Tetrahedron Letters,Vol.29,No.50,pp 6545-6548,1988
Printed in Great Britain

0040-4039/88 \$3.00 + .00
Pergamon Press plc

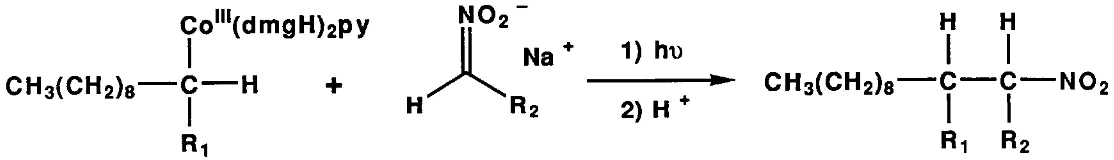
COBALOXIME-MEDIATED RADICAL ALKYL-NITROALKYLANION CROSS COUPLING

Bruce P. Branchaud*[1] and Gui-Xue Yu
Department of Chemistry
University of Oregon
Eugene, OR 97403-1210

Summary: Anaerobic photolysis of aqueous ethanol solutions of alkyl cobaloximes $RCo^{III}(dmgH)_2py$ (dmgH = dimethylglyoxime monoanion) and nitroalkyl anions caused cross coupling in which an H α to the nitro was replaced with R.

In previous studies we found that the success of cobaloxime-mediated radical alkyl-alkenyl[2,3] and alkyl-heteroaromatic[4] cross couplings depended upon (1) having a cross coupling partner which is highly reactive with nucleophilic alkyl radicals and (2) having a concentration of the cross coupling partner high enough to provide a sufficient radical-trapping flux (rate constant x concentration) to efficiently trap alkyl radicals in competition with other side reactions. Nitroalkylanions are extraordinarily reactive with nucleophilic alkyl radicals.[5] For example, the rate of addition of $H_2C{=}CH(CH_2)_3CH_2^{\bullet}$ to $(CH_3)_2C{=}NO_2^-$ ($\sim 2.5 \times 10^5\ M^{-1}s^{-1}$ at 40 °C),[5b] with two alkyl substituents at the site of radical attack, is faster than addition of $H_2C{=}CH(CH_2)_3CH_2^{\bullet}$ to $H_2C{=}CHPh$ ($\sim 8.7 \times 10^4\ M^{-1}s^{-1}$ at 45 °C),[6] with no alkyl substituents at the site of radical attack. The relative rates of addition of $(CH_3)_3C^{\bullet}$ to $(CH_3)_2C{=}NO_2^-$, $CH_3CH{=}NO_2$, and $H_2C{=}NO_2^-$ at 35 °C are 1:6:35, respectively.[5a] Since we have successfully cross coupled $H_2C{=}CHPh$ with $RCo^{III}(dmgH)_2py$,[2] we decided to examine cobaloxime-mediated alkyl-nitroalkylanion cross coupling.

We found that anaerobic visible light photolyses[7] of $CH_3(CH_2)_8CH_2\text{-}Co^{III}(dmgH)_2py$ (1) with $H_2C{=}NO_2^-\ Na^+$ (3) or $CH_3CH_2CH{=}NO_2^-\ Na^+$ (4) led to cross coupling.[8,9,10] Cross couplings using secondary alkyl $CH_3(CH_2)_8CH(CH_3)Co^{III}(dmgH)_2py$ (2) were also successful but consistently led to somewhat lower yields than with primary 1 under comparable conditions.[8,9,10] The yields of 5, 6, 7, and 8 were linear with nitroalkylanion concentration at low to moderate concentrations of nitroalkylanions and reached a maximum plateau at higher concentrations of nitroalkylanions.



1 $R_1 = H$
2 $R_1 = CH_3$

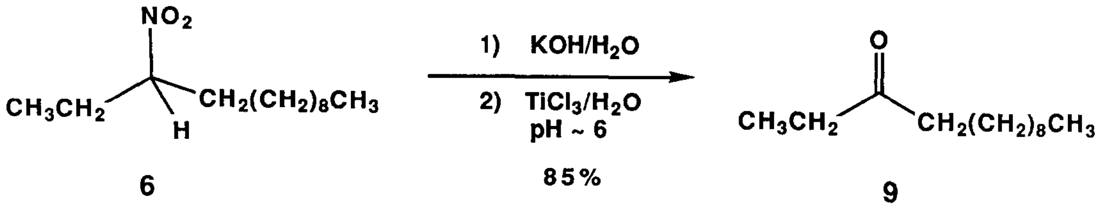
3 $R_2 = H$
4 $R_2 = CH_2CH_3$

5 $R_1 = H$ $R_2 = H$
6 $R_1 = H$ $R_2 = CH_2CH_3$
7 $R_1 = CH_3$ $R_2 = H$
8 $R_1 = CH_3$ $R_2 = CH_2CH_3$

RCo^{III}(dmgH)$_2$py[a]	Nitroalkylanion (concn, mM)	Solvent	Product (% Yield)[b,c]
1	3 (20)	95% EtOH/H_2O	**5** (16)
1	3 (40)	95% EtOH/H_2O	**5** (25)
1	3 (60)	95% EtOH/H_2O	**5** (48)
1	3 (100)	95% EtOH/H_2O	**5** (80)
1	3 (200)	95% EtOH/H_2O	**5** (85)
1	3 (400)	95% EtOH/H_2O	**5** (81)
1	4 (20)	95% EtOH/H_2O	**6** (25)
1	4 (40)	95% EtOH/H_2O	**6** (45)
1	4 (60)	95% EtOH/H_2O	**6** (70)
1	4 (80)	95% EtOH/H_2O	**6** (72)
1	4 (100)	95% EtOH/H_2O	**6** (77)
1	4 (200)	95% EtOH/H_2O	**6** (83)
1	4 (400)	95% EtOH/H_2O	**6** (83)
2	3 (60)	95% EtOH/H_2O	**7** (28)
2	3 (100)	80% EtOH/H_2O	**7** (37)
2	3 (200)	80% EtOH/H_2O	**7** (58)
2	3 (400)	80% EtOH/H_2O	**7** (58)
2	4 (20)	95% EtOH/H_2O	**8** (5)
2	4 (60)	95% EtOH/H_2O	**8** (28)
2	4 (100)	80% EtOH/H_2O	**8** (27)
2	4 (200)	80% EtOH/H_2O	**8** (56)
2	4 (400)	80% EtOH/H_2O	**8** (62)

[a] RCo^{III}(dmgH)$_2$py concn was 20 mM for all reactions. [b] Reactions were run at ~15 °C. [c] Reaction times were ~30 h in all cases.

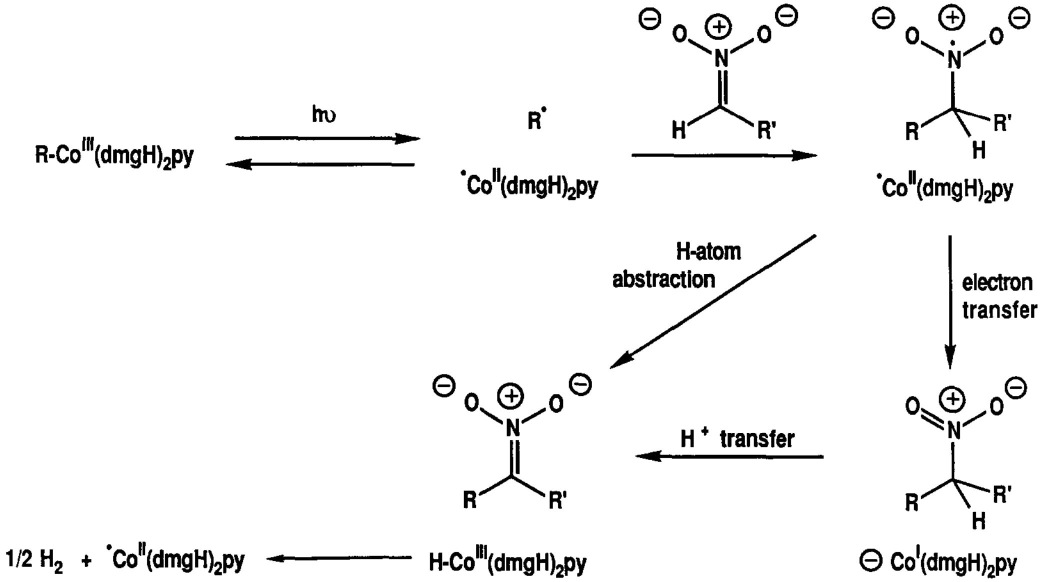
Since the nitro functional group can be converted into the important ketone or aldehyde groups under mild conditions (anaerobic aqueous $TiCl_3$),[11] we have formally developed an equivalent to carbanion-carbonyl addition that is compatible with hydroxylic solvents and should be compatible with common organic functional groups. As an illustration of that point, **the completely aqueous-compatible sequence of reactions**, $CH_3(CH_2)_8CH_2Br$ to **1** (91% average isolated yield) then **1** to **6** (83% isolated yield using 5 equiv of **4**) then **6** to **9** (85% isolated yield),[12] in 64% overall isolated yield for three steps (86% average for each step), is **equivalent to aqueous-incompatible standard carbanion-carbonyl couplings** such as carbanion-aldehyde addition followed by alcohol to ketone oxidation or cross coupling of organocadmium[13] or organomanganese[14] reagents with acid halides.



6

9

Reasonable non-chain and chain mechanisms can be formulated to rationalize our results. The non-chain model shown below is analogous to ones we have proposed for alkyl-alkenyl[2] and alkyl-heteroaromatic[4] cross couplings. The chain mechanisms that could be written are analogous to $S_{RN}1$ cross coupling of alkylmercuric halides with nitroalkylanions.[5] We strongly favor the non-chain mechanism for this and all cobaloxime-mediated cross couplings for fundamental reasons which have been discussed in detail elsewhere.[4] In brief here, a consideration of one electron reduction potentials of $^{\bullet}Co^{II}(dmgH)_2py$ versus $RCo^{III}(dmgH)_2py$ leads to the conclusion that $^{\bullet}Co^{II}(dmgH)_2py$ should act as a chain-terminating radical scavenger, diverting the reaction flux away from a chain reaction and into the non-chain pathway shown below.



Acknowledgements. The Alfred P. Sloan Foundation and NSF CHE 8806805 provided financial support. The General Electric QE-300 NMR used in this work was purchased with funds from NIH RR 02336 and NSF CHE 8411177. The VG ZAB-2FHF MS and VG 12/253 Quad MS used in this work were purchased with funds from NIH RR 03001, NSF DMB 8414627, and the M. J. Murdoch Charitable Trust.

References and Notes

1. Fellow of the Alfred P. Sloan Foundation, 1987-1989.
2. (a) Branchaud, B. P.; Meier, M. S.; Choi, Y. *Tetrahedron Lett.* **1988**, *29*, 167. (b) Branchaud, B. P.; Meier, M. S. *Tetrahedron Lett.* **1988**, *29*, 3191. (c) Branchaud, B. P.; Meier, M. S., *J. Org. Chem.*, in press.
3. For radical-alkene reactions via cobalt radical chemistry see: (a) Baldwin, J. E.; Li, C.-S. *J. Chem. Soc. Chem. Commun.* **1988**, 261. (b) Coveney, D. J.; Patel, V. F.; Pattenden, G. *Tetrahedron Lett.* **1987**, *28*, 5949. (c) Patel, V. F.; Pattenden, G. *J. Chem. Soc. Chem. Commun.* **1987**, 871. (d) Baldwin, J. E.; Li, C.-S. *J. Chem. Soc. Chem. Commun.* **1987**, 166. (e) Scheffold, R. *Pure Appl. Chem.* **1987**, *59*, 363.
4. Branchaud, B. P.; Choi, Y. L. *J. Org. Chem.* **1988**, *53*, in press.
5. (a) Russell, G. A.; Khanna, R. K. In *Nucleophilicity*; Harris, J. M.; McManus, S. P., Eds.; ACS Advances in Chemistry Series 215; American Chemical Society: Washington, D. C., 1987; pp 355-68. (b) Russell, G. A.; Guo, D. *Tetrahedron Lett.* **1984**, *25*, 5239. (c) Madden, K. P.; Taniguchi, H.; Fessenden, R. W. *J. Am. Chem. Soc.* **1988**, *110*, 2753.
6. Citterio, A.; Arnoldi, A.; Minisci, F. *J. Org. Chem.* **1979**, *44*, 2674.
7. Photolyses were performed using a 300 W incandescent light bulb in Pyrex test tube reaction vessels in a simple Pyrex apparatus previously described in detail in Branchaud, B. P.; Meier, M. S.; Malekzadeh, M. N. *J. Org. Chem.* **1987**, *52*, 212.
8. The R-$Co^{III}(dmgH)_2py$ 1 and 2 were prepared in moderate to good isolated yields as previously described in references 2 and 7.
9. Products **5**, **6**, **7**, and **8** were characterized by ^1H NMR, ^{13}C NMR, and MS.
10. All yields for cross-coupling products are for isolated, chromatographically purified materials. Yields were determined by ^1H NMR integration vs Ph_3CH added as an internal standard to chromatographically homogeneous samples prior to ^1H NMR analysis.
11. McMurry, J. E. *Accts. Chem. Res.* **1974**, *9*, 281.
12. 3-tridecanone **9** was characterized by ^1H NMR, and by ^1H NMR and ^{13}C NMR of its 2,4-DNP derivative (mp = 42.5-43.0 °C).
13. Jones, P. R.; Desio, P. J. *Chem. Rev.* **1978**, *78*, 491.
14. Cahiez, G.; Bernard, D.; Normant, J. F. *Synthesis* **1977**, *2*, 130.

(Received in USA 24 August 1988)