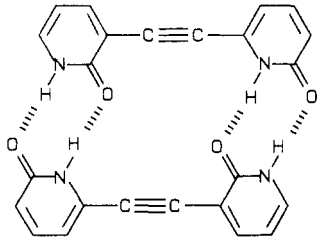
pyridine[10] with acetylene ($N(C_2H_5)_3$, 3 mol % $Pd(PPh_3)_4$, 1 mol % CuI, 79%), followed by deprotecting the resulting dibenzyl ether (93%).[14]

Vapor-pressure osmometric studies at 41 °C confirmed that both acetylenic dipyridones **5** and **6**, like 2-pyridone itself, exist as solvated monomers in CH_3OH and other strongly hydrogen-bonding polar solvents. In $CHCl_3$, however, all three compounds are associated. The ratio of absorbances at 1672 cm^{-1} (monomer) and 1654 cm^{-1} (dimer) in the infrared spectrum of 2-pyridone at 25 °C indicates about 20% dimerization at 1.1×10^{-3} M, and the behavior of symmetric dipyridone **6** is similar. In contrast, asymmetric dipyridone **5** is almost exclusively dimeric (>90%) even at distinctly lower concentrations (3.6×10^{-4} M). We attribute the particularly strong association of self-complementary dipyridone **5** to the formation of dimer **7** with $-\Delta G° > 6.5$ kcal/mol at 25 °C.

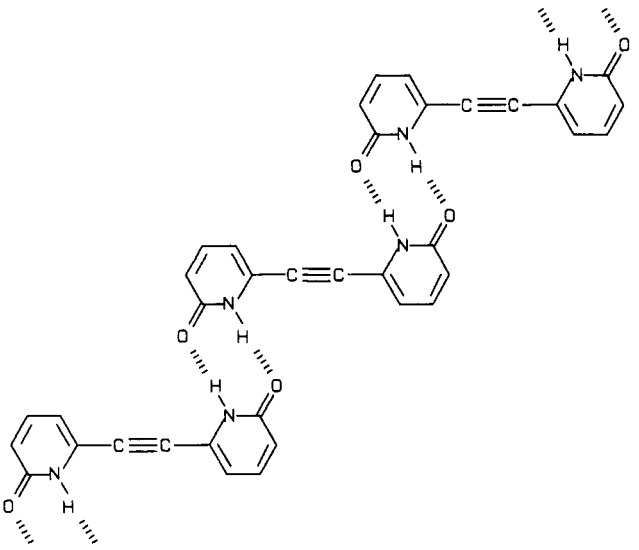


7

X-ray crystallographic studies established that dipyridones **5** and **6** also have different modes of aggregation in the solid state. As expected, asymmetric isomer **5** exists as discrete dimers **7**, and symmetric isomer **6** adopts the planar polymeric motif **8**.[16] Dimer **7** is distinctly nonplanar; in each dipyridone subunit **5** the average planes of the pyridone rings make an angle of 29°, presumably to minimize repulsion of the carbonyl oxygens directed toward the interior of the dimer.[17] Otherwise, the bond lengths and angles in each structure are closely similar to those of related molecules.[5,19]

Our strategy for amplifying the strength of simple hydrogen-bonding motifs can clearly be extended to produce self-complementary arrays with even lower free energies of aggregation. Creative incorporation of these sticky subunits in larger molecules may produce the elements of a molecular Lego construction set that allows chemists to make predictably ordered supramolecular aggregates with useful properties.

Acknowledgment. This work was financially supported by the Natural Sciences and Engineering Research Council of Canada and the Ministère de l'Education du Québec. We thank Professor Peter Beak for helpful discussions.



8

Registry No. **5**, 117068-69-6; **6**, 117068-70-9; 2-(benzyloxy)-6-bromopyridine, 117068-71-0; (trimethylsilyl)acetylene, 1066-54-2; acetylene, 74-86-2; 2-(benzyloxy)-3-bromopyridine, 52200-49-4.

Supplementary Material Available: Spectroscopic and analytic data and atomic positional and thermal parameters for **5** and **6** (5 pages). Ordering information is given on any current masthead page.

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Received September 8, 1988

(15) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467–4470.

(16) (a) Ducharme, Y.; Simard, M.; Wuest, J. D., unpublished results. (b) Crystals of the asymmetric dipyridone **5** belong to the monoclinic space group $P2_1/c$ with $a = 8.930$ (9) Å, $b = 13.299$ (9) Å, $c = 10.781$ (9) Å, $\beta = 126.08$ (9)°, and $V = 1034.8$ Å^3. An Enraf-Nonius CAD-4 diffractometer was used to collect a set of intensity data at 220 K ($2\theta \leq 140.0°$, Cu Kα, 1614 nonzero reflections). The structure was solved by direct methods and refined by full-matrix least-squares calculations to $R = 0.044$, $Rw = 0.054$, and goodness-of-fit ratio = 1.94. (c) Crystals of the symmetric dipyridone **6** belong to the same space group with $a = 4.900$ (3) Å, $b = 13.184$ (5) Å, $c = 8.989$ (3) Å, $\beta = 115.97°$, and $V = 522.1$ Å^3. Similar collection and treatment of the data led to $R = 0.12$, $Rw = 0.098$, and goodness-of-fit ratio = 3.40 for 652 nonzero reflections. The atomic positional and thermal parameters for both structures are included in the supplementary material.

(17) This deformation produces hydrogen bonds bent about 13° from linearity, which should not be energetically costly.[4b,18]

(18) Taylor, R.; Kennard, O.; Versichel, W. *J. Am. Chem. Soc.* **1983**, *105*, 5761–5766.

(19) Mavridis, A.; Moustakali-Mavridis, I. *Acta Crystallogr., Sect. B.: Struct. Crystallogr. Cryst. Chem.* **1977**, *B33*, 3612–3615.

General Approach to Highly Functionalized Benzylic Organometallics of Zinc and Copper

Summary: A general synthesis of highly functionalized benzylic zinc organometallics is described. The corresponding copper derivatives, formed by a transmetalation with CuCN·2LiCl, react in high yields with allylic halides, enones, acyl chlorides, and aldehydes.

Sir: Benzylic lithium and magnesium compounds are often difficult to prepare by conventional methods. When metal–halogen exchange reactions are used, there is often formation of cross-coupling products[1] even at low temperature, and thus special reaction conditions[2] had to be developed. Direct metalation[3] requires the use of strong

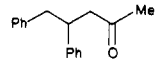
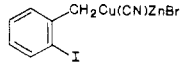
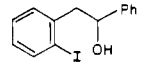
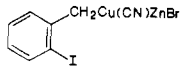
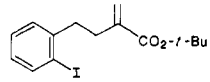
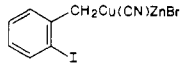
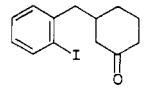
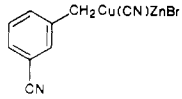
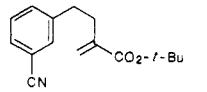
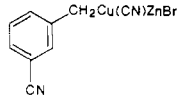
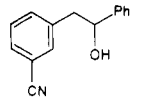
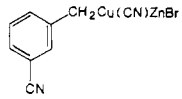
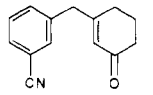
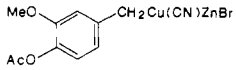
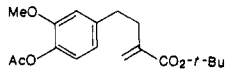
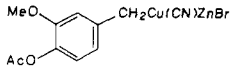
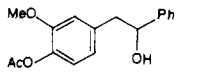
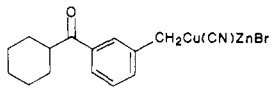
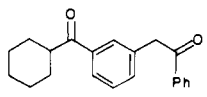
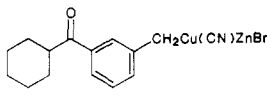
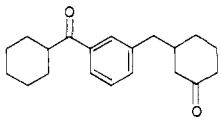
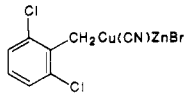
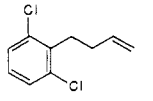
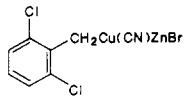
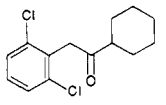
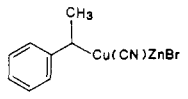
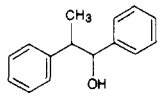
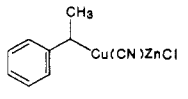
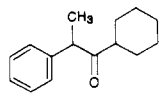
(1) Parham, W. E.; Jones, L. D.; Sayed, Y. A. *J. Org. Chem.* **1976**, *41*, 1184.

(2) (a) Raston, C. L.; Salem, G. *J. Chem. Soc., Chem. Commun.* **1984**, 1702. (b) Raston, C. L.; Harvey, S. *J. Chem. Soc., Chem. Commun.* **1988**, 652. (c) For the synthesis of some functionalized benzylic organocadmium bromides by using highly reactive cadmium metal powder, see: Burkhardt, E. R.; Rieke, R. D. *J. Org. Chem.* **1985**, *50*, 416. (d) Harvey, S.; Junk, P. C.; Raston, C. L.; Salem, G. *J. Org. Chem.* **1988**, *53*, 3134. (e) Bogdanovic, B. *Acc. Chem. Res.* **1988**, *21*, 261.

(3) For a review, see: Wardell, J. L. Preparation and Use in Organic Synthesis of Organolithium and Group IA Organometallics; The Chemistry of the Metal-Carbon Bond. *The Chemistry of Functional Groups*; Patai, S., Ed.; Wiley: New York, 1987; Vol. 4, pp 35–42.

0022-3263/88/1953-5789$01.50/0

Table I. Products of Type 4 Obtained by the Reaction of Benzylic Copper Organometallics 3 with Electrophiles[a]

entry	benzylic organocopper 3	electrophile	product of type 4	yield, %
1	$PhCH_2Cu(CN)ZnBr$	butanal	$PhCH_2CH(OH)CH_2CH_2CH_3$	94
2	$PhCH_2Cu(CN)ZnBr$	*trans*-4-phenyl-3-buten-2-one		91
3		benzaldehyde		93
4		*tert*-butyl α-(bromomethyl)acrylate		95
5		cyclohexenone		93
6		*tert*-butyl α-(bromomethyl)acrylate		97
7		benzaldehyde		94
8		3-iodo-2-cyclohexen-1-one		84
9		*tert*-butyl α-(bromomethyl)acrylate		98
10		benzaldehyde		85
11		benzoyl chloride		90
12		cyclohexenone		95
13		allyl bromide		96
14		cyclohexanecarbonyl chloride		92
15		benzaldehyde		97[b]
16		cyclohexanecarbonyl chloride		93

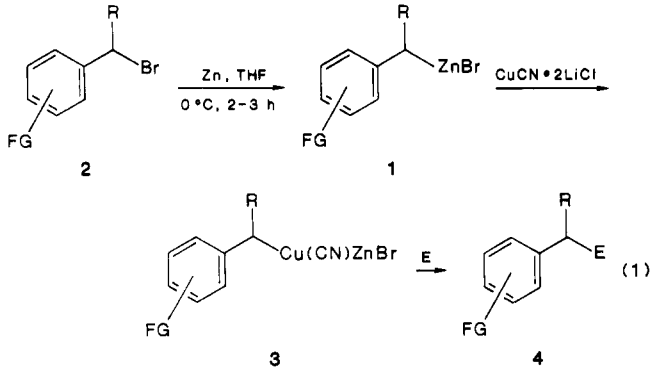
[a] All indicated yields are isolated yields. Satisfactory spectral data (IR, ^1H and ^{13}C NMR, high-resolution mass spectra) were obtained for all new compounds. [b] The product was a 1:1 mixture of diastereomers.

bases and can be complicated by the formation of ring-metalated products. Benzyltin derivatives,[4] benzyl ethers,[5] benzyl thioethers,[6] and recently benzyl selenides[7] have also been used to prepare mostly nonfunctionalized benzyllithiums.

We now report a mild and general synthesis of benzylic zinc bromides **1** which tolerates the presence of important functional groups like esters, cyanides, halides, or even ketones. The reaction of the benzylic bromides **2** with zinc activated with 1,2-dibromoethane[8] in THF[9] furnishes the

(4) (a) Seyferth, D.; Suzuki, R.; Murphy, C. J.; Sabet, C. R. *J. Organomet. Chem.* **1964**, *2*, 431. (b) Kronzer, F. J.; Sandel, V. R. *J. Am. Chem. Soc.* **1972**, *94*, 5705. (c) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.
(5) Gilman, H.; McNinch, H. A. *J. Org. Chem.* **1961**, *26*, 3723.
(6) Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1979**, *44*, 713.
(7) Clarembeau, M.; Krief, A. *Tetrahedron Lett.* **1985**, *26*, 1093.

benzylic zinc bromides 1 in over 90% yield[10] (5 °C, 2–3 h; see eq 1 and Table I). Under our reaction conditions, only very small amounts of cross-coupling products (usually less than 5%) were observed with primary benzylic bromides. In the case of a secondary benzylic bromide (entry 15 of Table I), a slow addition (3.5 h) of (1-bromoethyl)benzene (10 mmol in 15 mL of THF) to activated zinc (2.5 equiv) at −15 °C was required to prepare the corresponding zinc derivative in 75% yield (20% of coupling products was formed). The reaction of (1-chloroethyl)benzene (10 mmol in 10 mL of THF) led to a further improvement. In this case, less than 8% of coupling products was formed and over 90% yield of the corresponding zinc compound could be obtained (2 equiv of Zn; 30 °C, 12–16 h; see entry 16 of Table I).



FG = COR, OAc, CN, Cl, I; E = aldehydes, acid chlorides, enones, allylic bromides; R = CH_3, H

The reactivity of 1 toward electrophiles E is considerably enhanced by performing a transmetalation to the copper derivatives **3** by using the new soluble copper salt[8] CuCN·2LiCl (see eq 1 and Table I). These copper species are highly stable below −20 °C but decompose slowly at higher temperatures. Reactions of **3** with various electrophiles afford very high yields of products **4** (85–97%). Allylic bromides react very rapidly (−70 to 0 °C, 5 min at 0 °C); see entries 4, 6, 9, and 13. The Michael addition of the copper reagents **3** to enones proceeds smoothly in the presence of Me_3SiCl[11] (2 equiv); see entries 2, 5, and 12. Without Me_3SiCl, enones react far more slowly and 3-iodo-2-cyclohexen-1-one selectively furnishes the corresponding unsaturated ketone (see entry 8) upon treatment with the (3-cyanobenzyl)copper derivative. Aldehydes react rapidly in the presence of BF_3·OEt_2[12] and afford secondary alcohols (see entries 1, 3, 7, 10, and 15). Finally, acid chlorides lead to the corresponding ketones in high yields (entries 11 and 14).

In conclusion, a general approach to highly functionalized benzylic zinc and copper organometallics is described and their good reactivity toward various organic electrophiles has been established. Extensions of this methodology are currently studied in our laboratory.

Acknowledgment. We thank the Chemistry Department of The University of Michigan, the Horace H. Rackham School of Graduate Studies of The University of Michigan, and the Moses Gomberg Fellowship Fund for the generous support of this work and La Vieille Montagne Co. (Paris, France) for a generous gift of zinc.

Supplementary Material Available: Spectral data for new compounds (5 pages). Ordering information is given on any current masthead page.

(8) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

(9) Gaudemar, M. *Bull. Soc. Chim. Fr.* **1962**, 974.

(10) Typical procedure: A solution of 21.5 mmol of the benzylic bromide in 11 mL of THF was slowly added (1 drop each 5 s) at 0 °C to 1.7 g (26 mmol) of cut zinc foil (99.99% purity) which had been activated with 200 mg of 1,2-dibromoethane. After 2–3 h of stirring at 5 °C, the benzylic zinc organometallic was ready to use. Ten millimoles of this solution was then added at −70 °C to a solution of 0.9 g (10 mmol) of CuCN and 0.9 g (21 mmol) of LiCl in 10 mL of THF. After warming up to −20 °C for 5 min, the reaction mixture was cooled to −70 °C and ready to use. (a) Reaction with acid chlorides and allylic bromides: A solution of 8 mmol (0.8 equiv) of the acid chloride or of the allylic bromide in 2 mL of THF was added at −70 °C. The reaction mixture was in the first case warmed up to −20 °C, stirred for 12 h at this temperature, and worked up. In the second case, the reaction mixture was slowly warmed up to 0 °C and worked up after 5 min. (b) Reaction with enones: Me_3SiCl (2.50 mL, 20 mmol) was added to the benzylic copper solution at −70 °C followed by 8 mmol (0.8 equiv) of the enone in 2 mL of THF. After 3 h at −70 °C, the reaction mixture was warmed up to −20 °C, stirred for 12 h at this temperature, and worked up as usual. (c) Reaction with aldehydes: BF_3·OEt_2 (2.50 mL, 20 mmol) was added to the benzylic copper solution at −78 °C, followed by 8 mmol (0.8 equiv) of the aldehyde in 2 mL of THF. The reaction mixture was warmed up to −30 °C, stirred for 4–6 h at this temperature, and worked up.

(11) (a) Chuit, C.; Foulon, J. P.; Normant, J. F. *Tetrahedron* **1981**, *37*, 1385; *Ibid.* **1980**, *36*, 2305. (b) Bourgain-Commercon, M.; Foulon, J. P.; Normant, J. F. *J. Organomet. Chem.* **1982**, *228*, 321. (c) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015, 6019. (d) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047. (e) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025. (f) Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4029.

(12) Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887.

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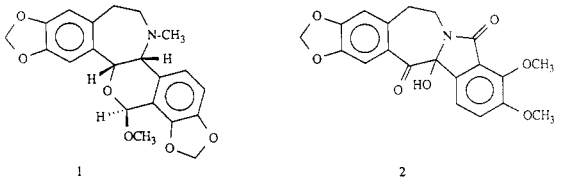
Oxidative Ring Expansion of Isoquinoline Enamides. Facile Formation of 3-Benzazepines

Summary: The reaction of enamides (acylenamines), derived from various substituted 1-methyl- and 1-ethyldihydroisoquinolines, with lead tetraacetate proceeds through an oxidative rearrangement to form 3-benzazepin-2-ones in high yield.

Sir: The benzazepine ring system occurs in the biologically active rhoeadine alkaloids, e.g., rhoeadine (**1**),[1] as well as in other isoquinoline-derived alkaloids like chilenine (**2**).[2]



1 2

Other simpler substituted benzazepines are being intensively developed as central nervous system and cardiovascular pharmaceutical agents.[3] Several approaches to the synthesis of this ring system have been described[4] and excellent methods exist for the preparation of aryl-substituted benzazepines.[3] However, benzazepines that are either unsubstituted or alkyl substituted on the azepine

(1) (a) Ronsch, H. *Alkaloids (N.Y.)* **1986**, *28*, 1–93. (b) Montgomery, C. T.; Cassels, B. K.; Shamma, M. *J. Nat. Prod.* **1983**, *46*, 441–53.

(2) Fajardo, V.; Elango, V.; Cassels, B.; Shamma, M. *Tetrahedron Lett.* **1982**, *23*, 39–42.

(3) Weinstock, J.; Hieble, J. P.; Wilson, J. W. *Drugs Fut.* **1985**, *10*, 646–97.

(4) Kasparek, S. *Adv. Heterocycl. Chem.* **1974**, *17*, 45.

0022-3263/88/1953-5791$01.50/0