3, 75.1, 68.9, 6.8, 5.4; TLC (95:5 hexanes/EtOAc) R_f 0.35. Anal. Calcd for $C_{22}H_{27}NO_3Si$: C, 69.25; H, 7.13; N, 3.67. Found: C, 69.37; H, 7.28; N, 3.60.

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Supporting Information Available: Experimental details and analytical data for all new compounds, CSP−SFC traces of racemic and enantioenriched compounds, and details of stereochemical proofs. This material is available free of charge via the Internet at http://pubs.acs.org.

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