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α-Chlorobenzylation of Nitroarenes via Vicarious Nucleophilic Substitution with Benzylidene Dichloride. Umpolung of the Friedel-Crafts Reaction

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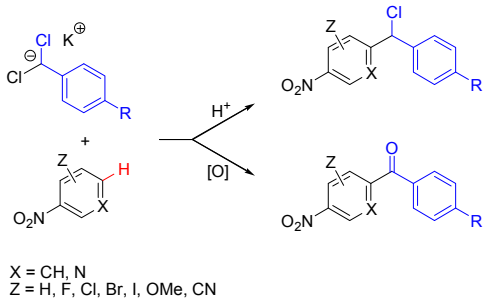


X = CH, N
Z = H, F, Cl, Br, I, OMe, CN

ABSTRACT: Readily available α,α-dichlorotoluenes enter a vicarious nucleophilic substitution (VNS) reaction with electron-deficient arenes to give α-chlorobenzylated nitrobenzenes, as well as six- and five-membered heterocycles. Oxidation of the initially formed α-chlorobenzylic carbanions instead of protonation results in formation of diaryl ketones, providing a means of overall nucleophilic C–H-benzoylation of electron-deficient aromatic rings. Alternatively, benzoylated nitroarenes can be obtained via the reaction of isolated α-chlorodiarylmethanes with sodium azide.

Keywords: α-halocarbanions, nitroarenes, vicarious nucleophilic substitution, hydrogen substitution, chloroalkylation, benzoylation

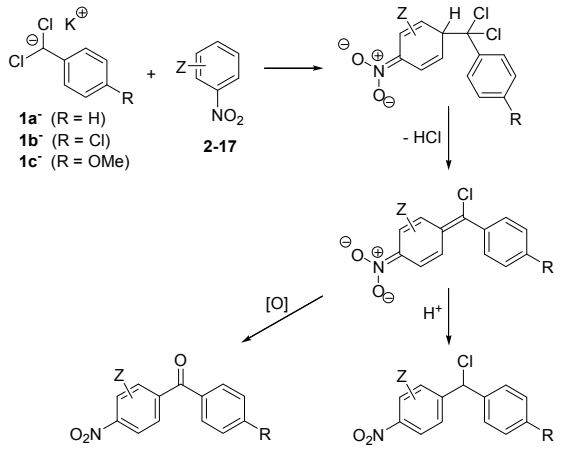
INTRODUCTION

Vicarious Nucleophilic Substitution (VNS) is a versatile process for introduction of functionalized carbon substituents into electron-deficient aromatic rings (particularly nitroarenes), at positions occupied by hydrogen atoms.[1] The reaction proceeds via reversible addition of α-halocarbanions (and carbanions with other nucleofugal groups X) to nitroarenes and other electron-deficient arenes to form σ^H adducts, followed by base-induced β-elimination of HX to form nitrobenzylic carbanions of the products. The final products are isolated upon protonation. It should be stressed that VNS of hydrogen in *o*-and *p*-halonitroarenes proceeds much faster than conventional S_NAr substitution, which involves much slower, but irreversible addition of nucleophiles at positions occupied by halogens. This is in accord with the recently formulated general mechanism of substitution in electron-poor aromatic compounds.[1c-e]

Particularly valuable are VNS reactions of nitroarenes with tri- and dihalocarbanions as they lead to nitrobenzylic halides, potentially useful in further transformations. Treatment of chloroform or bromoform with an excess of strong base at low temperature in the presence of nitroarenes resulted in introduction of dihalomethyl groups in positions *ortho* and/or *para* to the nitro group.[2] Hydrolysis of these groups provides *o*- or/and *p*-nitrobenzaldehydes. The VNS with haloforms can be therefore considered as nucleophilic formylation of carbo- and heterocyclic nitroarenes.[2] Even more valuable is VNS with carbanions of alkyl dichloroacetates that produces esters of α-chloro-α-nitroaryl acetic acids.[3] Further reaction of ethyl α-chloro-α-nitroaryl acetates with sodium azide results in substitution of chlorine with azide anion followed by spontaneous conversion of the azides into ethyl nitrobenzoylformates. Acidic hydrolysis of *tert*-butyl α-chloro-α-nitroarylacetates is followed by instantaneous decarboxylation to form chloromethyl nitroarenes.[3c,d] VNS in electron deficient arenes with *t*-butyl dichloroacetate can therefore be considered as nucleophilic chloromethylation of nitroarenes. Nitrobenzylic α-chlorocarbanions generated in a VNS reaction between nitroarenes and

carbanions of alkyl dichloroacetates may also undergo one-pot reactions with electrophiles, for example addition to Michael acceptors with the formation of nitrophenyl cyclopropanes in a one pot process,[4] or to aromatic aldehydes giving oxiranes.[5] A VNS reaction of carbanions proceeds also between 2-dichloromethylimidazolines and nitroarenes to give α-chloronitrobenzylic carbanions, reacting in situ with aromatic aldehydes with formation of oxiranes.[6]

SCHEME 1 The Concept of α-Chlorobenzylation and Benzoylation of Electron-deficient Arenes in a VNS Reaction with Dichlorotoluene Carbanions



Considering high value of α-chloronitrobenzylic carbanions as versatile active intermediates, we were looking for a further extension of the scope of the VNS reaction. In this endeavor, we expected that benzylidene dichlorides (α,α-dichlorotoluenes) **1** would be the proper choice as precursors of dichlorocarbanions capable of entering VNS (Scheme 1).The VNS reaction between nitroarenes and α,α-dichlorobenzyl carbanions would provide synthetically useful α-chlorobenzylated products (nitrobenzhydryl chlorides). In fact, there is a lack of a general method for preparation of such compounds with various substitution pattern. The simplest representative of this type of compounds – *p*-nitrobenzhydryl chloride – has been synthesized from *p*-nitrobenzophenone via ketone reduction and OH to Cl exchange.[7] Moreover, we envisioned that oxidation of the intermediate chlorobenzyl

carbanions could provide a method of direct, nucleophilic benzoylation of electron-deficient arenes. Apart from the classical Friedel-Crafts acylation (applicable to electron-rich substrates),[8] C–H benzoylation of aromatic rings is currently possible using transition-metal catalyzed aromatic C–H activation[9] using arylpyruvates,[10] aroyl chlorides and aromatic aldehydes[11] as cross-coupling partners. A few reports of nucleophilic benzoylation of C–H positions in nitroarenes have been published. A moderately efficient method has been reported by Katritzky who used α-alkoxy-α-benzotriazolyl-substituted carbanions in oxidative substitution of hydrogen, followed by hydrolysis.[12] Very recently, two protocols of oxidative nucleophilic benzoylation of nitrobenzene derivatives have been disclosed, both employing arylacetic esters as nucleophile precursors.[13,14] Another approach has been developed by Suzuki and co-workers, who achieved benzoylation of nitroarenes by nucleophilic substitution of ring fluorine with the Breslow intermediates formed from aromatic aldehydes and *N*-heterocyclic carbenes.[15]

It should be mentioned that there is only one published report of VNS with carbanion of a benzyl chloride derivative – the reaction between *p*-nitrobenzyl chloride and *m*-dinitrobenzene resulted in introduction of a *p*-nitrobenzyl group into the dinitrobenzene ring.[16] A similar reaction of chloromethyl-substituted heterocycles has also been described that provides an efficient method of synthesis of nitroaryl heteroaryl methanes.[17]

Similarly to deprotonation of chloroform, leading to a CCl_3^- carbanion that dissociates rapidly to dichlorocarbene particularly under PTC conditions,[18] but can be trapped by nitroarenes when generated at low temperature,[2] deprotonation of benzylidene dichloride **1a** generates phenyl dichloromethyl carbanion that dissociates rapidly to phenyl chlorocarbene.[19] Lithiation of benzylidene dichloride via its reaction with butyllithium at -100 °C results in formation of phenyldichloromethyl lithium which is stable at such temperatures. This metaloorganic compound can be trapped by carbon dioxide or, upon warming to -65 °C, it decomposes to phenyldichlorocarbene.[20] An opposite process, involving addition of chloride anion to phenyl chlorocarbene generated by thermolysis of phenyl chlorodiazirine, followed by addition of the carbanion to an electrophile – acrylonitrile, has also been described.[21] It was therefore

of interest to examine whether α,α-dichlorocarbanion generated via deprotonation of readily available benzylidene dichloride can enter VNS reactions with nitroarenes.

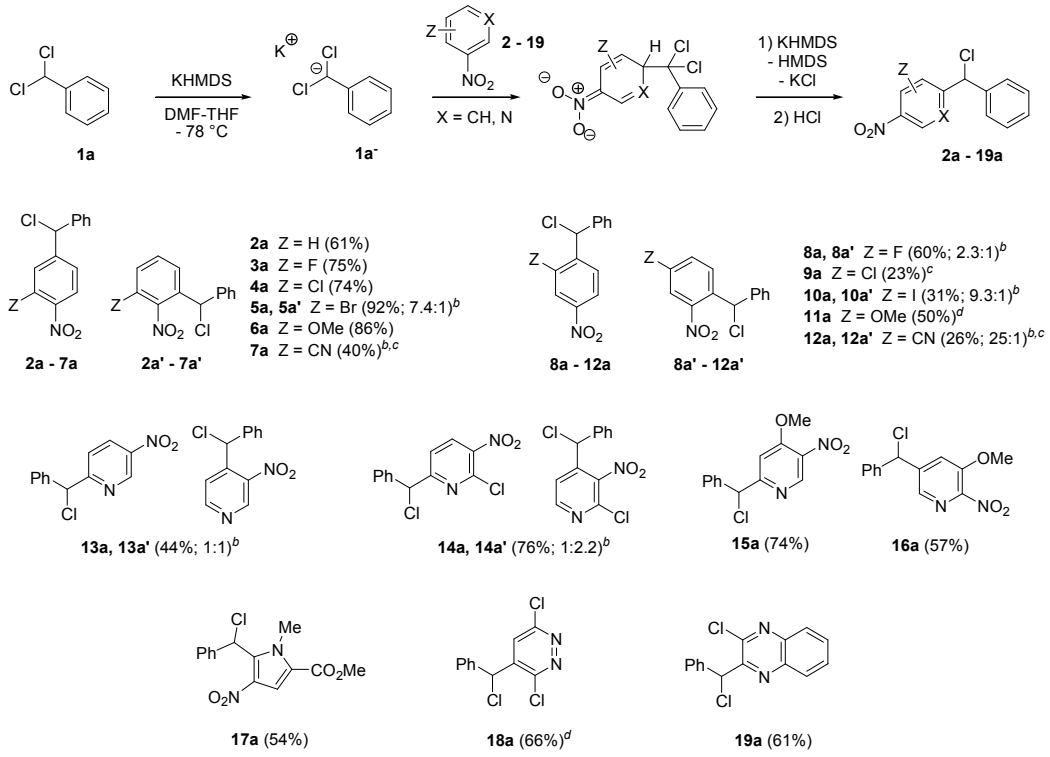
RESULTS AND DISCUSSION

Carbanions of nitrobenzyl chlorides and nitrobenzylidene dichlorides (such as those produced in the VNS reaction with chloroform) are very unstable entities. Therefore, deprotonation of benzylidene dichloride **1a** and the reaction between **1a**$^-$ and nitroarenes should be carried out at low temperature. Treatment of a mixture of **1a** and nitrobenzene **2** in DMF/THF at -78 °C with potassium *tert*-butoxide resulted in coloration of the mixture, indicating formation of nitrobenzylic carbanions of the VNS products. However, the yield of the expected *p*-nitrodiphenyl chloromethane (nitrobenzhydryl chloride) **2a** obtained in preliminary experiments were moderate, perhaps due to insufficient basicity of *t*-BuOK. Under similar conditions but using a stronger base, that is upon addition of a solution of **1a** (0.6 mmol) and nitrobenzene **2** (0.5 mmol) in DMF to a stirred solution of potassium bis(trimethylsilyl)amide (KHMDS; 2.5 equiv. in THF cooled to -78 °C, followed by quenching of the mixture with aqueous HCl after 15 min, the expected product **2a** was obtained in much better yield of 61%. Increasing the excess of base or of **1a** with respect to nitroarene did not have any significant effect on the final yield. The addition of the bulky methinic carbanion **1a**$^-$ proceeded selectively at position *para*; the product of *ortho* substitution was not detected.

Under these conditions: -78 °C, 2.5 equiv. of KHMDS, DMF/THF 1:1, 15 min, **1a** reacted with nitroarenes containing a variety of substituents in *ortho* and *meta* positions, giving the expected VNS products **2a - 19a** (Scheme 2). With nitrobenzene and its *ortho*-substituted derivatives, the reaction proceeded selectively at position *para* to the nitro group due to the steric requirements of the bulky methinic carbanion **1a**$^-$. *m*-Substituted nitroarenes reacted with lower yields and lower *ortho*/*para* selectivity, probably due to steric hindrance associated with addition of **1a**$^-$ at the position *ortho* to the substituent Z. The VNS reaction with carbanion of **1a** proceeds also with some nitroheterocycles such as

nitropyridines or a nitropyrrole derivative, or even azines without an activating nitro group - 1,4-dichloropyridazine **18** or 2-chloroquinoxaline **19**.

SCHEME 2 VNS Reaction of Electron-deficient Arenes with Dichlorotoluene Carbanion 1a$^-$ [a]



[a] Reaction conditions: nitroarene (1 equiv.) and **1a** (1.2 equiv.) in DMF were added dropwise to KHMDS (2.5 equiv; 1M in THF) cooled to -78 °C, stirred for 15 min, then quenched with 2M HCl. [b] Ratio of isomers resulting from attack at *para* and *ortho* position to the nitro group. [c] Reaction time: 5 min. [d] Reaction time: 1 min.

In some cases, under the standard conditions we observed very low yields of the VNS reaction, or the expected products were not obtained at all, particularly with substrates **7**, **9**, **11**, **12**, 3,6-dichloropyridazine **18** and 2-chloroquinoxaline **19**. It was surprising because these nitroarene are highly electrophilic and usually react satisfactorily in other VNS reactions, including those with CCl_3^- carbanions. As all starting materials were consumed in these cases, it appeared that the initially formed α-chloronitrobenzylic carbanions were unstable even at low temperature. In order to verify this supposition, the reactions of these nitroarenes were carried out in shorter time: 5 min or even 1 min. To our satisfaction, the expected products could be obtained in acceptable yields and only minor quantities

of nitroarenes were recovered unchanged. It should be stressed how fast these multistep reactions are being completed below -70 °C (within 1-5 min).

Generally, nitroarenes exhibited very low propensity to react with **1a**$^-$ (or carbanions derived from other α,α-dihalotoluenes, see below) at the position *ortho* to the nitro group. Moreover, an attempt to force *ortho* substitution in a reaction of **1a**$^-$ with a substrate with blocked *para* position (*p*-chloronitrobenzene) led to recovery of substrate and formation of small amounts of a few products, one of which was the expected products of VNS. Unfortunately, this compound turned out to be too unstable for isolation in pure form, unlike *ortho* isomers obtained in some reactions in Scheme 2 (**5a'**, **8a'**, **10a'**). On the other hand, in the case of some nitropyridines the reaction proceeded with low *ortho*/*para* selectivity or even preferentially at the position vicinal to NO_2 (**14a**, **14a'**).

Noteworthy, **1a**$^-$ reacts with 2-chloroquinoxaline **19** along the VNS pathway to give **19a**. This reaction takes a completely different course than the reactions of quinoxaline with carbanions of chloromethyl aryl sulfones described in the literature that lead to annulated bis(aziridine)derivatives of quinoxaline.[22] In those reactions, the intermediate anionic σ^H adducts undergo 1,3-intramolecular substitution rather than β-elimination. Apparently, the chlorine substituent in **19** contributes to negative charge delocalization, promoting β-elimination to an α-chlorobenzyl carbanion, instead of nucleophilic substitution with the negatively charged nitrogen atom of the heterocyclic ring.

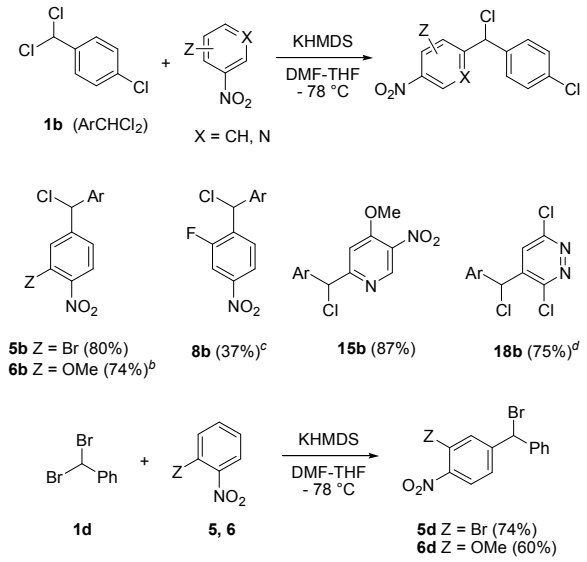
Similarly to CCl_3^- carbanions, α,α-dichlorocarbanions formed from **1a** may undergo fast dissociation to phenyl chlorocarbene. The success of the VNS reaction with **1a**$^-$ relies upon its generation in the presence of electrophilic nitroarenes, so addition and formation of the σ^H adducts is faster than α-elimination. While studying VNS with CCl_3^- anions, we demonstrated that its fast and reversible dissociation indeed proceeds in the solvent cage.[2a] Thus, dichloromethylation of moderately electrophilic mononitroarenes by trichloromethyl carbanions proceeded satisfactorily at -70 °C in THF/DMF but not in liquid ammonia that otherwise is an excellent solvent for VNS reactions with other α-chlorocarbanions.[1b,c] It appears that dichlorocarbene generated by fast and reversible dissociation of

CCl_3^- in the solvent cage is immediately quenched by ammonia solvent, whereas in THF/DMF the carbanion can be trapped by nitroarene. This supposition was supported by the observation that very active nitroarenes such as nitroquinolines are entering VNS with chloroform even in liquid ammonia. On the other hand, we found that the reaction of **1a**$^-$ in liquid ammonia proceeds efficiently even with weakly electrophilic 2-nitroanisole (75%). It demonstrates that spontaneous dissociation of **1**$^-$ is considerably slower than that of CCl_3^-.

4-Chlorobenzylidene dichloride **1b**, readily prepared from 4-chlorobenzaldehyde,[23] satisfactorily enters the VNS reaction as demonstrated by formation of products **5b**, **6b**, **8b**, **15b** and **18b** in high yields (Scheme 3). Regioselectivity was usually higher than in similar reactions of **1a**, for example *m*-fluoronitrobenzene underwent nearly exclusive attack *para* to the NO_2 group (compare with 2.3:1 mixture of **8a** and **8a'** in Scheme 2). In some cases (e.g. reactions of **6** and **8**) we observed formation of considerable amounts of 4-chlorobenzoyl-substituted nitroarenes. Only traces of similar ketones were formed in the reactions of **1a**.

On the other hand, similar reactions of 4-methoxybenzylidene dichloride **1c** led to complex mixtures containing unreacted nitroarenes and only traces of the expected VNS products. Such reaction course may be associated with greater instability of **1c**$^-$ anion. Changing the α-halogen substituents, we found that α,α-dibromotoluene **1d** provided α-bromobenzylated nitroarenes in slightly lower yields (74% for **5d**, 60% for **6d**) compared to those observed with **1a** under identical conditions (92% for **5a**, 96% for **6a**; see Scheme 2), probably due to greater steric hindrance and faster dissociation of the C–Br bond in **1d**$^-$ (Scheme 3). On the other hand, reactions of **1d** were more regioselective in favor of the *para* substitution. α,α-Difluorotoluene failed to undergo deprotonation in the presence of KHMDS and in consequence only the starting materials were recovered when its reaction with nitrobenzene was attempted.

SCHEME 3 VNS Reactions of 4-Chlorobenzylidene Dichloride 1b and Benzylidene Dibromide 1d



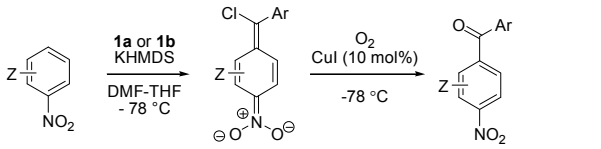
[a] Reaction conditions: nitroarene (1 equiv.) and **1** (1.2 equiv.) in DMF were added dropwise to KHMDS (2.5 equiv; 1M in THF) cooled to -78 °C, then stirred for 15 min, then quenched with 2M HCl. [b] 4'-Chloro-3-methoxy-4-nitrobenzophenone (**6f**) formed as side product in 13% yield. [c] 4-Chloro-2'-fluoro-4'-nitrobenzophenone (**8f**) formed as side product in 16% yield. [d] Reaction time: 1 min.

The VNS reactions described above were equally efficient when performed at a 10 times larger scale. For example, 5 mmol of nitroarene **5** was converted into **5b** in 82% yield, and pyridine **15** into **15a** in 78% yield.

In some cases products of the VNS reactions of **1a** and particularly **1b** were accompanied by minor amounts of nitrobenzophenones, such as 4-nitrobenzophenone **2e** in the reaction of nitrobenzene and **1a**, or ketones **6f** and **8f** in Scheme 3. Their formation can be probably attributed to nitroarene substrates acting as oxidants, or traces of molecular oxygen present in the reaction mixture. Therefore, we expected that a one-pot benzoylation of nitroarenes could be achieved if the intermediate α-chloronitrobenzylic carbanions formed in the VNS process described above were subjected to direct oxidation rather than protonation. In preliminary experiments, addition of a DMF solution of **1a** and 2-bromo- or 2-methoxynitrobenzene to 1M KHMDS in THF at -78, followed after 15 min by bubbling dried air (passed through a layer of solid KOH) through the reaction mixture until the characteristic color of α-chlorobenzylic anions has disappeared (about 30 min), resulted in the formation of the respective 4-benzoylation products in about 50% yield. After some experimentation, we found that the reaction gives higher yields and proceeds much faster with oxygen instead of air. Further improvement

can be obtained using 10 mol% of CuI as an additive. Under these optimized conditions, nitrobenzophenone derivatives could be obtained in good or sometimes moderate yields, together with varying amounts of unoxidized VNS products (Scheme 4).

SCHEME 4 Benzoylation of Nitroarenes in a One-pot Procedure

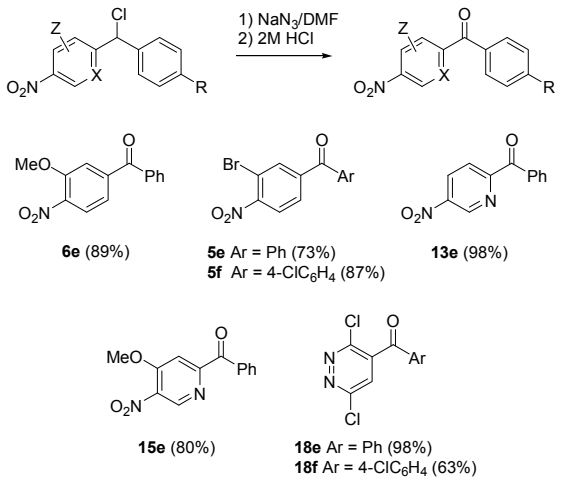


Ar = Ph
2e, 2e' Z = H (78%; 4.2:1)[a]
3e Z = 3-F (55%)
5e, 5e' Z = 3-Br (73%; 5:1)[a,b]
6e Z = 3-OMe (79%)
8e Z = 2-F (36%)
11e Z = 2-OMe (30%)
Ar = 4-ClC_6H_4
2f, 2f' Z = H (74%; 10:1)[a]

[a] Ratio of regioisomers. [b] Air used instead of oxygen gas.

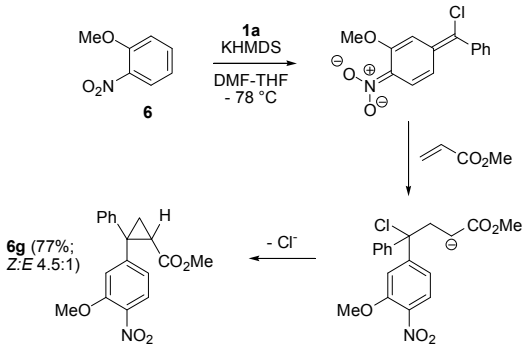
Unfortunately, the one-pot protocol shown in Scheme 4 proved efficient only for simple nitrobenzene derivatives, and failed altogether for benzoylation of heterocyclic substrates. Therefore, a two-step benzoylation protocol has been established, based upon the reaction of sodium azide with α-chlorobenzylated products isolated after the VNS reaction. Spontaneous conversion of nitrobenzyl azides into ketones was observed earlier.[3a] Nucleophilic substitution of chloride with azide, presumably followed by a rearrangement to an imine and its hydrolysis, provides diaryl ketones in high (sometimes quantitative) yields, as demonstrated by the examples in Scheme 5.

SCHEME 5 Transformation of the VNS Products into Diaryl Ketones



Synthetic utility of the α-chlorobenzyl carbanions formed in VNS with α,α-dichlorotoluenes can be also demonstrated by the reaction with a Michael acceptor, methyl acrylate, which gives a diarylcyclopropane derivative in good yield and 4.5:1 ratio of diastereoisomers, after intramolecular substitution of the remaining chlorine atom (Scheme 6). The configuration of the main diastereoisomer has been determined to be *Z* in NOE NMR experiments. This example of the cyclopropane resembles a similar, but somewhat less general cyclopropanation of enals with carbanions of dinitrobenzyl chlorides.[24]

SCHEME 6 Formation of a Cyclopropane Derivative in a Tandem VNS-Michael Addition Process



CONCLUSIONS

Carbanions of benzylidene dichloride and its analogues enter VNS reaction with a variety of nitroarenes, nitroheteroarenes and even some azines to give products of substitution of the ring hydrogen with α-chlorobenzyl substituents. This process, which can be considered a nucleophilic analogue (umpolung) of the Friedel-Crafts reaction, is an efficient way of synthesis of substituted benzhydryl chlorides – versatile intermediates in further synthetic transformations. The α-chlorocarbanions generated in the VNS process can be directly oxidized by oxygen to form respective benzophenones. Alternatively, isolated α-chlorobenzyl nitroarenes can be converted into benzophenones via reaction with sodium azide. The overall process is an example of nucleophilic benzoylation and can be regarded as an umpolung of the Friedel-Crafts acylation.

EXPERIMENTAL SECTION

General information. All ^{1}H and ^{13}C NMR spectra were recorded at 298 K in $CDCl_3$ solutions with a 400 MHz (400, 100 and 376 MHz for ^{1}H, ^{13}C and ^{19}F, respectively). The ^{1}H and ^{13}C NMR chemical shifts are given relative to the TMS signal at 0.0 ppm and relative to $CFCl_3$ for ^{19}F spectra. Mass spectra and HR MS measurements were obtained using a mass spectrometer equipped with an electrospray ion source and q-TOF type mass analyzer (ES), or a magnetic sector mass spectrometer equipped with an electron impact (EI) ion source and the EBE double focusing geometry mass analyzer. IR spectra were obtained using a FT-IR spectrometer. Melting point temperatures were measured at a heating rate of 5 °C/min. Column chromatography was performed using silica gel 60 (0.040−0.063 mm). Thin-layer chromatography was performed on precoated silica gel plates and visualized under a UV lamp. Hexanes for column chromatography were distilled before use. Dry DMF, α,α-dichlorotoluene and KHMDS (1M in THF) were commercial and used as received. 4-Chloro- and 4-methoxybenzylidene dichloride,[23] as well as α,α-dibromotoluene[25] were obtained from the respective aldehydes following the literature procedures.

General synthetic procedure for α-chlorobenzylation. KHMDS solution in THF (1M, 1.25 mmol, 1.25 mL) was placed in a flame-dried Schlenk flask under Ar and cooled to -78 °C. A solution of nitroarene (0.5 mmol) and **1a**, **1b** or **1d** (0.6 mmol) in DMF (1.25 mL) was added dropwise with vigorous magnetic stirring. After 15 min (or 5 min, or 1 min; see notes to Scheme 2 and 3) 2M $HCl_{(aq)}$ (1 mL) was added, followed by AcOEt (5 mL) and brine (5 mL). The phases were separated, the organic phase was washed with brine (3x10 mL), dried over anhydrous Na_2SO_4 and evaporated. The products were purified by column chromatography on silica gel using hexanes–AcOEt 10:1 or hexanes–DCM 5:1 as eluent, unless specified otherwise in the descriptions of particular compounds.

*4-Nitro-1'-phenylbenzyl chloride (**2a**)*. 76 mg (61%) yield; colorless oil; IR (DCM) ν_{max} 3080, 2855, 1606, 1522, 1348, 1111, 837, 750, 701, 600 cm^{-1}; ^1H NMR δ 6.17 (1H, s), 7.38 (5H, m), 7.60 (2H, d, $^3J_{HH}$ = 8.6 Hz), 8.19 (2H, d, $^3J_{HH}$ = 8.8 Hz); ^{13}C NMR δ 62.7, 123.8, 127.7, 128.7, 128.7, 128.9, 139.7, 147.5, 147.9; MS (EI 70 eV, *m/z*, %) 247 (M^+, 12), 212 (100), 165 (59), 153 (18), 77 (20); HR MS (EI+) calcd for $C_{13}H_{10}ClNO_2$ $[M]^+$ 247.0400, found 247.0400. Elemental analysis calcd for $C_{13}H_{10}ClNO_2$: C, 63.04; H, 4.07; Cl, 14.31; N, 5.66. Found: C, 63.11; H, 4.12; Cl, 14.13; N, 5.66.

*3-Fluoro-4-nitro-1'-phenylbenzyl chloride (**3a**)*. 100 mg (75%) yield; pale yellow oil; IR (DCM) ν_{max} 3063, 3033, 2928, 2866, 1613, 1529, 1454, 1428, 1350, 844, 733, 700 cm^{-1}; ^1H NMR δ 6.10 (1H, s), 7.37 (7H, m), 8.03 (1H, t, ^3J = 8.1 Hz); ^{13}C NMR δ 62.0, 117.8 (d, $^2J_{CF}$ = 22.5 Hz), 123.7 (d, $^3J_{CF}$ = 4.1 Hz), 126.3 (d, $^4J_{CF}$ = 2.4 Hz), 127.6, 129.0, 129.1, 136.6 (m), 139.1, 149.6 (d, $^2J_{CF}$ = 7.6 Hz), 155.4 (d, $^1J_{CF}$ = 265.8 Hz); ^{19}F NMR δ -116.01 (dd, $^3J_{FH}$ = 11.5 Hz, $^4J_{HF}$ = 7.5 Hz); MS (EI 70 eV, *m/z*, %) 265 (M^+, 7), 230 (100), 183 (66), 171 (18); HR MS (EI+) calcd for $C_{13}H_9FClNO_2$ $[M]^+$ 265.0306, found 265.0311. Elemental analysis calcd for $C_{13}H_9FClNO_2$: C, 58.77; H, 3.41; F, 7.15; Cl, 13.34; N, 5.27. Found: C, 58.70; H, 3.44; F, 7.08; Cl, 13.30; N, 5.23.

*3-Chloro-4-nitro-1'-phenylbenzyl chloride (**4a**)*. 105 mg (74%) yield; pale yellow oil; IR (DCM) ν_{max} 3064, 3033, 2926, 2856, 1582, 1529, 1352, 1050, 840, 707 cm^{-1}; ^1H NMR δ 6.09 (1H, s), 7.38 (5H, m), 7.45 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 2.0 Hz), 7.62 (1H, d, $^4J_{HH}$ = 1.9 Hz), 7.85 (1H, d, $^3J_{HH}$ = 8.5 Hz);

^{13}C NMR δ 62.0, 125.8, 126.9, 127.4, 127.7, 129.0, 129.1, 131.1, 139.2, 146.9, 147.1; HR MS (ES+) calcd for $C_{13}H_{10}Cl_2NO_2$ $[M + H]^+$ 282.0089, found 282.0092. Elemental analysis calcd for $C_{13}H_9Cl_2NO_2$: C, 55.34; H, 3.22; N, 4.96; Cl, 25.13. Found: C, 55.44; H, 3.34; N, 4.94; Cl, 24.39.

*3-Bromo-4-nitro-1'-phenylbenzyl chloride (**5a**)*. Chromatography with hexanes–DCM 2:1 as eluent; 132 mg (81%) yield; pale yellow oil; IR (DCM) ν_{max} 3092, 3063, 3031, 2925, 2866, 1808, 1589, 1530, 1351, 1216, 1039, 838, 703 cm^{-1}; ^{1}H NMR δ 6.09 (1H, s), 7.38 (5H, m), 7.49 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.5 Hz), 7.81 (2H, m); ^{13}C NMR δ 61.9, 114.8, 125.8, 127.6, 127.7, 128.9, 129.1, 134.2, 139.2, 146.8, 149.0; MS (EI 70 eV, *m/z*, %) 325 (M^+, 11), 290 (91), 181 (24), 165 (100), 153 (37), 115 (29); HR MS (EI+) calcd for $C_{13}H_9ClBrNO_2$ $[M]^+$ 324.9505, found 324.9512. Elemental analysis calcd for $C_{13}H_9ClBrNO_2$: C, 47.81; H, 2.78; N, 4.29. Found: C, 48.04; H, 2.86; N, 4.33.

*3-Bromo-2-nitro-1'-phenylbenzyl chloride (**5a'**)*. Chromatography with hexanes–DCM 2:1 as eluent; 18 mg (11%) yield; pale yellow oil; ^{1}H NMR δ 6.13 (1H, s), 7.37 (6H, m), 7.63 (2H, m); ^{13}C NMR δ 57.4, 113.2, 127.4, 128.8, 128.8, 129.0, 131.4, 133.5, 135.0, 138.4, 149.8; HR MS (ES–) calcd for $C_{13}H_8ClBrNO_2$ $[M-H]^-$ 323.9427, found 323.9424.

*3-Methoxy-4-nitro-1'-phenylbenzyl chloride (**6a**)*. 119 mg (86%) yield; pale yellow oil; IR (DCM) ν_{max} 3062, 3031, 2945, 2847, 1609, 1520, 1455, 1416, 1353, 1285, 1168, 1094, 1027, 845, 728. cm^{-1}; ^{1}H NMR δ 3.93 (3H, s), 6.11 (1H, s), 7.03 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.7, Hz), 7.19 (1H, d, $^4J_{HH}$ = 1.6 Hz), 7.37 (5H, m), 7.80 (1H, d, $^3J_{HH}$ = 8.4 Hz); ^{13}C NMR δ 56.6, 63.0, 113.0, 119.6, 125.9, 127.7, 128.7, 128.9, 138.9, 139.7, 147.6, 153.0; HR MS (ES+) $C_{14}H_{12}ClNO_3Na$ $[M + Na]^+$ calcd. 300.0403, found 300.0395.

*3-Cyano-4-nitro-1'-phenylbenzyl chloride (**7a**)*. 42 mg (31%) yield; pale yellow oil; IR (DCM) ν_{max} 3111, 3064, 2928, 2868, 2236, 1587, 1534, 1454, 1346, 1219, 844, 721 cm^{-1}; ^{1}H NMR δ 6.16 (1H, s), 7.38 (5H, m), 7.85 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.0 Hz), 7.94 (1H, d, $^4J_{HH}$ = 2.0 Hz), 8.30 (1H, d, $^3J_{HH}$ = 8.7 Hz); ^{13}C NMR δ 61.5, 108.4, 114.7, 125.9, 127.6, 129.3, 132.8, 134.7, 138.5, 147.6, 148.4; HR MS (ES+) calcd for $C_{14}H_9ClN_2O_2Na$ $[M + Na]^+$ 295.0250, found 295.0244.

*2-Fluoro-4-nitro-1'-phenylbenzyl chloride (**8a**)*. 56 mg (42%) yield; pale yellow oil; IR (DCM) ν_{max} 3087, 3033, 2962, 2871, 1532, 1490, 1453, 1424, 1354, 1236, 1072, 943, 884, 809, 741, 697 cm^{-1}; ^1H NMR δ 6.42 (1H, s), 7.29-7.45 (5H, m), 7.80 (dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HF}$ = 7.5 Hz), 7.92 (dd, $^3J_{HF}$ = 9.7 Hz, $^4J_{HH}$ = 2.2 Hz), 8.06 (dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 1.8 Hz); ^{13}C NMR δ 55.9 (d, $^3J_{CF}$ = 3.7 Hz), 111.5 (d, $^2J_{CF}$ = 27.1 Hz), 119.6 (d, J_{CF} = 3.7 Hz), 127.4, 128.8, 128.9, 130.2 (d, J_{CF} = 2.9 Hz), 135.7 (d, $^2J_{CF}$ = 13.2 Hz), 138.5, 148.4 (d, $^3J_{CF}$ = 8.8 Hz), 158.7 (d, $^1J_{CF}$ = 252.8 Hz); ^{19}F NMR δ -112.12 (dd, $^3J_{FH}$ = 9.2 Hz, $^4J_{FH}$ = 7.8 Hz); MS (EI 70 eV, *m/z*, %) 265 (M^+, 7), 230 (100), 183 (57), 171 (15); HR MS (EI+) calcd for $C_{13}H_9FClNO_2$ $[M]^+$ 265.0306, found 265.0305. Elemental analysis calcd for $C_{13}H_9FClNO_2$: C, 58.77; H, 3.41; F, 7.15; Cl, 13.34; N, 5.27. Found: C, 58.85; H, 3.46; F, 7.11; Cl, 13.35; N, 5.15.

*4-Fluoro-2-nitro-1'-phenylbenzyl chloride (**8a'**)*. 24 mg (18%) yield; pale yellow oil; IR (DCM) ν_{max} 3093, 3061, 1953, 1880, 1809, 1750, 1681, 1536, 1465, 1358, 1256, 952, 838, 806, 738, 698 cm^{-1}; ^1H NMR δ 6.70 (1H, s), 7.28-7.39 (4H, m), 7.46-7.53 (3H, m), 7.67 (1H, dm, J = 8.2 Hz); ^{13}C NMR δ 53.4 (d, J_{CF} = 2.9 Hz), 120.1 (d, J_{CF} = 3.7 Hz), 121.3 (d, $^2J_{CF}$ = 22.7 Hz), 124.1 (d, $^2J_{CF}$ = 14.7 Hz), 126.8 (d, J_{CF} = 2.2 Hz), 128.1, 128.4, 130.4 (d, J_{CF} = 9.5 Hz), 137.5, 149.6 (d, $^3J_{CF}$ = 4.4 Hz), 161.3 (d, $^1J_{CF}$ = 258.2 Hz); ^{19}F NMR δ -103.53 (m); MS (EI 70 eV, *m/z*, %) 230 (45), 213 (82), 183 (100), 199 (47), 105 (45), 77 (43).

*2-Chloro-4-nitro-1'-phenylbenzyl chloride (**9a**)*. 32 mg (23%) yield; pale yellow oil; IR (DCM) ν_{max} 3101, 3033, 2928, 2857, 1588, 1525, 1352, 1117, 894, 736, 696 cm^{-1}; ^1H NMR δ 6.56 (1H, s), 7.38 (5H, m), 7.88 (1H, d, $^3J_{HH}$ = 8.7 Hz), 8.16 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.3 Hz), 8.26 (1H, d, $^4J_{HH}$ = 2.3 Hz); ^{13}C NMR δ 59.1, 122.1, 124.9, 127.7, 128.8, 128.9, 130.7, 133.6, 138.3, 145.3, 147.7; MS (EI 70 eV, *m/z*, %) 281 (M^+, 7), 246 (100), 199 (23), 165 (63); HR MS (EI+) calcd for $C_{13}H_9Cl_2NO_2$ $[M]^+$ 281.0010, found 280.9998.

*2-Iodo-4-nitro-1'-phenylbenzyl chloride (**10a**)*. Chromatography with hexanes–Et_2O 20:1 as eluent; 52 mg (28%) yield; pale yellow oil; IR (DCM) ν_{max} 3092, 3029, 2925, 2856, 1523, 1347, 1114, 1031, 815,

729, 696 cm^{-1}; ^1H NMR δ 6.44 (1H, s), 7.38 (5H, m), 7.79 (1H, d, $^3J_{HH}$ = 8.7 Hz), 8.23 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.3 Hz), 8.69 (1H, d, $^3J_{HH}$ = 2.3 Hz); ^{13}C NMR δ 66.1, 98.2, 123.5, 128.0, 128.8, 128.9, 130.2, 134.5, 138.4, 147.3, 149.9; MS (EI 70 eV, *m/z*, %) 373 (M^+, 31), 338 (100), 210 (35), 165 (93), 152 (19); HR MS (EI+) calcd for $C_{13}H_9ClINO_2$ $[M]^+$ 372.9367, found 372.9362. Elemental analysis calcd for $C_{13}H_9ClINO_2$: C, 41.80; H, 2.43; N, 3.75. Found: C, 42.01; H, 2.52; N, 3.79.

*2-Methoxy-4-nitro-1'-phenylbenzyl chloride (**11a**)*. Chromatography with toluene as eluent; 69 mg (50%) yield; pale yellow oil; IR (DCM) ν_{max} 3090, 3030, 2942, 2845, 1524, 1412, 1351, 1253, 1092, 1029, 802, 740 cm^{-1}; ^1H NMR δ 3.93 (3H, s), 6.54 (1H, s), 7.26-7.37 (3H, m), 7.40 (2H, m), 7.73 (2H, m), 7.86 (1H, dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.2 Hz); ^{13}C NMR δ 56.3, 57.0, 105.8, 115.9, 127.6, 128.3, 128.6, 129.5, 136.6, 139.7, 146.5, 148.5, 156.2; MS (EI 70 eV, *m/z*, %) 277 (M^+, 7), 242 (86), 165 (27), 152 (38), 91 (100); HR MS (EI+) calcd for $C_{14}H_{12}ClNO_3$ $[M]^+$ 277.0506, found 277.0513. Elemental analysis calcd for $C_{14}H_{12}ClNO_3$: C, 60.55; H, 4.36; Cl, 12.77; N, 5.04. Found: C, 60.84; H, 4.48; Cl, 12.69; N, 4.97.

*2-Cyano-4-nitro-1'-phenylbenzyl chloride (**12a**)*. 35 mg (26%) yield; pale yellow oil; IR (DCM) ν_{max} 3085, 2930, 2233, 1764, 1616, 1532, 1454, 1355, 790, 740, 696 cm^{-1}; ^1H NMR δ 6.52 (1H, s), 7.39 (5H, m), 8.01 (1H, d, $^3J_{HH}$ = 8.7 Hz), 8.45 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.3 Hz), 8.49 (1H, d, $^4J_{HH}$ = 2.4 Hz); ^{13}C NMR δ 59.8, 112.8, 115.0, 127.6, 127.9, 128.0, 129.2, 129.3, 130.3, 137.7, 147.2, 150.7; MS (EI 70 eV, *m/z*, %) 272 (M^+, 17), 237 (100), 190 (68), 178 (18), 163 (19); HR MS (EI+) calcd for $C_{14}H_9ClN_2O_2$ $[M]^+$ 272.0353, found 272.0350.

*4-(1'-Chlorobenzyl)-3-nitropyridine (**13a**)*. 27 mg (22%) yield; pale yellow oil; IR (DCM) ν_{max} 3460, 3065, 2928, 2866, 1956, 1886, 1699, 1601, 1578, 1525, 1452, 1353, 1185, 1115, 1017, 840, 758, 722, 697, 601 cm^{-1}; ^1H NMR δ 6.22 (1H, s), 7.35 (3H, m), 7.46 (2H, m), 7.80 (1H, d, $^3J_{HH}$ = 8.7 Hz), 8.49 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.6 Hz), 9.36 (1H, d, $^4J_{HH}$ = 2.6 Hz); ^{13}C NMR δ 63.5, 122.3, 127.7, 128.9, 128.9, 132.3, 138.5, 143.3, 144.6, 165.7; MS (EI 70 eV, *m/z*, %) 248 (M^+, 8), 213 (100), 167 (81), 139 (23), 105 (43), 77 (24); HR MS (EI+) calcd for $C_{12}H_9ClN_2O_2$ $[M]^+$ 248.0353, found 248.0348.

*2-(1'-Chlorobenzyl)-5-nitropyridine (**13a'**)*. 27 mg (22%) yield; pale yellow oil; IR (DCM) ν_{max} 3457, 3063, 3033, 2868, 1599, 1529, 1453, 1405, 1351, 1210, 1053, 872, 822, 757, 697, 635, 589 cm^{-1}; ^1H NMR δ 6.95 (1H, s), 7.34 (5H, m), 7.90 (1H, $^3J_{HH}$ = 5.2 Hz), 8.87 (1H, $^3J_{HH}$ = 5.2 Hz), 9.16 (1H, s); ^{13}C NMR δ 57.3, 124.2, 127.9, 129.0, 129.1, 137.9, 143.6, 144.1, 146.0, 154.0; MS (EI 70 eV, *m/z*, %) 213 (60), 196 (100), 168 (87), 139 (87), 105 (97), 77 (87). Elemental analysis calcd for $C_{12}H_9ClN_2O_2$: C, 57.96; H, 3.65; Cl, 14.26; N, 11.27. Found: C, 57.99; H, 3.47; Cl, 14.32; N, 11.12.

*6-(1'-Chlorobenzyl)-2-chloro-3-nitropyridine (**14a**) and 4-(1'-chlorobenzyl)-2-chloro-3-nitropyridine (**14a'**)*. 108 mg (76%) yield; pale yellow oil; IR (DCM) ν_{max} 3067, 3033, 2887, 1955, 1581, 1452, 1356, 1203, 1058, 852, 698, 604 cm^{-1}; **14a:** ^1H NMR δ 6.13 (1H, s), 7.36 (3H, m), 7.46 (2H, m), 7.70 (1H, d, $^3J_{HH}$ = 8.3 Hz) 8.22 (1H, d, $^3J_{HH}$ = 8.3 Hz). ^{13}C NMR δ 62.8, 121.3, 127.6, 129.0, 129.5, 135.4, 137.9, 142.7, 143.6, 163.7; **14a':** ^1H NMR δ 6.13 (1H, s), 7.36 (5H, m), 7.65 (1H, d, $^3J_{HH}$ = 5.2 Hz), 8.53 (1H, d, $^3J_{HH}$ = 5.2 Hz); ^{13}C NMR δ 56.3, 122.8, 127.5, 129.0, 129.2, 136.7, 142.4, 144.0, 144.3, 150.8; MS (EI 70 eV, *m/z*, %) 282 (M^+, 11), 247 (100), 201 (68), 166 (42), 139 (27); HR MS (EI+) calcd for $C_{12}H_8N_2O_2Cl_2$ $[M]^+$ 281.9963, found 281.9966.

*2-(1'-Chlorobenzyl)-4-methoxy-5-nitropyridine (**15a**)*. Chromatography with hexanes–AcOEt 2:1 as eluent; 103 mg (74%) yield; pale yellow oil; IR (DCM) ν_{max} 3063, 3031, 2949, 2863, 1601, 1522, 1355, 1289, 1019, 846, 740, 699 cm^{-1}; ^1H NMR δ 4.04 (3H, s), 6.13 (1H, s), 7.35 (4H, m), 7.44 (2H, m), 8.92 (1H, s); ^{13}C NMR δ 56.8, 63.8, 106.7, 127.7, 128.8, 128.9, 135.5, 138.7, 146.6, 159.8, 165.7; MS (EI 70 eV, *m/z*, %) 278 (M^+, 7), 243 (100), 196 (54), 167 (52), 139 (22); HR MS (EI+) calcd for $C_{13}H_{11}ClN_2O_3$ $[M]^+$ 278.0458, found 278.0450.

*5-(1'-Chlorobenzyl)-3-methoxy-2-nitropyridine (**16a**)*. 79 mg (57%) yield; pale yellow oil; IR (DCM) ν_{max} 3066, 2947, 1984, 1665, 1540, 1409, 1300, 1112, 1029, 965, 846, 723 cm^{-1}; ^1H NMR δ 3.93 (3H, s), 6.16 (1H, s), 7.38 (5H, m), 7.58 (1H, d, $^4J_{HH}$ = 1.7 Hz), 8.03 (1H, d, $^4J_{HH}$ = 1.8 Hz); ^{13}C NMR δ 56.7, 60.2, 121.9, 127.6, 129.1, 129.1, 138.0, 138.8, 142.9, 147.7, 147.9; MS (EI 70 eV, *m/z*, %) 278 (M^+, 27),

243 (100), 202 (58), 167 (54), 127 (49), 77 (43); HR MS (EI+) calcd for $C_{13}H_{11}ClN_2O_3$ $[M]^+$ 278.0458, found 278.0456.

*Methyl 5-(1'-chlorobenzyl)-1-methyl-4-nitro-1H-pyrrole-2-carboxylate (**17a**)*. 83 mg (54%) yield; yellow oil; IR (DCM) ν_{max} 3147, 2994, 2954, 1725, 1515, 1373, 1324, 1246, 1139, 1086, 870, 751 cm^{-1}; ^1H NMR δ 3.71 (3H, s), 3.85 (3H, s), 7.36 (5H, m), 7.55 (1H, s), 7.69 (1H, d, J_{HH} = 0.6 Hz); ^{13}C NMR δ 35.5, 51.5, 52.0, 113.4, 123.2, 126.4, 128.4, 128.9, 133.6, 135.0, 135.9, 160.3; MS (EI 70 eV, *m/z*, %) 308 (M^+, 24), 273 (87), 227 (52), 168 (100), 105 (71), 77 (56); HR MS (EI+) calcd for $C_{14}H_{13}ClN_2O_4$ $[M]^+$ 308.0564, found 308.0568.

*4-(1'-Chlorobenzyl)-3,6-dichloro-1,2-diazine (**18a**)*. 90 mg (66%) yield; pale yellow oil; IR (DCM) ν_{max} 3063, 2959, 2853, 1564, 1453, 1354, 1315, 1137, 1098, 735, 696, 542 cm^{-1}; ^1H NMR δ 6.25 (1H, s), 7.33 (2H, m), 7.39 (3H, m), 7.87 (1H, s); ^{13}C NMR δ 58.1, 128.0, 128.8, 129.3, 129.6, 136.2, 142.2, 154.2, 156.7; HR MS (ES+) calcd for $C_{11}H_8N_2Cl_3$ $[M + H]^+$ 272.9753, found 272.9745. Elemental analysis calcd for $C_{11}H_7Cl_3N_2$: C, 48.30; H, 2.58; Cl, 38.88; N, 10.24. Found: C, 48.49; H, 2.68; Cl, 38.95; N, 10.10.

*2-Chloro-3-(1'-chlorobenzyl)quinoxaline (**19a**)*. (61%) yield; pale yellow oil*;* IR (DCM) ν_{max} 3064, 3032, 1561, 1483, 1453, 1256, 1181, 1121, 1041, 828, 764, 724, 695, 595 cm^{-1}; ^1H NMR δ 6.73 (1H, s), 7.30-7.41 (3H, m), 7.63 (2H, m), 7.78 (2H, m), 8.00 (1H, m), 8.18 (1H, m); ^{13}C NMR δ 59.6, 128.1, 128.6, 128.6, 128.8, 129.4, 130.6, 131.5, 137.5, 140.7, 141.5, 145.4, 151.4; MS (EI 70 eV, *m/z*, %) 288 (M^+, 10), 253 (100), 218 (26), 190 (14), 125 (20), 116 (17), 102 (14), 89 (23); HR MS (EI+) calcd for $C_{15}H_{10}Cl_2N_2$ $[M]^+$ 288.0221, found 288.0220.

*3-Bromo-4-nitrophenyl-(4-chlorophenyl)chloromethane (**5b**)*. 144 mg (80%) yield; pale yellow oil that solidified on standing, mp 43–45 °C; IR (DCM) ν_{max} 3094, 3031, 1906, 1588, 1530, 1491, 1351, 1092, 1014, 810, 742 cm^{-1}; ^1H NMR δ 6.05 (1H, s), 7.30 (2H, d, $^3J_{HH}$ = 8.7 Hz), 7.36 (2H, d, $^3J_{HH}$ = 8.5 Hz), 7.47 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.9 Hz), 7.77 (1H, d, $^4J_{HH}$ = 1.9 Hz), 7.82 (1H, d, $^3J_{HH}$ = 8.5 Hz); ^{13}C NMR δ 61.1, 114.9, 125.9, 127.5, 129.0, 129.3, 134.2, 135.0, 137.7, 146.2, 149.1; MS (EI 70 eV,

m/z, %) 359 (M^+, 7), 326 (100), 280 (22), 243 (7), 199 (43), 163 (37), 152 (26), 139 (44); HR MS (EI+) calcd for $C_{13}H_8Cl_2BrNO_2$ $[M]^+$ 358.9115, found 358.9116. Elemental analysis calcd for $C_{13}H_8Cl_2BrNO_2$: C, 43.25; H, 2.23; N, 3.88. Found: C, 43.21; H, 2.29; N, 3.88.

*4-Chlorophenyl-(3-methoxy-4-nitrophenyl)chloromethane (**6b**)*. 115 mg (74%) yield; pale yellow oil; IR (DCM) ν_{max} 2926, 2852, 1609, 1522, 1492, 1408, 1352, 1281, 1168, 1092, 1027, 846, 820, 752 cm^{-1}; ^1H NMR δ 3.95 (3H, s), 6.07 (1H, s), 7.01 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.4 Hz), 7.16 (d, $^4J_{HH}$ = 1.3 Hz), 7.31 (d, $^3J_{HH}$ = 8.6 Hz), 7.35 (d, $^3J_{HH}$ = 8.6 Hz), 7.81 (d, $^3J_{HH}$ = 8.4 Hz); ^{13}C NMR δ 56.6, 62.1, 112.9, 119.5, 126.0, 129.1, 129.1, 134.7, 138.3, 139.1, 146.9, 153.1; HR MS (ES-) calcd for $C_{14}H_{10}NO_3Cl_2$ $[M - H]^-$ 310.0038, found 310.0042.

*4'-Chloro-3-methoxy-4-nitrobenzophenone (**6f**)*. 20 mg (13%) yield; light yellow crystals; IR (DCM) ν_{max} 3087, 2925, 2855, 1665, 1586, 1524, 1487, 1406, 1353, 1287, 1243, 1091, 1028, 983, 856, 747 cm^{-1}; ^1H NMR δ 3.15 (3H, s), 7.32 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.5 Hz), 7.50 (3H, m), 7.76 (2H, dm, $^3J_{HH}$ = 8.5 Hz), 7.87 (1H, d, $^3J_{HH}$ = 8.2 Hz); ^{13}C NMR δ 56.8, 114.4, 121.6, 125.2, 129.0, 131.4, 134.7, 140.0, 141.9, 152.8, 193.5; MS (EI 70 eV, *m/z*, %) 291 (M^+, 19), 244 (11), 180 (26), 139 (100), 119 (26), 111 (41), 75 (25); HR MS (EI+) calcd for $C_{14}H_{10}ClNO_4$ $[M]^+$ 291.0298, found 291.0303. Elemental analysis calcd for $C_{14}H_{10}ClNO_4$: C 57.65; H, 3.46; N, 4.80; Cl, 12.15. Found: C, 57.50; H, 3.70; N, 4.86; Cl, 12.07.

*4-Chlorophenyl-(2-fluoro-4-nitrophenyl)chloromethane (**8b**)*. 56 mg (37%) yield; pale yellow oil; IR (DCM) ν_{max} 3111, 3087, 2926, 1531, 1490, 1353, 1236, 1093, 1015, 811, 741 cm^{-1}; ^1H NMR δ 6.37 (1H, s), 7.34 (4H, s), 7.78 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HF}$ = 7.5 Hz), 7.93 (1H, dd, $^3J_{HF}$ = 9.6 Hz, $^4J_{HH}$ = 2.2 Hz), 8.08 (1H, dd, $^3J_{HH}$ = 8.6 Hz, $^4J_{HH}$ = 1.3 Hz); ^{13}C NMR δ 55.2, 111.6 (d, $^2J_{CF}$ = 27.0 Hz), 119.7 (d, $^4J_{CF}$ = 3.7 Hz), 128.8, 129.1, 130.1 (d, $^3J_{CF}$ = 3.0 Hz), 134.9, 135.2 (d, $^2J_{CF}$ = 13.1 Hz), 137.1, 148.5 (d, $^3J_{CF}$ = 8.2 Hz), 158.6 (d, $^1J_{CF}$ = 253.3 Hz); ^{19}F NMR δ -111.95 (dd, $^3J_{FH}$ = 9.6 Hz, $^4J_{FH}$ = 7.5 Hz); MS (EI 70 eV, *m/z*, %) 299 (M^+, 12), 264 (100), 218 (31), 183 (39); HR MS (EI+) calcd for $C_{13}H_8FCl_2NO_2$ $[M]^+$ 298.9916, found 298.9922.

*4-Chloro-2'-fluoro-4'-nitrobenzophenone (**8f**)*. 22 mg (16%) yield; yellow crystals (heptane–DCM), mp 99–101 °C; IR (DCM) ν_{max} 3107, 2925, 2853, 1673, 1586, 1531, 1417, 1353, 1282, 1227, 1092, 952, 912, 849, 810, 740, 613 cm^{-1}; ^1H NMR δ 7.49 (2H, dm, $^3J_{HH}$ = 8.6 Hz), 7.71 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HF}$ = 6.6 Hz), 7.76 (2H, m), 8.06 (1H, dd, $^3J_{HF}$ = 9.0 Hz, $^4J_{HH}$ = 2.0 Hz), 8.17 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 2.0 Hz); ^{13}C NMR δ 112.4 (d, $^2J_{CF}$ = 27.1 Hz), 119.6 (d, $^3J_{CF}$ = 3.7 Hz), 129.3, 131.1, 131.3 (d, $^4J_{CF}$ = 3.3 Hz), 132.4 (d, $^2J_{CF}$ = 16.6 Hz), 134.5, 141.1, 150.2 (d, $^3J_{CF}$ = 8.5 Hz), 159.3 (d, $^1J_{CF}$ = 256.5 Hz), 190.1; ^{19}F NMR δ -107.01 (m); MS (EI 70 eV, *m/z*, %) 279 (M^+, 53), 168 (30), 139 (100), 122 (25), 111 (46); HR MS (EI+) calcd for $C_{13}H_7NO_3FCl$ $[M]^+$ 279.0098, found 279.0092.

*4-Chlorophenyl-(4-methoxy-5-nitropyrid-2-yl)chloromethane (**15b**)*. Chromatography with hexanes–AcOEt 2:1 as eluent; 136 mg (87%) yield; pale yellow oil; IR (DCM) ν_{max} 3104, 2949, 2863, 1602, 1523, 1491, 1354, 1288, 1092, 1017, 846, 791, 758 cm^{-1}; ^1H NMR δ 4.05 (3H, s), 6.09 (1H, s), 7.33 (3H, m), 7.38 (2H, d, $^3J_{HH}$ = 8.5 Hz), 8.91 (1H, s); ^{13}C NMR δ 56.9, 62.9, 106.7, 129.1, 129.1, 134.8, 135.6, 137.3, 146.6, 159.8, 165.1; HR MS (ES-) $C_{13}H_9Cl_2N_2O_3$ $[M - H]^-$ 310.9990, found 310.9991.

*4-Chlorophenyl-(3,6-dichloro-1,2-pyridazin-4-yl)chloromethane (**18b**)*. 115 mg (75%) yield; pale yellow oil; IR (DCM) ν_{max} 3065, 2961, 1565, 1491, 1350, 1316, 1138, 1092, 1015, 829, 767, 543 cm^{-1}; ^1H NMR δ 6.21 (1H, s), 7.27 (2H, dm, $^3J_{HH}$ = 8.6 Hz), 7.37 (2H, dm, $^3J_{HH}$ = 8.6 Hz), 7.87 (1H, d, J_{HH} = 0.6 Hz); ^{13}C NMR δ 57.4, 128.7, 129.3, 129.6, 134.8, 135.7, 141.7, 154.1, 156.7; MS (EI 70 eV, *m/z*, %) 306 (M^+, 33), 271 (100), 207 (27), 200 (17), 173 (29); HR MS (EI+) calcd for $C_{11}H_6Cl_4N_2$ $[M]^+$ 305.9285, found 305.9284. Elemental analysis calcd for $C_{11}H_6Cl_4N_2$: C, 42.90; H, 1.96; N, 9.10; Cl, 46.04. Found: C, 43.03; H, 1.75; N, 9.19; Cl, 46.16.

*3-Bromo-4-nitro-1'-phenylbenzyl bromide (**5d**)*. Chromatography with hexanes–DCM 5:1 as eluent; 137 mg (74%) yield; yellow oil; IR (DCM) ν_{max} 3089, 3063, 3030, 1955, 1909, 1804, 1588, 1529, 1351, 1196, 1158, 1039, 895, 838, 763, 700, 502 cm^{-1}; ^1H NMR δ 6.20 (1H, s), 7.29-7.45 (5H, m), 7.53 (1H,

dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.0 Hz), 7.81 (2H, m); ^{13}C NMR δ 51.9, 114.7, 125.8, 128.3, 128.3, 128.9, 129.1, 134.9, 139.1, 146.9, 148.9; MS (EI 70 eV, *m/z*, %) 290 (100), 165 (99), 153 (37), 115 (31).

*3-Methoxy-4-nitro-1'-phenylbenzyl bromide (**6d**)*. 97 mg (60%) yield; pale yellow oil; IR (DCM) ν_{max} 3062, 3028, 2976, 2944, 1608, 1522, 1415, 1353, 1166, 1027, 845, 699 cm^{-1}; ^{1}H NMR δ 3.93 (3H, s), 6.24 (1H, s), 7.28-7.40 (3H, m), 7.42 (2H, m), 7.07 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.8 Hz), 7.21 (1H, d, $^4J_{HH}$ = 1.8 Hz), 7.80 (1H, d, $^3J_{HH}$ = 8.4 Hz); ^{13}C NMR δ 53.4, 56.6, 113.9, 120.2, 125.9, 128.3, 128.7, 128.9, 138.9, 139.7, 147.6, 153.0; HR MS (ES+) calcd for $C_{14}H_{12}BrNO_3Na$ $[M + Na]^+$ 343.9898, found 343.9895. Elemental analysis calcd for $C_{14}H_{12}BrNO_3$: C, 52.20; H, 3.75; Br, 24.80; N, 4.35. Found: C, 52.24; H, 3.54; Br, 24.63; N, 4.60.

One-pot preparation of nitrobenzophenones. KHMDS solution in THF (1M, 1.25 mmol, 1.25 mL) was placed in a flame-dried Schlenk flask under Ar and cooled to -78 °C. A solution of nitroarene (0.75 mmol) and **1a** or **1b** (0.6 mmol) in DMF (1.25 mL) was added dropwise with vigorous magnetic stirring. After 15 min (or 5 min for preparation of **11e**) CuI (0.06 mmol, 11.4 mg) was added and oxygen (or, in the case of **5e**/**5e'**, air dried by passing through a layer of powdered KOH) was bubbled through the reaction mixture using a metal needle (0.8 mm in diameter) for 30 min (or 90 min for preparation of **5e**/**5e'** and **6e**). After that period, 2M $HCl_{(aq)}$ (1 mL) was added, followed by AcOEt (5 mL) and brine (5 mL). The phases were separated, the organic phase was washed with brine (3x10 mL), dried over anhydrous Na_2SO_4 and evaporated. The products were purified by column chromatography on silica gel using hexanes–AcOEt from 10:1 or hexanes–DCM–Et_2O 20:4:1.

*4-Nitrobenzophenone (**2e**)*. 86 mg (63%) yield; yellow crystals (heptane–DCM), mp 131–133 °C; IR (DCM) ν_{max} 3282, 3101, 3062, 1947, 1650, 1596, 1514, 1358, 1318, 872, 705, 692 cm^{-1}; ^{1}H NMR δ 7.52 (2H, t, $^3J_{HH}$ = 7.7 Hz), 7.64 (1H, t, $^3J_{HH}$ = 7.4 Hz), 7.8 (2H, d, $^3J_{HH}$ = 7.1 Hz), 7.92 (2H, d, $^3J_{HH}$ = 8.8 Hz), 8.33 (2H, d, $^3J_{HH}$ = 8.8 Hz); ^{13}C NMR δ 123.5, 128.7, 130.1, 130.7, 133.4, 136.3, 142.9, 149.8, 194.7; MS (EI 70 eV, *m/z*, %) 227 (M^+, 40), 150 (21), 105 (100), 77 (65); HR MS (EI+) calcd for

$C_{13}H_9NO_3$ $[M]^+$ 227.0582, found 227.0589. Elemental analysis calcd for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.16. Found: C, 68.94; H, 3.98; N, 6.12.

*2-Nitrobenzophenone (**2e'**)*. 20 mg (15%) yield; yellow oil that solidified on standing, mp 92–94 °C; IR (DCM) ν_{max} 3064, 2924, 2854, 1675, 1529, 1448, 1348, 1280, 931, 853, 711, 633 cm^{-1}; ^1H NMR δ 7.45 (2H, t, $^3J_{HH}$ = 7.7 Hz), 7.50 (1H, d, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.3 Hz), 7.59 (1H, tm, $^3J_{HH}$ = 7.4 Hz), 7.68 (1H, m), 7.72 - 7.82 (3H, m), 8.24 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 0.7 Hz); ^{13}C NMR δ 124.5, 128.8, 128.9, 129.2, 130.5, 133.8, 134.1, 136.0, 136.3, 193.4; MS (EI 70 eV, *m/z*, %) 227 (M^+, 14), 152 (27), 134 (69), 105 (100), 77 (66); HR MS (EI+) calcd for $C_{13}H_9NO_3$ $[M]^+$ 227.0582, found 227.0571. Elemental analysis calcd for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.16. Found: C, 68.84; H, 4.03; N, 6.09.

*3-Fluoro-4-nitrobenzophenone (**3e**)*. 81 mg (55%) yield; pale yellow crystals (heptane–DCM), mp 84–86 °C; IR (KBr) ν_{max} 3112, 3058, 2869, 1817, 1665, 1597, 1526, 1358, 1280, 909, 869, 725 cm^{-1}; ^1H NMR δ 7.54 (2H, t, $^3J_{HH}$ = 7.7 Hz), 7.68 (3H, m), 7.79 (2H, m), 8.15 (1H, dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HF}$ = 7.2 Hz); ^{13}C NMR δ 119.6 (d, $^2J_{CF}$ = 22.0 Hz), 125.5 (d, $^3J_{CF}$ = 4.4 Hz), 126.2 (d, $^4J_{CF}$ = 2.9 Hz), 128.8, 130.0, 133.7, 135.7, 144.0 (d, $^2J_{CF}$ = 6.6 Hz), 155.1 (d, $^1J_{CF}$ = 267.2 Hz), 193.2; ^{19}F NMR -116.10 (dd, $^3J_{FH}$ = 10.7 Hz, $^4J_{FH}$ = 7.4 Hz); MS (EI 70 eV, *m/z*, %) 245 (M^+, 46), 168 (12), 122 (20), 105 (100), 94 (18), 77 (53); HR MS (EI+) calcd for $C_{13}H_8FNO_3$ $[M]^+$ 245.0488, found 245.0477.

*3-Bromo-4-nitrobenzophenone (**5e**)*. 112 mg (61%) yield; pale yellow oil; IR (DCM) ν_{max} 3087, 3027, 2864, 1664, 1574, 1532, 1447, 1360, 1277, 1038, 957, 853, 716, 672 cm^{-1}; ^1H NMR δ 7.53 (2H, t, $^3J_{HH}$ = 7.7 Hz), 7.66 (1H, m), 7.78 (2H, m), 7.82 (1H, dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 1.7 Hz), 7.90 (1H, d, $^3J_{HH}$ = 8.3 Hz), 8.11 (1H, d, $^4J_{HH}$ = 1.6 Hz); ^{13}C NMR δ 114.5, 125.3, 128.8, 129.4, 130.0, 133.7, 135.9, 136.0, 141.7, 151.7, 193.2; MS (EI 70 eV, *m/z*, %) 305 (M^+, 27), 228 (8), 182 (5), 152 (8), 105 (100), 77 (51); HR MS (EI+) calcd for $C_{13}H_8BrNO_3$ $[M]^+$ 304.9688, found 304.9689; Elemental analysis calcd for $C_{13}H_8BrNO_3$: C, 51.01; H, 2.63; Br, 26.10; N, 4.58. Found: C, 51.24; H, 2.53; Br, 26.04; N, 4.55.

*3-Bromo-2-nitrobenzophenone (**5e'**)*. 22 mg (12%) yield; pale yellow oil; IR (DCM) ν_{max} 3068, 2921, 2852, 1668, 1539, 1448, 1361, 1276, 955, 716, 649 cm^{-1}; ^1H NMR δ 7.43-7.52 (4H, m), 7.64 (1H, m),

7.79 (2H, m), 7.86 (1H, dd, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.9 Hz); ^{13}C NMR δ 114.9, 128.7, 128.8, 130.1, 131.2, 134.2, 135.0, 135.2, 136.4, 149.8, 191.6; MS (EI 70 eV, *m/z*, %) 305 (M^+, 6), 212 (27), 152 (24), 105 (100), 77 (73); HR MS (EI+) calcd for $C_{13}H_8BrNO_3$ $[M]^+$ 304.9688, found 304.9691.

*3-Methoxy-4-nitrobenzophenone (**6e**)*. 122 mg (79%) yield; pale yellow crystals (heptane–DCM), mp 91–93 °C; IR (DCM) ν_{max} 3061, 2925, 2853, 1983, 1737, 1663, 1603, 1524, 1406, 1027, 856, 722 cm^{-1}; ^{1}H NMR δ 4.01 (3H, s), 7.35 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.5 Hz), 7.52 (3H, m), 7.65 (1H, tm, $^3J_{HH}$ = 7.5 Hz), 7.80 (2H, m), 7.87 (1H, d, $^3J_{HH}$ = 8.2 Hz); ^{13}C NMR δ 56.8, 114.5, 121.8, 125.1, 128.6, 130.1, 133.3, 136.4, 142.3, 152.7, 194.7; MS (EI 70 eV, *m/z*, %) 257 (M^+, 63), 227 (5), 210 (6), 180 (21), 119 (18), 105 (100), 77 (60); HR MS (EI+) calcd for $C_{14}H_{11}NO_4$ $[M]^+$ 257.0688, found 257.0680. Elemental analysis calcd for $C_{14}H_{11}NO_4$ C, 65.37; H, 4.31; N, 5.44. Found: C, 65.10; H, 4.24; N, 5.46.

*2-Fluoro-4-nitrobenzophenone (**8e**)*. 53 mg (36%) yield; pale yellow oil; IR (DCM) ν_{max} 3107, 2925, 2855, 1673, 1531, 1417, 1355, 1284, 1226, 952, 812, 733 cm^{-1}; ^{1}H NMR δ 7.51 (1H, t, $^3J_{HH}$ = 7.7 Hz), 7.66 (1H, t, $^3J_{HH}$ = 7.4 Hz), 7.71 (1H, dd, $^3J_{HH}$ = 8.3, $^4J_{HF}$ = 6.6 Hz), 7.82 (1H, d, $^3J_{HH}$ = 8.2 Hz), 8.05 (1H, dd, $^3J_{HF}$ = 9.0, $^4J_{HH}$ = 2.0 Hz), 8.16 (1H, dd, $^3J_{HH}$ = 8.4, $^4J_{HH}$ = 1.6 Hz); ^{13}C NMR δ 112.3 (d, $^2J_{CF}$ = 27.0 Hz), 119.5 (d, $^3J_{CF}$ = 4.0 Hz), 128.8, 129.8, 131.3 (d, $^4J_{CF}$ = 3.6 Hz), 132.9 (d, $^2J_{CF}$ = 16.4 Hz), 134.4, 136.1, 150.1 (d, $^3J_{CF}$ = 7.7 Hz), 159.4 (d, $^1J_{CF}$ = 256.3 Hz), 191.3; ^{19}F NMR δ -107.33 (m); MS (EI 70 eV, *m/z*, %) 245 (M^+, 52), 168 (21), 122 (22), 105 (100), 77 (55); HR MS (EI+) calcd for $C_{13}H_8FNO_3$ $[M]^+$ 245.0488, found 245.0483. Elemental analysis calcd for $C_{13}H_8FNO_3$: C, 63.68; H, 3.29; F, 7.75; N, 5.71. Found: C, 63.75; H, 3.44; F, 7.77; N, 5.51.

*2-Methoxy-4-nitrobenzophenone (**11e**)*. 46 mg (30%) yield; orange crystals (heptane–DCM), mp 131–133 °C; IR (KBr) ν_{max} 3105, 2980, 2944, 1924, 1680, 1593, 1516, 1248, 1016, 936, 801, 714 cm^{-1}; ^{1}H NMR δ 3.84 (3H, s), 7.47 (3H, m), 7.60 (1H, t, $^3J_{HH}$ = 7.4 Hz), 7.78 (2H, d, $^3J_{HH}$ = 7.4 Hz), 7.84 (1H, d, $^4J_{HH}$ = 1.9 Hz), 7.93 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 2.0 Hz); ^{13}C NMR δ 56.2, 106.5, 115.8, 128.6, 129.6, 129.7, 133.8, 134.9, 136.5, 150.0, 157.6, 194.4; MS (EI 70 eV, *m/z*, %) 257 (M^+, 59), 240 (19), 180 (62), 166 (23), 134 (32), 105 (100), 77 (83); HR MS (EI+) calcd for $C_{14}H_{11}NO_4$ $[M]^+$ 257.0688,

found 257.0680. Elemental analysis calcd for $C_{14}H_{11}NO_4$: C, 65.37; H, 4.31; N, 5.44. Found: C, 65.36; H, 4.27; N, 5.38.

*4-Chloro-4'-nitrobenzophenone (**2f**)*. 105 mg (67%) yield; light brown crystals (heptane–DCM), mp 98–100 °C; IR (KBr) ν_{max} 3097, 3060, 1668, 1583, 1519, 1400, 1347, 1270, 1087, 1012, 928, 849, 737, 701 cm^{-1}; ^1H NMR δ 7.48 (2H, dm, $^3J_{HH}$ = 8.6 Hz), 7.74 (2H, d, $^3J_{HH}$ = 8.6 Hz), 7.89 (2H, d, $^3J_{HH}$ = 8.8 Hz), 8.32 (2H, d, $^3J_{HH}$ = 8.8 Hz); ^{13}C NMR δ 123.6, 129.0, 130.6, 131.4, 134.6, 140.1, 142.5, 149.9, 193.5; MS (EI 70 eV, *m/z*, %) 261 (M^+, 53), 226 (5), 180 (8), 150 (30), 139 (100), 111 (40); HR MS (EI+) calcd for $C_{13}H_8NO_3Cl$ $[M]^+$ 261.0193, found 261.0185. Elemental analysis calcd for $C_{13}H_8ClNO_3$: C, 59.67; H, 3.08; N, 5.35; Cl, 13.55. Found: C, 59.64; H, 3.15; N, 5.64; Cl, 13.59.

*4-Chloro-2'-nitrobenzophenone (**2f'**)*. 11 mg (7%) yield; yellow crystalline powder; IR (DCM) ν_{max} 3088, 2923, 2856, 1675, 1586, 1527, 1347, 1286, 1092, 930, 845, 745, 704 cm^{-1}; ^1H NMR δ 7.43 (1H, dm, $^3J_{HH}$ = 8.6 Hz), 7.48 (1H, dd, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.4 Hz), 7.70 (3H, m), 7.81 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.2 Hz), 8.25 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.1 Hz); ^{13}C NMR δ 124.6, 128.8, 129.2, 130.5, 130.7, 134.3, 134.4, 135.8, 140.4, 145.0, 192.2; MS (EI 70 eV, *m/z*, %) 261 (M^+, 11), 152 (33), 139 (94), 134 (100), 111 (56), 104 (37), 75 (39); HR MS (EI+) calcd for $C_{13}H_8ClNO_3$ $[M]^+$ 261.0193, found 261.0198.

Preparation of nitrobenzophenones using sodium azide. α-Chlorobenzylated arene (0.25 mmol) was dissolved in DMF (1 mL) and sodium azide (0.5 mmol, 33 mg) was added in one portion. The reaction mixture was stirred vigorously in open flask at rt. After substrate consumption (TLC control), which required 30 min (**13e**, **15e**, **18e**, **18f**), 3h (**5e**, **5f**) or 24h (**6e**), 2M $HCl_{(aq)}$ (1 mL) was added and stirring continued for another 30 min. **Warning: At large reaction scale, potentially dangerous amounts of toxic HN_3 might be liberated at this point.** The mixture was then separated between AcOEt (5 mL) and brine (5 mL) and neutralized with saturated $NaHCO_3$(aq). The organic phase was washed with brine (3 x 5 mL), dried over Na_2SO_4 and concentrated. The products were purified by column chromatography on silica gel using hexanes–DCM–Et_2O 20:4:1 as eluent.

*3-Bromo-4'-chloro-4-nitrobenzophenone (**5f**)*. 74 mg (87%) yield; light yellow crystals (heptane–DCM), mp 129–131 °C; IR (KBr) ν_{max} 3097, 3064, 3027, 2956, 1669, 1581, 1522, 1362, 1266, 1091, 958, 901, 851, 741 cm^{-1}; ^1H NMR δ 7.52 (2H, dm, $^3J_{HH}$ = 8.8 Hz), 7.74 (2H, dm, $^3J_{HH}$ = 8.7 Hz), 7.80 (1H, dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 1.7 Hz), 7.91 (1H, d, $^3J_{HH}$ = 8.3 Hz), 8.09 (1H, d, $^4J_{HH}$ = 1.7 Hz); ^{13}C NMR δ 114.7, 125.4, 129.2, 129.2, 131.4, 134.1, 135.9, 140.4, 141.2, 151.8, 192.0; MS (EI 70 eV, *m/z*, %) 339 (M^+, 24), 304 (2), 258 (2), 228 (8), 198 (3), 139 (100), 111 (44), 75 (45); HR MS (EI+) calcd for $C_{13}H_7ClBrNO_3$ $[M]^+$ 338.9298, found 338.9297; Elemental analysis calcd for $C_{13}H_7ClBrNO_3$ C, 45.85; H, 2.07; N, 4.11. Found: C, 45.62; H, 2.08; N, 4.18.

*2-Benzoyl-5-nitropyridine (**13e**)*. 56 mg (98%) yield; light yellow crystals (heptane–DCM), mp 83–85 °C; IR (KBr) ν_{max} 3062, 2862, 1983, 1876, 1827, 1674, 1597, 1518, 1446, 1358, 1318, 1273, 1246, 1166, 1016, 932, 854, 724, 697 cm^{-1}; ^1H NMR δ 7.50 (2H, t, $^3J_{HH}$ = 7.7 Hz), 7.64 (1H, t, $^3J_{HH}$ = 7.4 Hz), 8.06 (1H, d, $^3J_{HH}$ = 7.2 Hz), 8.19 (1H, d, $^3J_{HH}$ = 8.6 Hz), 8.65 (1H, dd, $^3J_{HH}$ = 8.6 Hz, $^4J_{HH}$ = 2.5 Hz), 9.49 (1H, d, $^4J_{HH}$ = 2.4 Hz); ^{13}C NMR δ 125.0, 128.4, 131.0, 132.3, 133.8, 135.1, 143.9, 145.0, 159.2, 191.6; HR MS (ES+) calcd for $C_{12}H_8N_2O_3Na$ $[M + Na]^+$ 251.0433, found 251.0423; Elemental analysis calcd for $C_{12}H_8N_2O_3$ C, 63.16; H, 3.53; N, 12.28. Found: C, 63.22; H, 3.34; N, 12.31.

*2-Benzoyl-4-methoxy-5-nitropyridine (**15e**)*. 52 mg (80%) yield; light yellow crystals (heptane–DCM), mp 144–146 °C; IR (KBr) ν_{max} 3093, 3022, 2949, 2864, 1924, 1661, 1594, 1520, 1484, 1393, 1361, 1284, 1148, 1017, 977, 859, 824, 742, 715, 694, 613 cm^{-1}; ^1H NMR δ 4.13 (3H, s), 7.50 (2H, m), 7.63 (1H, m), 7.77 (1H, s), 8.08 (2H, m), 9.03 (1H, s); ^{13}C NMR δ 57.2, 109.5, 128.4, 131.1, 133.7, 135.2, 137.5, 145.6, 159.4, 159.7, 191.7; MS (EI 70 eV, *m/z*, %) 258 (M^+, 35), 230 (24), 200 (30), 154 (13), 105 (100), 77 (90); HR MS (EI+) calcd for $C_{13}H_{10}N_2O_4$ $[M]^+$ 258.0641, found 258.0638; Elemental analysis calcd for $C_{13}H_{10}N_2O_4$ C, 60.47; H, 3.90; N, 10.85. Found: C, 60.41; H, 4.05; N, 10.68.

*4-Benzoyl-3,6-dichloro-1,2-diazine (**18e**)*. 62 mg (98%) yield; light yellow crystals (heptane-DCM), mp >180 °C (decomp.); IR (DCM) ν_{max} 3060, 2925, 2853, 1678, 1595, 1450, 1326, 1258, 1141, 968, 822, 800, 713, 560 cm^{-1}; ^1H NMR δ 7.50 (1H, s), 7.55 (2H, t, $^3J_{HH}$ = 7.8 Hz), 7.72 (1H, m), 7.77 (2H,

m); ^{13}C NMR δ 127.7, 129.3, 130.0, 134.0, 135.4, 140.0, 151.7, 156.2, 189.0; MS (EI 70 eV, *m/z*, %) 252 (M^+, 21), 105 (100), 77 (55); HR MS (EI+) calcd for $C_{11}H_6Cl_2N_2O$ $[M]^+$ 251.9857, found 251.9861. Elemental analysis calcd for $C_{11}H_6Cl_2N_2O$: C, 52.20; H, 2.39; N, 11.07; Cl, 28.02. Found: C, 52.25; H, 2.52; N, 10.92; Cl, 27.22.

*4-(4'-Chlorobenzoyl)-3,6-dichloro-1,2-diazine (**18f**)*. 45 mg (63%) yield; colorless crystals (heptane–DCM), mp 97–98 °C; IR (KBr) ν_{max} 3042, 1919, 1674, 1587, 1401, 1323, 1254, 1142, 1089, 965, 907, 842, 824, 750, 566 cm^{-1}; ^{1}H NMR δ 7.50 (1H, s), 7.52 (2H, m), 7.72 (2H, dm, $^3J_{HH}$ = 8.6 Hz); ^{13}C NMR δ 127.8, 129.8, 131.2, 132.4, 139.5, 142.4, 151.5, 156.3, 187.9; MS (EI 70 eV, *m/z*, %) 286 (M^+, 24), 139 (100), 111 (43), 75 (28); HR MS (EI+) calcd for $C_{11}H_5Cl_3N_2O$ 285.9467, found 285.9478; Elemental analysis calcd for $C_{11}H_5Cl_3N_2O$ C, 45.95; H, 1.75; Cl, 36.99; N, 9.74. Found: C, 46.00; H, 1.96; Cl, 37.05; N, 9.67.

Preparation of cyclopropane 6g. The general synthetic procedure for α-chlorobenzylation described above was followed, but instead of quenching the reaction with 2M $HCl_{(aq)}$, methyl acrylate (1.5 mmol, 129 mg, 135 μL) was added, the cooling bath was removed and the reaction mixture was stirred for another 1.5h. 2M $HCl_{(aq)}$ (1 mL) was added, followed by AcOEt (5 mL) and brine (5 mL). The phases were separated, the organic phase was washed with brine (3x10 mL), dried over anhydrous Na_2SO_4 and evaporated. Column chromatography on silica gel using hexanes–AcOEt 5:1 gave 94 mg (57%) of *cis*-**6g** and 32 mg (20%) of 1:0.4 *trans*:*cis* mixture. Cyclopropane *cis*-**6g**: bright yellow crystals (heptane–DCM), mp 91–92 °C; IR (DCM) ν_{max} 3024, 2950, 2850, 1733, 1606, 1519, 1439, 1348, 1242, 1173, 1092, 1023, 843, 757, 700 cm^{-1}; ^{1}H NMR δ 1.68 (1H, dd, $^3J_{HH}$ = 8.2 Hz, $^2J_{HH}$ = 5.0 Hz), 2.17 (1H, dd, $^3J_{HH}$ = 5.8 Hz, $^2J_{HH}$ = 5.1 Hz), 2.62 (1H, dd, $^3J_{HH}$ = 8.2 Hz, 5.9 Hz), 3.56 (3H, s), 3.92 (3H, s), 7.00 (1H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.7 Hz), 7.04 (1H, d, $^4J_{HH}$ = 1.6 Hz), 7.26 (5H, m), 7.80 (1H, d, $^3J_{HH}$ = 8.4 Hz); ^{13}C NMR δ 20.5, 28.9, 39.9, 52.1, 56.5, 114.7, 121.6, 126.0, 127.3, 127.6, 128.8, 138.2, 143.0, 147.8, 153.1, 170.7; HR MS (ES+) calcd for $C_{18}H_{17}NO_5Na$ $[M + Na]^+$ 350.1004, found 350.0998; Elemental analysis calcd for $C_{18}H_{17}NO_5$ C, 66.05; H, 5.23; N, 4.28. Found: C, 65.94; H, 5.22; N, 4.29.

trans-**6g**: ^{1}H NMR δ 1.63 (1H, dd, $^{3}J_{HH}$ = 8.3 Hz, $^{2}J_{HH}$ = 5.1 Hz), 2.24 (1H, dd, $^{3}J_{HH}$ = 5.9, $^{2}J_{HH}$ = 5.3 Hz), 2.58 (1H, dd, $^{3}J_{HH}$ = 8.3 Hz, 6.1 Hz), 3.48 (3H, s), 3.86 (3H, s), 6.89 (2H, m), 7.31 (5H, m), 7.76 (1H, d, $^{3}J_{HH}$ = 8.3 Hz); ^{13}C NMR δ 20.5, 29.3, 39.5, 51.9, 56.4, 113.0, 119.0, 126.0, 127.7, 128.7, 129.6, 138.6, 151.9, 153.1, 170.2.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information available: copies of ^{1}H, ^{13}C and ^{19}F NMR spectra for all new compounds.

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REFERENCES

1. (a) Mąkosza, M.; Winiarski, J. Vicarious Nucleophilic Substitution of Hydrogen. *Acc. Chem. Res*. **1987**, *20*, 282. (b) Mąkosza, M.; Wojciechowski, K. Nucleophilic Substitution of Hydrogen in Heterocyclic Chemistry. *Chem. Rev*. **2004**, *104*, 2631. (c) Mąkosza, M. "How Does Nucleophilic Aromatic Substitution in Nitroarenes Really Proceed: General Mechanism. *Synthesis* **2017**, 3247. (d) Błaziak, K.; Danikiewicz, W.; Mąkosza, M. How Does Nucleophilic Substitution Really Proceed in Nitroarenes? Computational Prediction and Experimental Verification. *J. Am. Chem. Soc.* **2016**, *138*,

7276. (e) Mąkosza, M. Reaction of Nucleophiles with Nitroarenes – Multifacial and Versatile Electrophiles. *Chem. Eur. J.* **2014**, *20*, 5536.

2. (a) Mąkosza, M.; Owczarczyk, Z. Dihalomethylation of Nitroarenes via Vicarious Nucleophilic Substitution of Hydrogen with Trihalomethyl Carbanions. *J. Org. Chem*. **1989**, *54*, 5094. (b) Couch, G. D.; Burke, P. J.; Knox, R. J.; Moody, C. J. Synthesis of 2-Aryl-6-methyl-5-nitroquinoline Derivatives as Potential Prodrug Systems for Reductive Activation. *Tetrahedron* **2008**, *64*, 2816. (c) Ostrowski, S.; Kosmalska, M.; Mikus, A. A Vicarious Approach to Porphyrin Aldehydes. *Tetrahedron Lett.* **2017**, *58*, 2011. (d) Ellis, D. Versatile Synthesis of Fused Tricyclic 1,2,4-Triazole Derivatives. *Synth. Comm.* **2011**, *41*, 963. (e) Crozet, M. D.; Suspène, C.; Kaafarani, M.; Crozet M. P.; Vanelle, P. Synthesis of a New Imidazo[4,5-b]pyridin-5-one via a Vicarious Nucleophilic Substitution of Hydrogen. *Heterocycles* **2004**, *63*, 1629.

3. (a) Mąkosza, M.; Sienkiewicz, K.; Wojciechowski, K. Vicarious Nucleophilic Substitution of Hydrogen in Nitroarenes by Carbanions of Alkyl Dichloroacetates. Some new Transformations of Chloro(nitroaryl)acetates. *Synthesis* **1990**, 850. (b) Mąkosza, M.; Białecki, M. Synthesis of (Nitroaryl)chloromethanes via Vicarious Nucleophilic Substitution of Hydrogen. *Synlett* **1991**, 181. (c) Tercel, M.; Lee, A. E.; Hogg, A.; Anderson, R. F.; Lee, H. H.; Siim, B. G.; Denny, W. A.; Wilson, W. R. Hypoxia-Selective Antitumor Agents. 16. Nitroarylmethyl Quaternary Salts as Bioreductive Prodrugs of the Alkylating Agent Mechlorethamine. *J. Med. Chem*. **2001**, *44*, 3511.

4. Mąkosza, M.; Bester, K.; Cmoch, P. One-pot Synthesis of Esters of Cyclopropane Carboxylic Acids via Tandem Vicarious Substitution – Michael Addition. *J. Org. Chem.* **2015**, *80*, 5436.

5. Sakowicz, A.; Loska, R.; Mąkosza, M. One-Pot Synthesis of Oxiranes through Vicarious Nucleophilic Substitution (VNS)–Darzens Reaction. *Synlett* **2016**, 2443.

6. Florio, S.; Lorusso, P.; Granito, C.; Luisi, R.; Troisi, L. One-pot Regioselective Synthesis of Nitrophenyloxazolinyl Styrene Oxides by the Darzens Reaction of Vicarious Nucleophilic Substitution-Formed Carbanions of 2-Dichloromethyl-4,4-dimethyloxazoline. *J. Org. Chem*. **2004**, *69*, 4961.

7. Nishida, S. Diphenylcarbinyl Derivatives. I. Solvolysis of some Monosubstituted Benzhydryl Chlorides. *J. Org. Chem*. **1967**, *32*, 2692.

8. Sartori, G.; Maggi, R. Use of Solid Catalysts in Friedel-Crafts Acylation Reactions. *Chem. Rev.* **2006**, *106*, 1077.

9. (a) Pan, C.; Jia, X.; Cheng, J. Transition-Metal-Catalyzed Synthesis of Aromatic Ketones via Direct CH Bond Activation. *Synthesis* **2012**, *44*, 677. (b) Wu, X.-F. Acylation of (Hetero)Arenes through C–H Activation with Aroyl Surrogates. *Chem. Eur. J.* **2015**, *21*, 12252. (c) Hummel, J. R.; Boerth, J. A.; Ellman, J. A. Transition-Metal-Catalyzed C–H Bond Addition to Carbonyls, Imines, and Related Polarized π Bonds. *Chem. Rev.* **2017**, *117*, 9163.

10. Suresh, R.; Kumaran, R. S.; Senthilkumar, V.; Muthusubramanian, S. Silver Catalyzed Decarboxylative Acylation of Pyridine *N*-oxides Using α-Oxocarboxylic Acids. *RSC Adv.* **2014**, *4*, 31685.

11. Sharma, U. K.; Gemoets, H. P. L.; Schröder, F.; Noël, T.; Van der Eycken, E. V. Merger of Visible-Light Photoredox Catalysis and C–H Activation for the Room-Temperature C-2 Acylation of Indoles in Batch and Flow. *ACS Catal.* **2017**, *7*, 3818.

12. Katritzky, A. R.; Chassaing, C.; Toader, D.; Gill, K. Reactions of 1-(Benzotriazol-1-yl)-1-phenoxyalkane and (Benzotriazol-1-yl)ethoxyphenylmethane Anions with Nitroarenes: a New Approach to Alkyl and Aryl *p*-Nitroaryl Ketones. *J. Chem. Res. (S)* **1999**, 504.

13. Li, J.-S.; Yang, Q.; Yang, F.; Chen, G.-Q.; Li, Z.-W.; Kuang, Y.-J.; Zhang, W.-J.; Huang, P.-M. Aerobic Oxidative Acylation of Nitroarenes with Arylacetic Esters under Mild Conditions: Facile Access to Diarylketones. *Org. Biomol. Chem.* **2018**, *16*, 140.

14. Kumar, P.; Sharma, A. K.; Guntreddi, T.; Singh, R.; Singh, K. N. Transition-Metal-Free Regiospecific Aroylation of Nitroarenes Using Ethyl Arylacetates at Room Temperature. *Org. Lett.* **2018**, *20*, 744.

15. (a) Suzuki, Y.; Toyota, T.; Imada, F.; Sato, M.; Miyashita, A. Nucleophilic Acylation of Arylfluorides Catalyzed by Imidazolidenyl Carbine. *Chem. Commun.* **2003**, 1314. (b) Suzuki, Y.; Ota,

S.; Fukuta, Y.; Ueda, Y.; Sato, M. *N*-Heterocyclic Carbene-Catalyzed Nucleophilic Aroylation of Fluorobenzenes. *J. Org. Chem.* **2008**, *73*, 2420.

16. Chhaly, L.; Pritzkow, W. 4-Nitrobenzyl Chloride as a Nucleophile in VNS Reactions. *J. Prakt. Chem.* **1994**, *336*, 558.

17. Florio, S.; Lorusso, P.; Luisi, R.; Granito, C.; Ronzini, L.; Troisi, L. Vicarious Nucleophilic Substitution of (Chloroalkyl)heterocycles with Nitroarenes. *Eur. J. Org. Chem.* **2004**, 2118.

18. Mąkosza, M.; Wawrzyniewicz, M. Reactions of Organic Anions. XXIV. Catalytic Method for Preparation of Dichlorocyclopropane Derivatives in Aqueous Medium. *Tetrahedron Lett*. **1969**, 4659.

19. (a) Moss, R. A. Improved Production of Phenylchlorocarbene. *J. Org. Chem.* **1962**, *27*, 2683. (b) Closs, G. L.; Coyle, J. J. Stereochemistry and Reactivities of Carbenoids from Benzal Chloride. Salt Effects in Carbenoid Reactions. *J. Org. Chem*. **1966**, *31*, 2759. (c) Moss, R. A.; Pilkiewicz, F. G. Crown Ethers in Carbene Chemistry. Generation of Free Phenylhalocarbenes. *J. Am. Chem. Soc*. **1974**, *96*, 5632. (d) Jończyk, A.; Karwowska, H.; Furman, J. Application of Alkali Metal Hydroxides for the Preparation of *gem*-Chlorophenylcyclopropanes. *Synth. Commun*. **2006**, *36*, 3571.

20. Hoeg, D. F.; Lusk, D. I.; Crumbliss, A. L. Preparation and Chemistry of α-Chloroalkyllithium Compounds. Their Role as Carbenoid Intermediates. *J. Am. Chem. Soc.* **1965**, *87*, 4147.

21. (a) Moss, R. A.; Tian, J. Concurrent Cyclopropanation by Carbenes and Carbanions. *J. Am. Chem. Soc*. **2005**, *127*, 8960. (b) Moss, R. A.; Tian, J. Hammett Studies of Aryldichloromethide Carbanion Reactions. *Org. Lett*. **2006**, *8*, 1245.

22. (a) Goliński, J.; Mąkosza, M.; Rykowski, R. Formation of Aziridine and Cyclopropane Rings in Reaction of Quinozalines and Naphthyridines with α-Halocarbanions. *Tetrahedron. Lett.* **1983**, *24*, 3279. (b) Mąkosza, M.; Glinka, T.; Ostrowski, S.; Rykowski, A. Vicarious Nucleophilic Substitution of Hydrogen versus Bis-Annulation in the Reaction of Chloromethyl Aryl Sulfone Carbanion with Electrophilic Arenes. *Chem. Lett.* **1987**, *16*, 61.

23. An, J.; Tang, X.; Moore, J.; Lewis, W.; Denton, R. M. Phosphorus(V)-catalyzed Deoxydichlorination Reactions of Aldehydes. *Tetrahedron* **2013**, *69*, 8769.

24. Meazza, M.; Ashe, M.; Shin, H. Y.; Yang, H. S.; Mazzanti, A.; Yang, J. W.; Rios, R. Enantioselective Organocatalytic Cyclopropanation of Enals Using Benzyl Chlorides. *J. Org. Chem.* **2016**, *81*, 3488.

25. Zhao, Y.; Kang, J.; Park, C.-M.; Bagdon, P. E.; Peng, B.; Xian, M. Thiol-Activated *gem*-Dithiols: A New Class of Controllable Hydrogen Sulfide Donors. *Org. Lett.* **2014**, *16*, 4536.