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Nicholas Reactions of Alkynyl- and Alkenyltrifluoroborates

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This paper is dedicated to Prof. Victor Snieckus, in consideration of his many years of mentorship and friendship, and for his tireless and continuing dedication to progress in synthetic aromatic chemistry.

Abstract The Lewis acid mediated Nicholas reaction of potassium alkynyltrifluoroborates and propargyl acetate- hexacarbonyldicobalt complexes affords 1,4-diyne dicobalt hexacarbonyl complexes in good yields. The analogous Nicholas reactions of potassium alkenyltrifluoroborates give 1,3-enzyme dicobalt hexacarbonyl complexes in most cases, although the initial site of reaction can vary. Potassium vinyltrifluoroborate itself affords alkynylcyclopropane complexes.

Key words alkyn complexes, boron, carbocation, coupling, Lewis acids, alkynes, enynes

The generation and reaction of hexacarbonyldicobalt complexes of propargylic carbocations (1), or Nicholas reaction, has achieved a place of prominence in metal-organic chemistry due to high reaction site selectivity, good cation stability and reactivity, ease of handling of the alkynedicobalt complexes, and ready decomplexation of the organic unit. Many of the requirements for participation of the nucleophile are well-understood,1 and a wide range of heteroatom-based nucleophiles, hydride sources, and carbon-based nucleophiles are compatible (Scheme 1). For carbon-carbon bond formation processes, electron-rich arenes, enol derivatives, and allylmetals are particularly reliable reaction participants.

Nevertheless, some classes of carbon based nucleophiles remain problematic for the Nicholas reaction. Alkynyl nucleophiles are known, but solely as the trialkynylaluminums; there is little further work reported based on this transformation, perhaps due to reactivity issues with some of the alanes involved.2 Similarly, there are limited reports of intermolecular reactions with alkene nucleophiles that are not activated as either enol ethers or allylmetals. For simple alkene nucleophiles, modest yields of isomeric alkene mixtures are the norm, with pendant cation-trapping nucleophiles substituted on the alkene ameliorating the situation only somewhat.4,5 Simple vinylsilanes have not been reported to be reliable nucleophiles in this process.

In this context, our attention has been drawn to the chemistry of potassium organotrifluoroborates. Arguably most prominent as boronic acid equivalents for cross coupling procedures,6,7 the alkynyl- and alkenyltrifluoroborates recently have been shown to enter into reactions with carbocations or related electrophilic carbon centres.8 These trifluoroborates are water-stable and have good long-term storage capability, and they would appear to be useful in addressing the limitations with alkynyl- and alkanyl nucleophiles in Nicholas reaction chemistry. This letter reports our preliminary work on these reactions.

Figure 1 Starting potassium alkynyltrifluoroborates (2), propargyl acetate hexacarbonyldicobalt complexes (3).

Our initial experiments involved use of phenylalkynyltrifluoroborate 2a and 1-acetoxy-2-pentyne complex 3a (Figure 1). In the presence of BF3•OEt2 (2.5 equiv) in CH2Cl2 at 0 °C (1.5 equiv 3a), a reaction occurred that ceased...
progressing after 1.5 h, giving 4aa (65% yield). Reversing the stoichiometry (1.5 equiv BF₃·OEt₂, 2.5 equiv 2a) improved the yield significantly (4aa, 86%), while use of 2.5 equiv each of BF₃·OEt₂ and 2a gave 4aa in 91% yield. This latter procedure was adopted as standard conditions for subsequent experiments.

Using these standard conditions, the reactions of three potassium alkenyltrifluoroborates (2a, butyl-substituted 2b, and unsubstituted 2c) were investigated, with a number of cobalt hexacarbonyl complexes of propargyl acetates 3 (Equation 1, Table 1). The alkenyltrifluoroborates successfully reacted with ethyl substituted complex 3a (4aa, 91% yield; 4ba, 73% yield; 4ca, 67% yield), butyl substituted complex 3b (4ab, 73%), trimethylsilyl substituted complex 3c (4ac, 65% yield; 4bc, 77% yield), vinyl substituted complex 3d (4bd, 65% yield), phenyl substituted complex 3e (4be, 60% yield) and unsubstituted complex 3f (4bf, 63% yield). Monosubstitution at the propargylic site of the alkynedicobalt complex was well tolerated, as methyl substituted complex 3g (4ag, 90% yield) and phenyl substituted 3h (4ah, 97% yield) each gave high yields of condensation product with 2a. Conversely, tertiary acetate 3i gave only elimination product 5 (54% yield) with 2a to the exclusion of any C-C bond forming product. Finally, a remote ester function on the propargyl ether complex (3j) was tolerated, giving γ-carbonyl cation reaction product 4aj (65% yield) employing Bu₂BOTf in place of BF₃·OEt₂.11

Table 1 Reactions of alkenyltrifluoroborates (2) and propargyl acetyl hexacarbonyldicobalt complexes (3).

Table 2 Reactions of alkenyltrifluoroborates (6) and propargyl acetyl hexacarbonyldicobalt complexes (3).

*Yields in parentheses based on recovered starting 3 (brsm). a Lewis acid Bu₂BOTf.

Four potassium alkenyltrifluoroborates were chosen for investigation with propargyl acetate complexes 3, including styryltrifluoroborate 6a, n-propenyltrifluoroborate 6b, isopropenyltrifluoroborate 6c, and vinyltrifluoroborate 6d (Figure 2). The styryl substituted trifluoroborates, reacted in a quite straightforward manner under the standard conditions, as 6a with 3b afforded 7ab (68% yield), and 6a with 3c gave 7ac (71% yield) each as (E)-isomers to the limits of detection by 1H NMR spectroscopy (Equation 1, Table 2). n-Proopinyltrifluoroborate 6b reacted analogously with 3a to give (E)-7ba (51% yield, 58% brsm) and with 3c to give (E)-7bc (35% yield, 69% brsm), but the reactions suffered from incomplete conversion under the standard conditions. Increasing the amounts of BF₃·OEt₂ and 6c to 4.0 equiv raised the yield of (E)-7bc to 42% (65% brsm).
conversion to cyclopropane products with only traces (ca. 7%) of alkene isomers evident by NMR spectroscopy; 3b afforded 8db (33% yield, 80% brsm), and 3c provided 8dc (57% yield, 89% brsm). An increase in the amounts of BF₃·OEt₂ and 6d (to 4.0 equiv each) with 3b gave somewhat improved yields of 8db, but still incomplete conversion (49% yield, 78% brsm).

Three Nicholas reaction products were selected for decomplexation, for illustration of the viability of the process for these substrates (Scheme 3). Employing ceric ammonium nitrate (CAN) in acetone, under carefully controlled conditions, skipped diyne complexes 4bd and 4bf, and enyne complex 7ab each afforded their metal-free counterparts in good to excellent yields (9bd, 86% yield; 9bf, 86% yield; 10ab, 96% yield).  

The Nicholas reactions with alkynyltrifluoroborates are quite successful in the anticipated manner. They give reasonable to excellent chemical yields in all cases except the elimination-prone tertiary case (3i), with the higher yielding cases generally coincident with the more stabilized propargylcobicalt cationic species. The modest amounts of starting propargyl acetate recovered in a few cases likely stems from a competitive defluorination reaction by BF₃·OEt₂ of the alkynyltrifluoroborate salt.  

For the alkynyltrifluoroborates, it is our belief that the reaction is being driven by attack of the propargylcobicalt cation by the most nucleophilic carbon of the alkene function, with ultimate alkene re-formation by way of BF₃ loss from a β-boryl cation. This results in straightforward substitution at boron-substituted site with styryltrifluoroborate 6a, and less efficiently for n-propenyltrifluoroborate 6b. For isopropenylborate 6c, attack at the terminal alkene carbon results in formation of carbocation 11, followed by hydride migration to give 12, which in turn undergoes BF₃ loss to give 7bc/7cg (Scheme 4). There are rare examples of reactions involving isopropenyltrifluoroborate that afford a 1-propenyl adduct; however, they likely are not proceeding by way of a carbocation. Finally, the reaction of vinyltrifluoroborate 6d is consistent with initial formation carbocation 11, a 1,3-hydride shift to give propargyl cation 13, and nucleophilic attack on the cation to give 8db/8dc. It is likely that 6d is a less nucleophilic trifluoroborate and that BF₃-induced defluorination competes more substantially in these cases. The reasons for the change in pattern of 6d from 6c are not clear at this time.

Future work will involve investigating other protocols for generation of the propargylcobicalt cation for the purpose of obtaining complete conversion in the more difficult cases, determining the borderline between divergent reaction processes with the alkynyltrifluoroborates, and exploration of aryl- and alkytrifluoroborates as potential Nicholas reaction partner. These are in progress and will be reported in due course.

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Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO (this text will be deleted prior to publication)

References and Notes


(10) Experimental Procedure. To a solution of 3a (89.7 mg, 0.218 mmol) and 2a (0.113 g, 0.544 mmol) in CH2Cl2 (8 mL) at 0 °C was added BF3·OEt2 (67 μL, 0.54 mmol). After 15 h, saturated NH4Cl(aq) was added and the mixture subjected to conventional extractive workup (CH2Cl2). Flash chromatography (methanol/petroleum ether: Et2O,0:51) afforded 4aa (90.3 mg, 91%) as a viscous red oil.

(11) Representative Characterization Data (4aa): 1H NMR: 8 7.30-7.44 (m, 5H), 4.00 (s, 2H), 2.92 (q, J = 7.3 Hz, 2H), 1.35 (t, J = 7.3 Hz, 3H). 13C NMR: 199.7, 131.5, 128.3, 120.3, 101.6, 93.7, 86.5, 82.3, 26.9, 25.0, 15.6; IR v(κ): 2971, 2084, 2043, 1989, 1600, 1490 cm−1; HRMS m/e for C2H12O2 calculated (M+CO2) 454.9376 found 454.9376.

(12) Nicholas reactions for carbonyl cation equivalents readily give more rapid reaction with Bu3SnH as Lewis acid relative to BF3·OEt2. See: Tai, R.; Green, J. R. J. Org. Chem. 2010, 75, 8258.

(13) Representative Characterization Data. 7b: 1H NMR: 8 7.29 – 7.44 (m, 5H), 6.61 (d, J = 15.7 Hz, 2H), 6.31 – 6.41 (dt, J = 15.7, 7.2 Hz, 1H), 3.77 – 3.79 (d, J = 7.2 Hz, 2H), 2.92 (t, J = 7.6 Hz, 2H), 1.48 – 1.77 (m, 4H), 1.00 (t, J = 7.2 Hz, 3H). 13C NMR: 200.3, 137.0, 132.3, 128.6, 127.5, 124.7, 126.9, 99.7, 97.6, 37.4, 33.8, 22.8, 13.9; IR v(κ): 3084, 3062, 3028, 2960, 2874, 2085, 2040, 1994, 1495 cm−1; HRMS m/e for C2H12O2 calculated (M+CO2) 456.9896, found 456.9907.

(14) Experimental Procedure. Complex 4bd (47.6 mg, 0.110 mmol) was dissolved in acetone (8 mL) and the solution cooled to −78°C. Cerium ammonium nitrate (0.302 g, 0.551 mmol, 5 equiv) was added and the solution allowed to warm to −30 °C (2 h), with monitoring by TLC. A saturated sodium chloride solution was added and the mixture subjected to a conventional extractive workup (EtOAc). The product was filtered through a silica plug using Et2O and concentrated under reduced pressure to give 4bd (13.9 mg, 86%).


(16) Our operating hypothesis for the predominant (Z)-isomer formation comes from the proposed larger size of the BF3·unit relative to a methyl group. Initial reaction consequently gives a cation 11 with the methyl nearly eclipsed to the homopropargyl-Co(CO)3 unit (Scheme 4); subsequent hydride migration then gives a cation 12 where rotation of the C=C bond to a co-linear orientation relative to the empty p-orbital of the cation is lower energy than a rotation of the methyl group anti- to the homopropargyl-Co(CO)3 group.


