ChemPubSoc Europe

DOI: 10.1002/ejoc.201801170

EurJOC European Journal of Organic Chemistry

Full Paper

Organocatalytic Mechanisms

Verkade's Superbase as an Organocatalyst for the Strecker Reaction

Jian Yang,[a] Bastien Chatelet,[a] Fabio Ziarelli,[b] Véronique Dufaud,[c] Damien Hérault,[a] and Alexandre Martinez*[a]

Abstract: Proazaphosphatranes -Verkade's superbases- proved to be efficient organocatalysts for the Strecker reaction between protected imines and trimethylsilyl cyanide (TMSCN). Excellent to quantitative yields were reached and, compared to other systems, only low catalyst loading and short reaction times were required for the reaction to proceed efficiently. A remarkable initial turnover frequency (TOF), close to 10^5 h^{-1}, was achieved, associated with an excellent selectivity since no side reactions were observed. A reaction mechanism was proposed and the key role played by the apical nitrogen in the proazaphosphatrane structure was demonstrated.

Introduction

Proazaphosphatranes, also named Verkade's superbases, were first described by J. G. Verkade in 1989.[1] In contrast to iminophosphine -phosphazenes- bases, the Verkade's superbases protonate on the phosphorus atom: upon this proton transfer, the apical nitrogen links to the positive phosphorus creating a highly stable azaphosphatrane structure.[2] The remarkable stability of this conjugated acid renders the Verkade's superbase highly basic (pK_a = 32),[3] one of the most basic nonionic base reported so far. Proazaphosphatranes have therefore attracted considerable interests as highly efficient basic and nucleophilic catalysts to promote a large number of reactions, such as trimerization of isocyanates,[4a] acylation of alcohols,[4b] dehydrohalogenations of alkyl halides,[4c] silylation of alcohols,[4d,4e] the Henry reaction,[4f] transesterification of esters,[4g] and additions of trimethylsilyl cyanide to aldehydes and ketones.[4h] The reaction conditions are generally milder with the Verkade's superbase than with other organocatalysts: lower temperatures and shorter reaction times are usually used and the reactions are often more selective.[4] Besides this remarkable activity as organocatalyst, new aspects of the chemistry of Verkade's superbases have recently been developed, i.e. they were found to act as highly donor ligand for transition metal complexes,[5] leading to very active organometallic catalysts, for Suzuki–Miyaura cross-coupling reactions,[6] or Buchwald–Hartwig amination reactions of aryl chlorides.[7] Proazaphosphatranes have also been confined in molecular cages or mesoporous silica leading to unexpected behavior and reactivity.[8] Recently, proazaphosphatranes turned out to be remarkable catalysts for the reductive functionalization of CO_2 into methylamines, in the presence of hydroborane.[9] Moreover, Krempner et al. demonstrated that Verkade's super-bases can be used to create intermolecular frustrated Lewis pairs (FLP) when associated to a weak boron-containing Lewis acid.[10] These "inverse" FLPs were able to cleave dihydrogen leading to efficient hydrogenation catalysts. The same group also reported the interactions and coordination properties of Verkade's superbases with strong Lewis acids by reaction of proazaphosphatranes with various gallium-, boron- and aluminium-containing Lewis acids.[11]

Although these recent developments bring new insight into the potentiality of such structure for new applications, the classical use of the Verkade's superbases as organocatalysts remains attractive because of their high performance in term of activity and selectivity.[12] Among the base-catalyzed transformations, the Strecker reaction is an appealing target reaction since it leads to the synthesis of α-aminonitriles which are important and versatile building blocks in organic synthesis as well as in biologically active products.[13] Consequently, numerous catalysts have been developed to perform this reaction.[14] One can cite the use of Lewis acids such as $BiCl_3$,[15] InI_3,[16] $RuCl_3$,[17] $NiCl_2$,[18] $La(NO_3)_3{\cdot}6H_2O$,[19] $Yb(OTf)_3$,[20] $Sc(OTf)_3$,[21] $Cu(OTf)_2$.[22] Generally, in those reactions, the aqueous workup is tedious and a large amount of toxic metal waste is generated inevitably. A few organocatalysts have also been reported to catalyze Strecker type reactions. *N*-heterocyclic carbenes were shown to catalyze the addition of trimethylsilyl cyanide to imines with excellent yields in the presence of 5 mol-% catalyst loading at 0 °C, but substrates were limited to tosyl protected imines, and, in most cases, long reaction times were needed (5–6 hours).[23] Heydari et al. showed that guanidine hydrochloride could act as catalyst for Strecker type reactions using aliphatic, aromatic, heterocyclic conjugated aldehydes, and primary, sec-

[a] *Aix Marseille Univ, CNRS, Centrale Marseille, iSm2, Marseille, France*
E-mail: alexandre.martinez@centrale-marseille.fr
[b] *Aix-Marseille Université, Centrale Marseille, CNRS, Fédération des Sciences Chimiques de Marseille (FR 1739), 13397 Marseille, France*
[c] *Laboratoire de Chimie, Catalyse, Polymères, Procédés CNRS, UMR 5265, Université Claude Bernard Lyon 1,*
CPE Lyon, 43 Bd du 11 novembre 1918, 69616, Villeurbanne cedex, France
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejoc.201801170.

ondary amines as substrates.[24] However, only moderate activity could be achieved with TON around 33 at 40 °C in 1 hour. Thiourea also performed well as catalyst with moderate to high yields in the presence of 5 mol-% catalyst loading at 0 °C, using primary amines and a range of aldehydes as substrates, in the presence of acyl cyanides as cyanide source. However, extended reaction times were required (1.5–2 days) for the reaction to proceed.[25] Besides, aqueous formic acid has proven to be an environment-friendly organocatalyst for the Strecker reaction between aniline, aromatic aldehydes and TMSCN at room temperature in 5–72 min, but a higher catalyst loading was necessary (20 mol-%) to achieve sufficient activity.[26] Recently, an ionic liquid was reported to be an efficient organocatalyst for the strecker reaction with TOF reaching 10 000 000 h^{-1}.[27] Although significant progress has been made, these methodologies are far from ideal from a sustainability viewpoint and greener organocatalysts able to function under milder reaction conditions while exhibiting high turnover numbers (TONs) and initial turnover frequencies (TOFs) still need to be developed.

Herein, we report on the use of differently substituted proazaphosphatranes **1a**–**d** (Figure 1) as catalysts for the Strecker reaction using Ts-, *N*-Boc-, and Bn- protected imines as substrates and TMSCN as cyanide source. These catalysts proved to be highly efficient under very mild reaction conditions providing at 0 °C high TOFs around 10^5 h^{-1} and TONs up to 10^4. Besides, a mechanism is proposed for the cyanation of imines catalyzed by proazaphosphatranes.

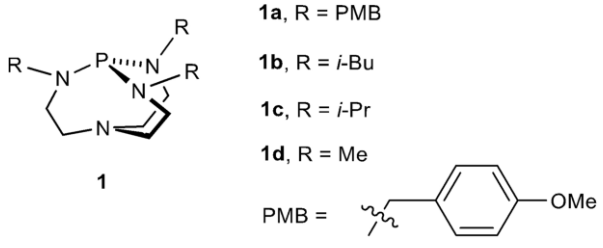


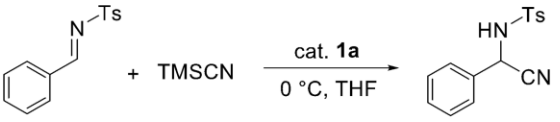
Figure 1. Proazaphosphatranes **1a**–**1d** used in this study.

Results and Discussion

The cyanation of imines was first investigated in the presence of proazaphosphatrane **1a** as catalyst using the addition of TMSCN (1.5 equiv.) to *N*-Tosyl-benzaldimine (1.0 equiv.) as a benchmark reaction (Table 1). We were pleased to observe that, in the presence of 1 mol-% of proazaphosphatrane **1a** in 20 minutes and at 0 °C, more than 99 % yield was reached (entry 1, Table 1), and even in very short reaction time (2 minutes), yield as high as 97 % could be achieved (entry 2, Table 1), highlighting the high efficiency of the Verkade's superbase as organocatalyst for this reaction. In addition, **1a** proved to be very selective leading to α-aminonitriles as the sole products, in line wih the results previously reported by J. G. Verkade for other transformations.[4]

Motivated by these results, we then decided to decrease the catalyst loading to explore further the performance scope of **1a**: with 0.1 mol-% loading, 83 % and 99 % yields were obtained in 2 and 20 minutes respectively (entries 3 and 4 respectively, Table 1). Decreasing further the amount of **1a** to 0.01 mol-%

Table 1. Optimization of catalyst loading and reaction time for proazaphosphatrane **1a** catalyzed cyanation of imines.[a]



Entry	**1a** (mol-%)	Time	Yield [%][b]
1	1	20 min	>99
2	1	2 min	97
3	0.1	20 min	99
4	0.1	2 min	83
5	0.01	20 min	58
6	0.01	2 min	31
7	0.01	12 h	99
8	–	12 h	<1

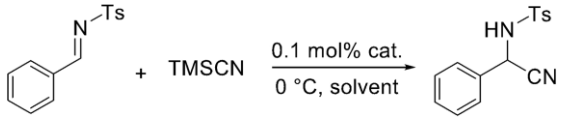
[a] Reaction conditions: *N*-Tosyl-benzaldimine (0.5 mmol), TMSCN (0.75 mmol), 1.5 mL of THF, under argon, then 3 mL of H_2O. [b] Isolated yields are given.

produced a 31 % yield in only 2 minutes which corresponds to a TOF of 9.3 10^4 h^{-1}, a remarkable activity value for an organocatalyst for the Strecker reaction (entry 6, Table 1). Prolonging the reaction time at this very low catalyst loading resulted in additional activity improvement with yields attaining 58 % in 20 minutes and up to 99 % after 12 hours, affording a total TON around 10^4 (entries 5 and 7, Table 1). It is noteworthy that no reaction occurred without catalyst (entry 8, Table 1), even after 12 hours, and that Et_3N failed to catalyze this reaction when used in the same reaction conditions as in entry 3 (0.1 mol-%, 20 min, 0 °C, <1 % yield). Thus, it appears that the Verkade's superbase is a powerful catalyst for the Strecker reaction displaying remarkable initial TOFs and TONs under mild conditions, underlining both its high catalytic activity and stability. It is worth mentioning that J. G. Verkade demonstrated in a previous report that an azaphosphatrane nitrate salt could catalyze the three-component Strecker reaction, however 20 mol-% of catalyst loading and long reaction times ranging from 15 to 35 hours were needed.[28]

We then chose to use the following reaction conditions to further screen the reaction parameters and catalyst structural pattern: 0.1 mol-% of catalyst loading at 0 °C for 20 minutes, as they allow for the reaction to proceed in high yield and in relatively short reaction timeframe. We first examined the influence of the solvent on catalytic performance. As shown from Table 2, high conversion levels were achieved in all the cases with yields of 93 % for DCM and up to 99 % for both THF and toluene (entries 1, 2, and 3, Table 2). The influence of the stereoelectronic properties and basicity of the proazaphosphatranes **1a**–**d** on catalytic activity was then investigated using THF as solvent (Table 2). In the presence of 0.1 mol-% catalyst within 20 minutes, all four proazaphosphatranes displayed excellent catalytic activity with yields approaching 100 % (entries 3, 4, 5 and 6, Table 2). In order to further discriminate catalytic activity among the proazaphosphatranes **1a**–**d**, a lower catalyst loading of 0.001 mol-% was used within the same reaction period. The results indicated that catalytic activity was correlated to the basicity of proazaphosphatranes: stronger basicity resulted in

higher yield (entries 3–6, Table 2). Indeed, the catalytic activity follows the same trend (**1a** < **1d** < **1b** < **1c**) as the basicity order of proazaphosphatranes (**1a** < **1d** < **1b** < **1c**).

Table 2. Influence of solvent and stereoelectronic properties of proazaphosphatranes on catalytic activity.[a]



Entry	Catalyst	Solvent	pK_a[b]	Yield [%][c]
1	**1a**	DCM	32.14	93
2	**1a**	Toluene	32.14	99
3	**1a**	THF	32.14	99 (15)[d]
4	**1b**	THF	33.53	99 (22)[d]
5	**1c**	THF	33.63	99 (28)[d]
6	**1d**	THF	32.90	99 (17)[d]

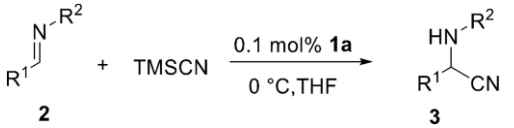
[a] Reaction conditions: *N*-Tosyl-benzaldimine (0.5 mmol), TMSCN (0.75 mmol), 0.1 mol-% catalyst, 1.5 mL of solvent, under argon for 20 min, then 3 mL of H_2O. [b] pK_a values of conjugate acids of proazaphosphatrane bases in acetonitrile.[8c,3] [c] Isolated yields are given. [d] 0.001 mol-% catalyst was used for 2 h.

With optimized conditions in hand, we then studied the scope of substrates for the cyanation of imines on representative examples. Tosyl-protected imines bearing phenyl groups differently substituted were first explored (entries 1–4, Table 3), for which nearly quantitative isolated yields were obtained. In addition to aromatic substituents, aliphatic analogue **2f** also proceeded well with 85 % yield (entry 6, Table 3). Furthermore, *N*-Boc and Bn-protected imines were tested in our system. Remarkably, excellent yields of 94 % and 92 % of corresponding products were reached, respectively (entries 7 and 8, Table 3). Clearly, different protecting groups are compatible with our methodology, which provides an attractive alternative for some specific low-reactive imines. Another key advantage is the use of TMSCN as cyanide source, which is more convenient and safer than typical cyanide salts such as NaCN, KCN or extremely toxic ones like HCN. Cyanation of an imine bearing a heterocyclic furan group was also successfully achieved in high yield (95 %) after 2 hours (entry 9, Table 3). Using ketimine **2j** as substrate also provides the expected product **3j** in 93 % yield (entry 10, Table 3).

A possible reaction mechanism is depicted in Scheme 1. The first step is the activation of TMSCN by attack of the superbase to form a tetra-coordinated silicon complex **A** which was confirmed by solid-state CP MAS ^{29}Si NMR: the appearance of a new signal was observed at 7.8 ppm by mixing 1 equiv. of TMSCN with 1 equiv. of **1a**, in addition to the resonance at –12.0 ppm for TMSCN, in agreement with the literature data (Figures S47–48).[4h] Then, the nucleophilic anion CN^- attacks the imine substrate affording the key intermediate ion pair **B**. Cleavage of the Si–P bond leads to the regeneration of the catalyst **1a** and the concomitant release of the TMS-protected amine product **C** which is subsequently hydrolyzed to give the desired amine product **D**.[29a,30]

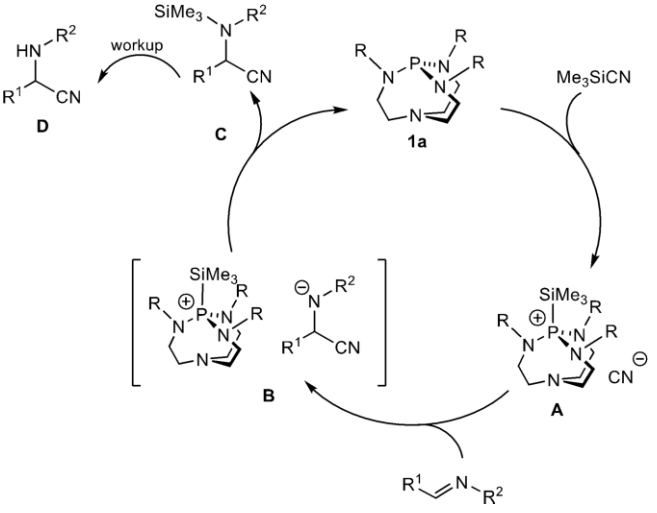
In order to shed light on the nature of the high efficiency of proazaphosphatranes, we carried out a control experiment using *N*-Tosyl-benzaldimine and TMSCN as substrates in the presence of 20 mol-% of HMPT at 0 °C in THF for 24 h (Scheme 2). Only 23 % yield was reached, which can be compared to the quantitative yield obtained with 0.1 mol-% of proazaphosphatrane **1a** in only 20 minutes (entry 1, Table 3). As can be seen, HMPT and **1a** have similar structure except for the bridgehead nitrogen in **1a**, the transannulation between bridgehead nitrogen and phosphorus enhanced the basicity and nucleophilicity of the phosphorus atom in **1a**, which makes it more reactive for activation of TMSCN in agreement with other reported proazaphosphatrane-catalyzed transformations.[4h,29a,30]

Table 3. Substrate scope of proazaphosphatrane **1a**-catalyzed cyanation of imines.[a]



Entry	Imine	R^1	R^2	PG	Product	Yield [%][b]
1	**2a**	Ph	H	Tosyl	**3a**	quant.
2	**2b**	*p*-MeC_6H_4	H	Tosyl	**3b**	quant.
3	**2c**	*p*-MeOC_6H_4	H	Tosyl	**3c**	quant.
4	**2d**	*p*-CNC_6H_4	H	Tosyl	**3d**	quant.
5	**2e**	2-naphthyl	H	Tosyl	**3e**	quant.
6	**2f**	*t*Bu	H	Tosyl	**3f**	85
7	**2g**	Ph	H	*N*-Boc	**3g**	94
8	**2h**	Ph	H	Bn	**3h**	92
9	**2i**	2-furan	H	Tosyl	**3i**	95[c]
10	**2j**	Ph	CH_3	Tosyl	**3j**	93[c,d]

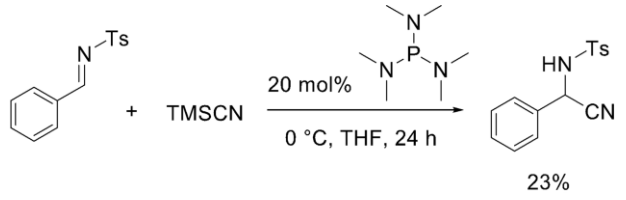
[a] Reaction conditions: imines (0.5 mmol), TMSCN (0.75 mmol), 0.1 mol-% **1a**, 1.5 mL of THF, 20 min, under argon, then 3 mL of H_2O. [b] Isolated yields are given. [c] 2 mol-% of catalyst was used. [d] The reaction was performed for 2 h.



Scheme 1. Proposed mechanism for the cyanation of imines catalyzed by proazaphosphatrane.

Conclusions

In summary, we have presented a mild, convenient and highly efficient methodology for the synthesis of α-aminonitriles using



Scheme 2. Cyanation of imine in the presence of HMPT.

proazaphosphatranes **1a**–**d** as catalysts. In general, our method tolerates a variety of substrates, ranging from aromatic, heteroaromatic to aliphatic imines with different protecting groups including Tosyl-, Bn-, and *N*-Boc. The very low catalyst loading, safer cyanide source and excellent yield and selectivity make **1a**–**d** outstanding among the best organocatalysts for the Strecker reaction.

Experimental Section

All commercial reagents and starting materials were used directly as received without further purification. Proazaphosphatrane **1a** was prepared using a reported procedure,[8d] **1b**–**d** were purchased from commercial sources. All dry solvents were purified prior to use through standard procedures or obtained from a solvent drying system (MB-SPS-800). All the reactions were carried out under an atmosphere of argon, unless otherwise noted. Flash column chromatography was performed using silica gel 60 (230–400 mesh). Thin-layer chromatography was per-formed on aluminum-coated plates with silica gel 60 F_{254} and was visualized with a UV lamp or by staining with potassium permanganate. ^{1}H NMR spectra were recorded at either 300 or 400 MHz on BRUKER Avance III nanobay spectrometers. ^{13}C NMR spectra were recorded at either 101 or 126 MHz and reported in ppm relative to $CDCl_3$ (δ = 77.4 ppm), unless otherwise noted. Single Pulse Magic Angle Spinning (CP MAS) ^{29}Si Solid State NMR spectra were obtained with a Bruker Avance 400 MHz WB spectrometer at the ^{29}Si resonance frequency of 79.5 MHz. Chemical shifts were referenced to tetramethylsilane, whose resonance was set to 0 ppm. High-resolution mass spectra (HRMS) were performed at Spectropole Analysis Service of Aix Marseille University.

General Procedure for Proazaphosphatrane-catalyzed Cyanation of Imines: To a solution of pro-azaphosphatrane (0.1 %mmol) and TMSCN (94 μL, 0.75 mmol) in THF (1.5 mL) was added imine (0.5 mmol) under an atmosphere of argon. The mixture was stirred at 0 °C for 20 minutes, upon completion monitored by TLC, 3 mL of H_2O was added and the mixture was stirred for another 30 minutes. The reaction mixture was then extracted with ethyl acetate (3 × 50 mL). The organic phase was collected, dried with anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash column chromatography using petroleum ether and ethyl acetate (10:1) as eluent to give products **3a**–**j**. All compounds have been described elsewhere, therefore only ^{1}H, ^{13}C and mass spectra are given, which are consistent with reported literatures.

***N*-[Cyano(phenyl)methyl]-4-methylbenzenesulfonamide (3a):**[31] Obtained as white solid, 143 mg (quant.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.8 Hz, 2 H), 7.50–7.39 (m, 5 H), 7.37 (d, *J* = 7.8 Hz, 2 H), 5.48 (s, 1 H), 5.12 (s, 1 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.7, 136.1, 132.1, 130.1, 129.9, 129.4, 127.3, 127.1, 116.3, 48.2, 21.7 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{15}H_{18}N_3O_2S^+$ $[M + NH_4]^+$, 304.1114, found 304.1112.

***N*-[Cyano(*p*-tolyl)methyl]-4-methylbenzenesulfonamide (3b):**[31] Obtained as white solid, 151 mg (quant.) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.3 Hz, 2 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 5.44 (d, *J* = 8.8 Hz, 1 H), 4.93 (d, *J* = 8.8 Hz, 1 H), 2.46 (s, 3 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.68, 140.12, 136.11, 130.05, 129.15, 127.36, 126.99, 116.39, 48.04, 21.66, 21.16 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{16}H_{20}N_3O_2S^+$ $[M + NH_4]^+$, 318.1271, found 318.1272.

***N*-[Cyano(4-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (3c):**[31] Obtained as white solid, 158 mg (quant.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.1 Hz, 2 H), 7.46–7.28 (m, 4 H), 6.90 (d, *J* = 7.4 Hz, 2 H), 5.42 (d, *J* = 8.5 Hz, 1 H), 5.00 (d, *J* = 8.2 Hz, 1 H), 3.81 (s, 3 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.72, 144.66, 136.12, 130.04, 128.54, 127.35, 124.03, 116.47, 114.74, 55.44, 47.78, 21.66 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{16}H_{20}N_3O_3S^+$ $[M + NH_4]^+$, 334.1220, found 334.1221.

***N*-[Cyano(4-cyanophenyl)methyl]-4-methylbenzenesulfonamide (3d):**[31] Obtained as white solid, 156 mg (quant.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.5 Hz, 2 H), 7.69–7.50 (m, 4 H), 7.34 (d, *J* = 7.1 Hz, 2 H), 5.95 (d, *J* = 9.3 Hz, 1 H), 5.50 (d, *J* = 9.4 Hz, 1 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.12, 137.14, 135.65, 133.02, 130.19, 127.95, 127.24, 117.76, 115.47, 113.73, 47.75, 21.69 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{16}H_{13}N_3O_2SNa^+$ $[M + Na]^+$, 334.0621, found 334.0621.

***N*-[Cyano(naphthalen-2-yl)methyl]-4-methylbenzenesulfonamide (3e):**[32] Obtained as white solid, 170 mg (quant.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.78 (m, 6 H), 7.56 (d, *J* = 4.5 Hz, 2 H), 7.47 (d, *J* = 8.7 Hz, 1 H), 7.36 (d, *J* = 8.0 Hz, 2 H), 5.65 (d, *J* = 8.8 Hz, 1 H), 5.12 (d, *J* = 9.1 Hz, 1 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.77, 136.08, 133.54, 132.87, 130.08, 129.70, 129.18, 128.24, 127.78, 127.49, 127.37, 127.17, 126.66, 123.91, 116.26, 48.47, 21.66 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{19}H_{20}N_3O_2S^+$ $[M + NH_4]^+$, 354.1271, found 354.1270.

***N*-(1-Cyano-2,2-dimethylpropyl)-4-methylbenzenesulfonamide (3f):**[33] Obtained as white solid, 133 mg (85 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.1 Hz, 2 H), 7.35 (d, *J* = 7.8 Hz, 2 H), 5.68 (d, *J* = 10.2 Hz, 1 H), 3.88 (d, *J* = 10.3 Hz, 1 H), 2.43 (s, 3 H), 1.04 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.49, 136.02, 130.04, 127.23, 116.68, 54.69, 35.30, 25.66, 21.63 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{13}H_{22}N_3O_2S^+$ $[M + NH_4]^+$, 284.1427, found 284.1422.

***tert*-Butyl [Cyano(phenyl)methyl]carbamate (3g):**[24] Obtained as white solid, 110 mg (94 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.30 (m, 5 H), 5.80 (s, 1 H), 5.16 (s, 1 H), 1.48 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 154.17, 133.49, 129.50, 129.32, 126.89, 117.74, 81.60, 46.13, 28.24 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{13}H_{16}N_2O_2Na^+$ $[M + Na]^+$, 255.1104, found 255.1104.

2-(Benzylamino)-2-phenylacetonitrile (3h):[33] Obtained as yellow oil, 102 mg (92 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.28 (m, 10 H), 4.77 (s, 1 H), 4.08 (d, *J* = 13.1 Hz, 1 H), 3.97 (d, *J* = 13.0 Hz, 1 H), 1.89 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.17, 134.81, 129.05, 128.99, 128.67, 128.44, 127.67, 127.33, 118.78, 53.49, 51.29 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{15}H_{15}N_2^+$ $[M + H]^+$, 223.1230, found 223.1228.

***N*-[Cyano(furan-2-yl)methyl]-4-methylbenzenesulfonamide (3i):**[33] Obtained as colorless solid, 131 mg (95 %) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.1 Hz, 2 H), 7.39–7.35 (m, 1 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 6.45 (d, *J* = 3.2 Hz, 1 H), 6.33 (t, *J* = 2.5 Hz, 1 H), 5.71 (d, *J* = 8.9 Hz, 1 H), 5.52 (d, *J* = 9.0 Hz, 1 H), 2.43 (s, 3 H)

ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.63, 144.43, 144.14, 136.09, 129.97, 127.25, 114.68, 110.97, 110.36, 42.26, 21.60 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{13}H_{16}N_3O_3S^+$ $[M + NH_4]^+$, 294.0907, found 294.0907.

***N*-(1-Cyano-1-phenylethyl)-4-methylbenzenesulfonamide (3j):**[34] Obtained as colorless solid, 139 mg (93 %) ^1H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.0 Hz, 2 H), 7.48 (d, *J* = 7.2 Hz, 2 H), 7.38–7.28 (m, 3 H), 7.26–7.18 (m, 2 H), 5.40 (s, 1 H), 2.42 (s, 3 H), 1.94 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.05, 137.38, 137.19, 129.56, 129.24, 128.90, 127.47, 125.58, 118.94, 56.62, 30.17, 21.55 ppm. HRMS (ESI-TOF) *m/z*: calcd. for $C_{16}H_{20}N_3O_2S^+$ $[M + NH_4]^+$, 318.1271, found 318.1271.

Keywords: Pro-Azaphophatranes · Verkade's superbase · Strecker reaction · Organocatalysis · Phosphorus

[1] a) C. Lensink, S.-K. Xi, L. M. Daniels, J. G. Verkade, *J. Am. Chem. Soc.* **1989**, *111*, 3478–3479; b) M. A. Laramay, J. G. H. Verkade, *J. Am. Chem. Soc.* **1990**, *112*, 9421–9422; c) J.-S. Tang, J. G. Verkade, *J. Am. Chem. Soc.* **1993**, *115*, 1660–1664; d) J.-S. Tang, J. G. Verkade, *Tetrahedron Lett.* **1993**, *34*, 2903–2904.

[2] J. G. Verkade, P. B. Kisanga, *Tetrahedron* **2003**, *59*, 7819–7858.

[3] P. B. Kisanga, J. G. Verkade, R. Schwesinger, *J. Org. Chem.* **2000**, *65*, 5431–5432.

[4] a) a) J.-S. Tang, J. G. Verkade, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 896–898; *Angew. Chem.* **1993**, *105*, 934–936; b) B. A. D'Sa, J. G. Verkade, *J. Org. Chem.* **1996**, *61*, 2963–2966; c) S. Arumugam, J. G. Verkade, *J. Org. Chem.* **1997**, *62*, 4827–4828; d) B. A. D'Sa, J. G. Verkade, *J. Am. Chem. Soc.* **1996**, *118*, 12832–12833; e) B. A. D'Sa, D. McLeod, J. G. Verkade, *J. Org. Chem.* **1997**, *62*, 5057–5061; f) P. B. Kisanga, J. G. Verkade, *J. Org. Chem.* **1999**, *64*, 4298–4303; g) P. Ilankumaran, J. G. Verkade, *J. Org. Chem.* **1999**, *64*, 3086–3089; h) Z. Wang, B. Fetterly, J. G. Verkade, *J. Organomet. Chem.* **2002**, *646*, 161–166.

[5] a) Z. Thammavongsy, J. F. Khosrowabadi Kotyk, C. Tsay, J. Y. Yang, *Inorg. Chem.* **2015**, *54*, 11505–11510; b) Z. Thammavongsy, I. M. Kha, J. W. Ziller, J. Y. Yang, *Dalton Trans.* **2016**, *45*, 9853–9859; c) B. Chatelet, P. Nava, H. Clavier, A. Martinez, *Eur. J. Inorg. Chem.* **2017**, *37*, 4311–4316

[6] J. V. Kingston, J. G. Verkade, *J. Org. Chem.* **2007**, *72*, 2816–2822.

[7] S. Urgaonkar, J. H. Xu, J. G. Verkade, *J. Org. Chem.* **2003**, *68*, 8416–8423

[8] a) P. D. Raytchev, A. Bendjeriou, J.-P. Dutasta, A. Martinez, V. Dufaud, *Adv. Synth. Catal.* **2011**, *353*, 2067–2077; b) P. D. Raytchev, L. Roussi, J.-P. Dutasta, A. Martinez, V. Dufaud, *Catal. Commun.* **2012**, *28*, 1–4; c) P. Dimitrov Raytchev, A. Martinez, H. Gornitzka, J.-P. Dutasta, *J. Am. Chem. Soc.* **2011**, *133*, 2157–2159; d) B. Chatelet, H. Gornitzka, V. Dufaud, E. Jeanneau, J.-P. Dutasta, A. Martinez, *J. Am. Chem. Soc.* **2013**, *135*, 18659–18664.

[9] E. Blondiaux, J. Pouessel, T. Cantat, *Angew. Chem. Int. Ed.* **2014**, *53*, 12186–12190; *Angew. Chem.* **2014**, *126*, 12382; E. Blondiaux, J. Pouessel, T. Cantat, *Angew. Chem. Int. Ed.* **2014**, *53*, 12186–12386; *Angew. Chem.* **2014**, *126*, 12382

[10] S. Mummadi, D. K. Unruh, J. Zhao, S. Li, C. Krempner, *J. Am. Chem. Soc.* **2016**, *138*, 3286–3289.

[11] S. Mummadi, D. Kenefake, R. Diaz, D. K. Unruh, C. Krempner, *Inorg. Chem.* **2017**, *56*, 10748–10759.

[12] X. Wang, Y. Liu, Z. Li, H. Wang, H. Gebru, S. Chen, H. Zhu, F. Wei, K. Guo, *ACS Macro Lett.* **2017**, *6*, 1331–1336.

[13] a) P. L. Feldman, M. F. Brackeen, *J. Org. Chem.* **1990**, *55*, 4207–4209; b) P. L. Feldman, M. K. James, M. F. Brackeen, J. M. Bilotta, S. V. Schuster, A. P. Lahey, M. W. Lutz, M. R. Johnson, M. J. Leighton, *J. Med. Chem.* **1991**, *34*, 2202–2208; c) A. J. Walz, F. L. Hsu, *Tetrahedron Lett.* **2014**, *55*, 501–502; d) F. G. Zhang, X. Y. Zhu, S. Li, J. Nie, J. A. Ma, *Chem. Commun.* **2012**, *48*, 11552–11554; e) A. Sadhukhan, S. Saravanan, N. U. H. Khan, R. I. Kureshy, S. H. Abdi, SH. C. Bajaj, *J. Org. Chem.* **2012**, *77*, 7076–7080; f) C. Bolm, R. Mocci, C. Schumacher, M. Turberg, F. Puccetti, J. G. Hernandez, *Angew. Chem. Int. Ed.* **2018**, *57*, 2423–2426; *Angew. Chem.* **2018**, *130*, 2447–2450.

[14] For reviews, see: a) H. Gröger, *Chem. Rev.* **2003**, *103*, 2795–2828; b) J. Wang, X. Liu, X. Feng, *Chem. Rev.* **2011**, *111*, 6947–6983; c) L. Yet, *Angew. Chem. Int. Ed.* **2001**, *40*, 875–877; *Angew. Chem.* **2001**, *113*, 900–902; d) P. Merino, E. Marqués-López, T. Tejero, R. P. Herrera, *Tetrahedron* **2009**, *65*, 1219–1234; e) V. V. Kouznetsov, C. E. P. Galvis, *Tetrahedron* **2018**, *74*, 773–810.

[15] S. K. De, R. A. Gibbs, *Tetrahedron Lett.* **2004**, *45*, 7407–7408.

[16] Z. L. Shen, S. J. Ji, T. P. Loh, *Tetrahedron* **2008**, *64*, 8159–8163.

[17] S. K. De, *Synth. Commun.* **2005**, *35*, 653–656.

[18] S. K. De, *J. Mol. Catal. A* **2005**, *225*, 169–171.

[19] M. Narasimhulu, T. S. Reddy, K. C. Mahesh, S. M. Reddy, A. V. Reddy, Y. Venkateswarlu, *J. Mol. Catal. A* **2007**, *264*, 288–292.

[20] S. Kobayashi, H. Ishitani, M. Ueno, *Synlett* **1997**, 115–116.

[21] S. Kobayashi, T. Busujima, *Chem. Commun.* **1998**, 981–982.

[22] A. S. Paraskar, A. Sudalai, *Tetrahedron Lett.* **2006**, *47*, 5759–5762.

[23] a) Y. Fukuda, Y. Maeda, K. Kondo, T. Aoyama, *Synthesis* **2006**, *12*, 1937–1939; b) Y. Fukuda, K. Kondo, T. Aoyama, *Synthesis* **2006**, *16*, 2649–2652.

[24] A. Heydari, A. Arefi, S. Khaksar, R. K. Shiroodi, *J. Mol. Catal. A* **2007**, *271*, 142–144.

[25] S. C. Pan, B. List, *Synlett* **2007**, *2*, 318–320.

[26] H. Ghafuri, M. Roshani, *RSC Adv.* **2014**, *4*, 58280–58286.

[27] B. Ullah, J. Chen, Z. Zhang, H. Xing, Q. Yang, Z. Bao, Q. Ren, *Scientific Reports* https://doi.org/10.1038/srep42699.

[28] B. M. Fetterly, N. K. Jana, J. G. Verkade, *Tetrahedron* **2006**, *62*, 440–456.

[29] a) K. Wadhwa, V. R. Chintareddy, J. G. Verkade, *J. Org. Chem.* **2009**, *74*, 6681–6690; b) P. B. Kisanga, P. Ilankumaran, B. M. Fetterly, J. G. Verkade, *J. Org. Chem.* **2002**, *67*, 3555–3560; c) B. A. D'Sa, P. Kisanga, J. G. Verkade, *J. Org. Chem.* **1998**, *63*, 3961–3967.

[30] V. R. Chintareddy, K. Wadhwa, J. G. Verkade, *J. Org. Chem.* **2009**, *74*, 8118–8132.

[31] S. T. Kadam, P. Thirupathi, S. S. Kim, *Synthesis* **2011**, *6*, 919–923.

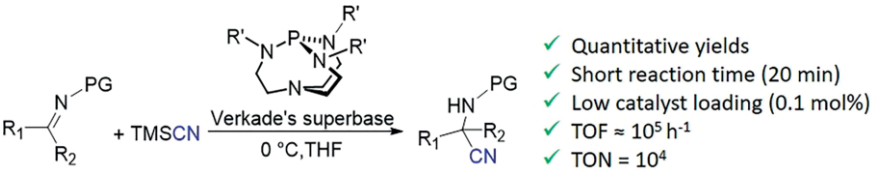
[32] J. Wang, X. Hu, J. Jiang, S. Gou, X. Huang, X. Liu, X. Feng, *Angew. Chem. Int. Ed.* **2007**, *46*, 8468–8470; *Angew. Chem.* **2007**, *119*, 8620–8622.

[33] N. H. Khan, S. Agrawal, R. I. Kureshy, S. H. R. Abdi, S. Singh, E. Suresh, R. V. Jasra, *Tetrahedron Lett.* **2008**, *49*, 640–644.

[34] X. Huang, J. Huang, Y. Wen, X. Feng, *Adv. Synth. Catal.* **2006**, *348*, 2579–2584.

Received: July 25, 2018

Organocatalytic Mechanisms



Verkade's superbases were found to be efficient organocatalysts for the Strecker reaction, leading to high yield, in short reaction time and requiring low catalyst loading.

DOI: 10.1002/ejoc.201801170