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Unusual Copper Salt Promoted Addition Reactions of Cyclic 1,3-Dicarbonylmethanides to Olefinic Bonds

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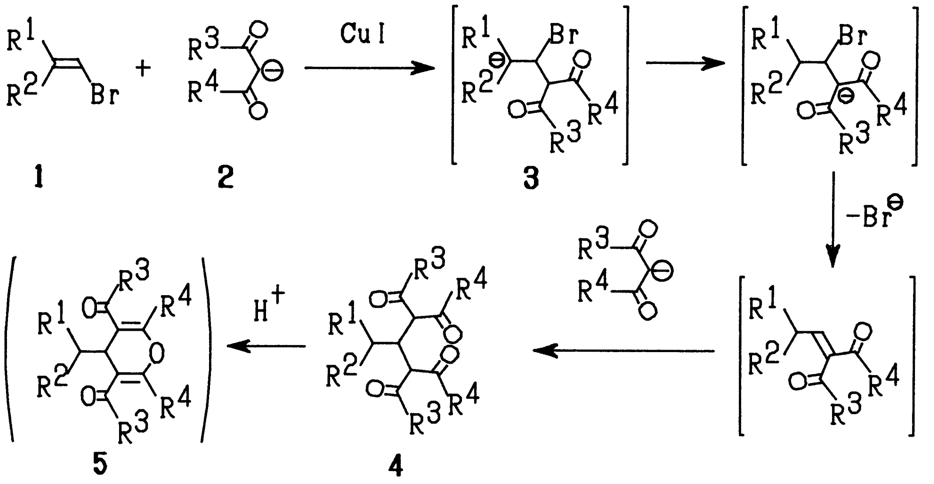
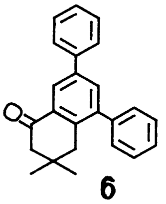
Carbanions derived from cyclic 1,3-dicarbonyl compounds reacted smoothly with some vinyl bromides and 1,3-enones in HMPA in the presence of copper(I) iodide to give geminally disubstituted alkanes in good yields. The products were easily dehydrated intramolecularly to form 4H-pyran derivatives almost quantitatively.

Although the <u>formal</u> addition reactions of carbanions to nonactivated olefins are often utilized for organic syntheses,$^{1)}$ the <u>real</u> addition reactions of nucleophiles to nonactivated olefins occur quite reluctantly because of their electronic repulsion.$^{2)}$ However, we have found herein a novel and unique reaction assisted by CuI and aprotic polar solvent,$^{3)}$ in which two molecules of carbanions <u>2</u> derived from cyclic 1,3-dicarbonyl compounds add geminally to nonac-

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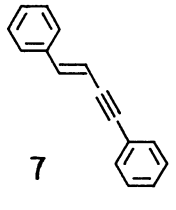
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tivated vinylbromides (**1**), 3-acetyl-4-nonen-2-one (**8a**), or 4-nonen-2-one (**8b**) to give 1,1-disubstituted alkanes (**4**) in good yields (Table 1).

Generally the reactions were performed as follows; to a carbanion solution prepared from 1,3-dicarbonyl compound **2** (3.0 mmol) and NaH (120 mg) in HMPA (2 cm^{-3}), dry CuI (3.0 mmol, 571 mg) and vinyl bromide **1** (1.0 mmol) were added, and heated at 120 °C under a nitrogen atmosphere. When the vinyl bromide was consumed completely, ca. 10% HCl aq. solution saturated with NaCl was added, and the organic layer was extracted with benzene. The extract was dried, evaporated, and the residue was purified by passing through a silica-gel column using CH_2Cl_2/hexane as an eluent. The products were assigned as 1,1-disubstituted alkanes **4** from their spectral and analytical data.[4] Further structure proof of **4** was made by the acid-catalyzed intramolecular dehydration to 4H-pyran derivatives **5**;[5] heating of **4a** in benzene for ca. 3 h in the presence of cat. amounts of sulfuric acid gave **5a** in a quantitative yield.

When the ratio of the carbanion and copper salt to the vinyl bromide was varied, the product distribution suffered significant changes. Thus, when 1-bromo-2-phenylethene was reacted with an equimolar amount of sodium dimedonide and copper(I) iodide, tetralone derivatives (**6**)[6] and conjugated alkenyne (**7**)[7] were obtained in 15% and 11% yields respectively (run 1). With 2.0 equiv. of carbanion and copper(I) iodide was used, 27% of **7** and 46% of **4a** were formed (run 2). And with 3.0 equiv. of the carbanion and copper(I) iodide, only **4a** was produced in 86% yield (run 5). Therefore, 3.0 equiv. of the reagents were preferably used toward the substrates under the standard conditions.

The reaction proceeded not only with moderately activated vinyl bromides such as **1a**, **1b**, or **1c** but also with nonactivated vinyl bromide such as 1-bromo-1-octene (**1d**). However, the reaction did not undergo smoothly with secondary vinyl bromides such as 1-alkyl-1-bromo-2-phenylethene and 2-bromo-1-octene, the complex mixtures being the only product obtained.

The carbanions derived from open chain 1,3-dicarbonyl compounds such as 2,4-pentanedione and dimethyl malonate gave poor results, which might be attributed to the chelate formation between 1,3-dicarbonyl compound and copper salt.

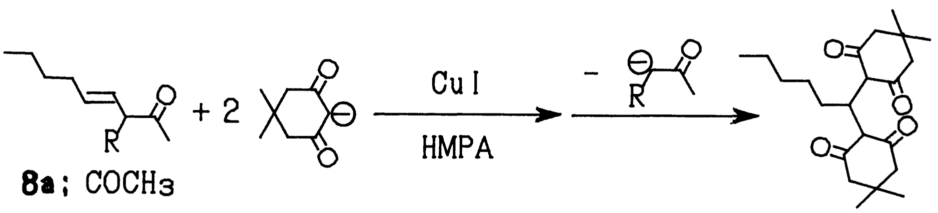
In the present reaction HMPA is not essential as the reaction medium. In other aprotic polar solvent systems, however, the product **4a** was obtained only in fair to moderate yields; reactions of 1-bromo-2-phenylethene with 3.0 equiv. of sodium dimedonide and CuI in DMSO for 2 h gave **4a** in 53% yield. In DMF for 7 h and in THF / HMPA (1:1) for 5 h the respective yields were 73% and 40%.

Table 1. Reactions of 1,3-dicarbonylmethanides with vinylbromides[a)]

Run	Vinyl bromide 1 (mmol) R^1	R^2		Carbanion 2 (mmol) R^3 R^4		CuI /mmol	Time /h	Product (%)[b)]	
1	Ph	H	1a (1.0)	$CH_2C(Me)_2CH_2$	(1.0)	1.0	24	6 (11)	7 (15)
2	Ph	H	1a (1.0)	$CH_2C(Me)_2CH_2$	(2.0)	2.0	9	4a (46)	7 (27)
3	Ph	H	1a (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	1.0	5	4a (32)	
4	Ph	H	1a (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	2.0	5	4a (56)	
5	Ph	H	1a (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	3.0	5	4a (86)	
6	Ph	H	1a (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	4.0	5	4a (>95)	
7	Ph	H	1a (1.0)	$CH_2CH_2CH_2$	(3.0)	3.0	10		5b (47)
8	Ph	H	1a (1.0)	CH_2CH_2	(3.0)	3.0	5	4c (60)	
9	Ph	Me	1b (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	3.0	8	4d (74)	
10	Ph	Me	1b (1.0)	$CH_2CH_2CH_2$	(3.0)	3.0	8	4e (46)	
11	Ph	CHMe	1c (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	3.0	5	4f (70)	
12	$CH_3(CH_2)_5$	H	1d (1.0)	$CH_2C(Me)_2CH_2$	(3.0)	3.0	5	4g (46)	

a) HMPA, 2 cm^{-3}; temperature, 120 °C; N_2 atmosphere. b) Yields refer to isolated products.

Quite surprising results were obtained when 3-acetyl-4-nonen-2-one (8a) or 4-nonen-2-one (8b) was reacted with sodium dimedonide; both ketones afforded 2,2'-(1,1-hexanediyl)-bis-5,5-dimethyl-1,3-cyclohexanedione (4h) as common product in 82% and 22% yields respectively. Replacement of the acetonyl group by the stabilized carbanion did occur!



8a; $COCH_3$

8b; H

2a

4h

Although the mechanism is not clear at present, this novel addition reaction is unique in its reaction mode and may provide potentials as a simple useful tool for the preparation of some substituted 4H-pyran ring systems.

References

1) B. M. Trost and S. J. Martin, J. Am. Chem. Soc., 106, 4263 (1984), and references therein.

2) Strong nucleophiles such as organolithium compounds or organomagnesium halides undergo addition reactions to non-activated olefins in only limited cases; B. J. Wakefield, "Organolithium Methods," Academic Press, Harcourt Brace Jovanovich, Publishers, London (1988), Chap. 4; H. Lehmkuhl, "Olefin Insertion into Organyl Metal Bonds," in "Organometallics in Organic Synthesis," ed by A. de Meijere and H. tom Dieck, Springer-Verlag, Berlin (1987), p. 185.

3) As for copper(I) iodide promoted substitution reactions of vinyl halides, see: T. Ogawa, K. Hayami, and H. Suzuki, Chem. Lett., 1989, 769, and references therein.

4) Spectral and analytical data of some representative products are as follows: **4a**: colorless crystals, mp 169-171 °C. ^{1}H NMR (CDCl$_3$) δ = 0.69 (S, 6H), 0.99 (s, 6H), 2.2 (m, 8H), 3.32 (d, J= 8.9 Hz, 2H), 4.37 (t, J= 8.9 Hz, 1H), 7.05-7.21 (m, 5H), and 12.78 (bs, 2H); IR (KBr) 3355, 2940, 1580, 1380, 1360, 1245, 925, and 695 cm^{-1}; MS (rel. intensity) 382 (M$^+$, 0.2), 291 (2), 242 (6), 185 (4), and 83 (100). Found: C, 75.56; H, 7.97%. Calcd for $C_{24}H_{30}O_4$: C, 75.40; H, 7.91%. **4c**: colorless crystals, mp 217-219 °C. ^{1}H NMR (CDCl$_3$) δ = 2.40-2.50 (m, 8H), 3.00 (d, J= 8.5 Hz, 2H), 4.27 (t, J= 8.5 Hz, 1H), 7.07-7.36 (m, 5H), 11.64 (bs, 2H); IR (KBr) 1610, 1570, 1390, 1350, and 1285 cm^{-1}; CI-MS (rel. intensity) 299 (M$^+$+1, 7), 201 (65), and 99 (100). Found: C, 72.49; H, 6.08%. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08%. **4g**: colorless crystals, mp 84-86 °C. ^{1}H NMR (CDCl$_3$) δ = 0.76 (t, J= 6.7 Hz, 3H), 0.967 (s, 6H), 0.956 (s, 6H), 1.12 (m, 10H), 1.90 (dt, J=7.7 and 7.7, 2H), 2.14 (ABq, J= 17 Hz, 4H), 2.21 (ABq, 17 Hz, 4H), 3.81 (t, J= 7.9 Hz, 1H), 12.4 (bs, 2H); IR (KBr) 1600, 1580, 1395, 1375, and 1260 cm^{-1}; MS (rel. intensity) 390 (M$^+$, 8), 291 (15), 250 (23), 193 (40), 165 (51), 83 (100). Found: C, 73.51; H, 9.67%. Calcd for $C_{24}H_{38}O_4$: C, 73.81; H, 9.81%. **6**: colorless crystals, mp 148-151 °C. ^{1}H NMR (CDCl$_3$) δ = 1.03 (s, 6H), 2.55 (s, 2H), 2.76 (s, 2H), and 7.26-8.35 (m, 12H); IR (KBr) 1670, 1590, 1440, 1340, 1265, 1240, and 760 cm^{-1}; MS (rel. intensity) 326 (M$^+$, 100), 270 (13), 242 (90), 165 (17), 135 (9), and 119 (8). **5b**: pale yellow crystals, mp 149-151 °C. ^{1}H NMR (CDCl$_3$) δ= 1.92-2.53 (m, 12H), 2.82 (d, J= 4.0 Hz, 2H), 4.09 (t, J= 4.0 Hz, 1H), 6.79-7.27 (m, 5H); IR (KBr) 1670, 1650, 1375, 1195, 1165, 1125, and 955 cm^{-1}; CI-MS (rel. intensity) 309 (M$^+$+1, 65), 217 (100), and 91 (8). Found: C, 77.56; H, 6.55%. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54%.

5) T. S. Vasundhara and D. B. Parihar, J. Chromatogr., 176, 225 (1979).

6) Formation of **6** is reasonably understood as a consequence of the addition reaction of intermediate **3** with another molecule of 1-bromo-2-phenylethene, and subsequent dehydrobromination and dehydration.

7) T. Ogawa, K. Kumiko, M. Tanaka, K. Hayami, and H. Suzuki, Synth. Commun., 19, 2199 (1989).

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