H3), 4.72 (dd, J = 18, 2.5, H18a), 4.82 (dd, J = 18, 2.5, H18b), 5.04 (tsep, J = 7.2, 1.0, H13), 5.45 (br s, H4); UV (EtOH) 227 (ε 6195), 208 (5162).

Reduction of 1 to 3. A solution of 14.3 mg of **1** in 1 mL of absolute ethanol was treated with 5 mg of $NaBH_4$. The mixture was stirred at room temperature for 80 min and then quenched with several drops of 5% HCl. After addition of 3 mL of water, the product was extracted four times with 3-mL portions of diethyl ether and then dried over anhydrous K_2CO_3. Filtration and evaporation of solvent left 12.7 mg of nearly pure **3**, which after HPLC had $[\alpha]_D$ 24.3° (c 1.07, $CHCl_3$).

Reduction of 2 to 4. This was analogous to preparation of **3** from **1** above. From 25 mg **2**, 22 mg of crude **4** was obtained. After purification by HPLC, its spectral properties matched those of natural **4**.

Acetylation of 3 to 4. To a solution of 13.0 mg of **3** in 1 mL of dry pyridine, 50 μL of freshly distilled acetic anhydride was added, and the reaction was allowed to proceed at room temperature for 17 h. Methylene chloride (10 mL) was added, and the solution was washed with 10% HCl (2×), saturated $CuSO_4$ (2×), and H_2O (1×) to remove the pyridine. After drying with anhydrous $MgSO_4$ and removal of solvent, 12 mg of **4** remained, about 95% pure by ^1H NMR. This material was purified by HPLC on Partisil M9 and Lichrosorb-ODS. From natural **3**, $[\alpha]_D$ 14.2° (c 1.21, $CHCl_3$); from synthetic **3**, $[\alpha]_D$ 20.5° (c 0.57, $CHCl_3$).

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Registry No. 1, 85443-36-3; 2, 85443-37-4; 3, 83845-31-2; 4, 65043-52-9.

Supplementary Material Available: Tables listing final atomic coordinates and thermal parameters (Table A) and bond distances and angles (Table B) for 1 (6 pages). Ordering information is given on any current masthead page.

An Efficient Method for Synthesis of Symmetrical Diketones via Reaction of α-Amino-α-arylacetonitriles (Masked Acyl Anion Equivalents) with Alkyl Dibromides

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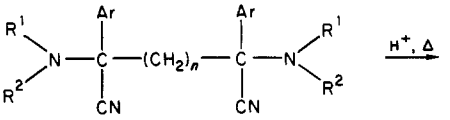
Anions derived from α-amino-α-arylacetonitriles are related as masked acyl anion equivalents. The utility of their anions in the formation of carbon–carbon bonds has been reported.[1] The utilization of such masked acyl anions is, however, not universal. The choice of substituents α to the nitrile group appears to be critical. We report here a new synthetic method for symmetrical diketones by reaction of the masked acyl anions formed from α-(dimethylamino)-α-arylacetonitrile (**1**) and derivatives with alkyl dibromides followed by hydrolysis. Many synthetic routes to 1,4-diketones have been reported.[2] However, this method is found to be useful for preparation of not only 1,4-diketones but also other symmetrical diketones having longer polymethylene chains.

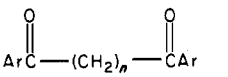
Various α-amino-α-phenylacetonitriles (**1a–e**) were prepared for investigation of the influence of the amino groups on the preferential formation of 2,5-diamino-2,5-diphenyladiponitriles (**2**) as the precursors of the corresponding diketones. The reactions of **1a–e** with 1,2-dibromoethane were carried out in a mixture of tetrahydrofuran (THF) and hexamethylphosphoramide (HMPA) containing lithium diisopropylamide (LDA). When the amino group was dimethylamine (**1a**), the yield of **2** was superior to that obtained in the case of diethyl-

Scheme I

1a, $R^1 = R^2$ = Me; Ar = Ph; 83%
b, $R^1 = R^2$ = Et; Ar = Ph; 81%
c, $R^1, R^2 = -(CH_2)_4-$; Ar = Ph; 81%
d, $R^1, R^2 = -(CH_2)_2O(CH_2)_2-$; Ar = Ph; 87%
e, R^1 = Me; R^2 = Ar = Ph; 67%
10a, $R^1 = R^2$ = Me; Ar = *p*-MeOPh; 75%
11a, $R^1 = R^2$ = Me; Ar = *p*-ClPh; 88%
12a, $R^1 = R^2$ = Me; Ar =  ; 74%



2a, $R^1 = R^2$ = Me; Ar = Ph; n = 2; 64%
b, $R^1 = R^2$ = Et; Ar = Ph; n = 2; 22%
c, $R^1, R^2 = -(CH_2)_4-$; Ar = Ph; n = 2; 48%
3a, $R^1 = R^2$ = Me; Ar = Ph; n = 3; 80%
4a, $R^1 = R^2$ = Me; Ar = Ph; n = 6; 88%
5a, $R^1 = R^2$ = Me; Ar = Ph; n = 10; >90%[a]
13a, $R^1 = R^2$ = Me; Ar = *p*-MeOPh; n = 2; 37%
14a, $R^1 = R^2$ = Me; Ar = *p*-ClPh; n = 2; 59%
15a, $R^1 = R^2$ = Me; Ar =  ; n = 2; 24%
16a, $R^1 = R^2$ = Me; Ar =  ; n = 3; 78%



6, Ar = Ph; n = 2; 92% from **2a**, 88% from **2c**
7, Ar = Ph; n = 3; 84%
8, Ar = Ph; n = 6; 98%
9, Ar = Ph; n = 10; 84%[b]
17, Ar = *p*-MeOPh; n = 2; 76%
18, Ar = *p*-ClPh; n = 2; 78%
19, Ar =  ; n = 2; 93%
20, Ar =  ; n = 3; 86%

[a] Not isolated. [b] Overall yield from **1a**.

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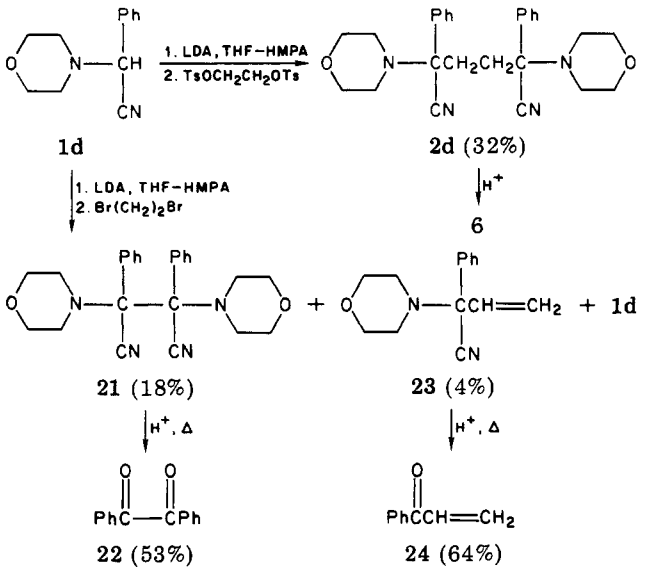
Scheme II



amine (**1b**) and pyrrolidine (**1c**) (see Scheme I). The subsequent hydrolysis of **2** in a mixture of THF and 30% oxalic acid gave 1,4-diphenyl-1,4-butanedione (**6**) in good yield. Interestingly, the reaction of α-morpholino-α-phenylacetonitrile (**1d**) with 1,2-dibromoethane did not give a **2** but afforded 2,3-dimorpholino-2,3-diphenylsuccinonitrile (**21**), 2-morpholino-2-phenyl-3-butenenitrile (**23**), and a substantial amount of unreacted **1d** (see Scheme II). Hydrolysis of **21** and **23** gave benzil (**22**) and vinyl phenyl ketone (**24**), respectively. The reaction of **1d** with 1,2-bis(tosyloxy)ethane on the other hand, gave 2,5-dimorpholino-2,5-diphenyladiponitrile (**2d**) together with a substantial amount of unreacted **1d**. The reaction of α-(*N*-methylanilino)-α-phenylacetonitrile (**1e**) with 1,2-dibromoethane did not proceed at all. Thus, the formation of **2** was affected significantly by the type of amino group in **1**.

The reaction of **1a** with 1,3-dibromopropane was superior to that with 1,2-dibromoethane, giving 1,5-bis(dimethylamino)-1,5-dicyano-1,5-diphenylpentane (**3a**) in 80% yield. Subsequent hydrolysis of **3a** gave 1,5-diphenyl-1,5-pentanedione (**7**) in 84% yield. Likewise, the reaction with 1,6-dibromohexane and 1,10-dibromodecane gave 1,8-bis(dimethylamino)-1,8-dicyano-1,8-diphenyloctane (**4a**) and 1,12-bis(dimethylamino)-1,12-dicyano-1,12-diphenyldodecane (**5a**) in good yields. Interestingly, **5a** was not isolated as a pure product, because part of the **5a** was hydrolyzed in a silica gel column, and a mixture of **5a** and the corresponding diketone (**9**) was always obtained. It has been reported that the silica gel procedure for hydrolysis transforms α-disubstituted aminonitriles directly into ketones.[7] In this work, however, only **5a** was hydrolyzed on a silica gel column. The hydrolysis of **4a** and crude **5a** containing a small amount of the diketone **9** afforded 1,8-diphenyl-1,8-octanedione (**8**) and 1,12-diphenyl-1,12-dodecanedione (**9**) in 98% and 84% overall yields from **1a**, respectively. When the number of methylene groups between the two bromines was larger than two, the reaction with **1a** proceeded more favorably. These results suggest that introduction of additional CH_2 groups between two bromines diminishes the repulsion toward access to the dibromides of two carbanions formed from **1a** having bulky substituents such as cyano, dimethylamino, and phenyl.

In addition, the treatment of α-(4-methoxyphenyl)-, α-(4-chlorophenyl)-, and α-(2-thienyl)-α-(dimethylamino)acetonitriles (**10a**, **11a**, and **12a**) with 1,2-dibromoethane and/or 1,3-dibromopropane afforded 2,5-bis(4-methoxyphenyl)-, 2,5-bis(4-chlorophenyl)-, and 2,5-bis(2-thienyl)-2,5-bis(dimethylamino)adiponitriles (**13a**, **14a**, and **15a**) and 1,5-dicyano-1,5-bis(dimethylamino)-1,5-bis(2-thienyl)pentane (**16a**), respectively. Hydrolysis of **13a**, **14a**, **15a**, and **16a** gave, in high yields, 1,4-bis(4-methoxyphenyl)-, 1,4-bis(4-chlorophenyl)-, and 1,4-bis(2-thienyl)-1,4-butanediones (**17**, **18**, and **19**) and 1,5-bis(2-thienyl)-1,5-pentanedione (**20**), respectively.

Experimental Section

All melting points were taken on a Yanagimoto micro-melting-point apparatus and are uncorrected. ^1H NMR spectra were determined with a Hitachi R-24 (60 MHz) nuclear magnetic resonance spectrometer by using tetramethylsilane (Me_4Si) as an internal standard. IR and mass spectra were taken with diffraction grating infrared (Japan Spectroscopic Co. Ltd., Type A-202) and high resolution mass (Hitachi, Type RMU-7M) spectrometers, respectively. Microanalytical data were obtained by using a Perkin-Elmer 240 elemental analyzer.

(I) Preparation of α-Amino-α-arylacetonitriles. Those used as the starting materials in this work were prepared according to the procedure reported in the literature[3] and are known compounds. Their physical properties agreed with those reported in the literature: α-(dimethylamino)-α-phenylacetonitrile (**1a**), bp 80–82 °C (2 mmHg) [lit.[3] bp 78–79 °C (1 mmHg)]; α-(diethylamino)-α-phenylacetonitrile (**1b**), bp 80–82 °C (5 mmHg) [lit.[4] bp 78–80 °C (0.08 mmHg)]; α-pyrrolidino-α-phenylacetonitrile (**1c**), bp 92–94 °C (2 mmHg) [lit.[8] bp 101–103 °C (0.01 mmHg)]; α-morpholino-α-phenylacetonitrile (**1d**), mp 68–69 °C (lit.[5] mp 68–70 °C); α-(*N*-methylanilino)-α-phenylacetonitrile (**1e**), mp 66–67 °C (lit.[6] mp 67 °C); α-(dimethylamino)-α-(4-methoxyphenyl)acetonitrile (**10a**), mp 34–35 °C (lit.[5] mp 32–35 °C); α-(dimethylamino)-α-(4-chlorophenyl)acetonitrile (**11a**), mp 46–47 °C (lit.[9] 46–48 °C); α-(dimethylamino)-α-(2-thienyl)acetonitrile (**12a**), bp 68–70 °C (3 mmHg) [lit.[10] bp 107–108 °C (10 mmhg)]. Boiling points of **1b** and **1c** do not agree with those in the literatures as described above, but they gave satisfactory microanalyses as follows. Anal. Calcd for $C_{12}H_{16}N_2$ (**1b**): C, 76.55; H, 8.57; N, 14.88. Found: C, 76.51; H, 8.53; N, 14.75. Calcd for $C_{12}H_{14}N_2$ (**1c**): C, 77.38; H, 7.58; N, 15.04. Found: C, 77.45; H, 7.56; N, 14.99.

(II) Reaction of α-Amino-α-Arylacetonitriles with Alkyl Dibromides. Preparation of 2,5-Bis(dimethylamino)-2,5-diphenyladiponitrile (2a) as a Typical Example. Under dry nitrogen, diisopropylamine (1.5 mL, 9 mmol) dissolved in a mixture of 5 mL each of dry THF and HMPA was treated with *n*-butyllithium (6 mL of a 1.67 M solution in hexane, 9 mmol) at −78 °C, the mixture was again cooled to −78 °C, α-(dimethylamino)-α-phenylacetonitrile (**1a**; 1.28 g, 8 mmol) dissolved in THF (1 mL) was added, and the reaction mixture was stirred for 15 min at −78 °C and for 1 h at 0 °C. To the mixture again cooled to −78 °C was added 1,2-dibromoethane (0.752 g, 4 mmol) dropwise. After the mixture was stirred for 20 min at −78 °C, the stirring was continued for several hours at the room temperature until the complete disappearance of **1a** was confirmed by means of TLC. The reaction mixture was poured into ice and water and then extracted with diethyl ether (3 × 50 mL). The combined ether layers were washed with brine and dried with anhydrous sodium sulfate. After the ether was distilled off, the residue was purified by means of column chromatography and

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recrystallization from ethyl alcohol. Thus, 2,5-bis(dimethylamino)-2,5-diphenyladiponitrile (**2a**) was obtained in 64% yield (886 mg): mp 134–136 °C; IR (KBr) ν_{CN} 2220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.80 (s, 4 H), 2.13 (s, 12 H), 7.50 (s-like, 10 H); MS, *m/e* 292 (M^+ – 2HCN). Anal. Calcd for $C_{22}H_{26}N_4$: C, 76.27; H, 7.56; N, 16.17. Found: C, 76.05; H, 7.69; N, 16.26.

2,5-Bis(diethylamino)-2,5-diphenyladiponitrile (2b). By use of the same procedure, the reaction of α-(diethylamino)-α-phenylacetonitrile (**1b**; 1.50 g, 8 mmol) with 1,2-dibromoethane (0.752 g, 4 mmol) was carried out to give 709 mg (22% yield) of **2b**: mp 133–135 °C; IR (KBr) ν_{CN} 2200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20 (t, 12 H, J = 8 Hz), 2.25 (s, 4 H), 3.52 (q-like, 8 H, J = 8 Hz), 7.60 (s, 10 H). Anal. Calcd for $C_{26}H_{34}N_4$: C, 77.57; H, 8.51; N, 13.92. Found: C, 77.71; H, 8.53; N, 13.76.

2,5-Dipyrrolidino-2,5-diphenyladiponitrile (2c). By use of the same procedure, the reaction of α-pyrrolidino-α-phenylacetonitrile (**1c**; 1.49 g, 8 mmol) with 1,2-dibromoethane (0.752 g, 4 mmol) was carried out to give 765 mg (48% yield) of **2c**: mp 132–135 °C; IR (KBr) ν_{CN} 2250 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.5–2.1 (m, 12 H), 2.2–2.7 (m, 8 H), 7.61 (s, 10 H); MS, *m/e* 344 ($M^{+\cdot}$ – 2HCN). Anal. Calcd for $C_{26}H_{30}N_4$: C, 78.36; H, 7.59; N, 14.06. Found: C, 78.09; H, 7.65; N, 14.26.

2,5-Dimorpholino-2,5-diphenyladiponitrile (2d). By use of the same procedure, the reaction of α-morpholino-α-phenylacetonitrile (**1d**; 1.62 g, 8 mmol) with 1,2-bis(tosyloxy)ethane (1.48 g, 4 mmol) was carried out to give 550 mg (32% yield) of **2d**: mp 160–162 °C; IR (KBr) ν_{CN} 2200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.89 (s, 4 H), 2.45 (t-like, 8 H, J = 4 Hz), 3.72 (t, 8 H, J = 4 Hz), 7.55 (s, 10 H); MS, *m/e* 376 ($M^{+\cdot}$ – 2HCN). Anal. Calcd for $C_{26}H_{30}N_4O_2$: C, 72.53; H, 7.02; N, 13.01. Found: C, 72.39; H, 7.10; N, 13.12.

1,5-Bis(dimethylamino)-1,5-dicyano-1,5-diphenylpentane (3a). By use of the same procedure, the reaction of α-(dimethylamino)-α-phenylacetonitrile (**1a**; 1.282 g, 8 mmol) with 1,3-dibromopropane (0.808 g, 4 mmol) was carried out to give 1.154 g (80% yield) of **3a**: mp 105–107 °C; IR (KBr) ν_{CN} 2220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.6–2.1 (m, 6 H), 2.27 (s-like, 12 H), 7.44 (s, 10 H); MS, *m/e* 304 ($M^{+\cdot}$ – 2HCN). Anal. Calcd for $C_{23}H_{28}N_4$: C, 76.63; H, 7.83; N, 15.54. Found: C, 76.43; H, 7.90; N, 15.67.

1,8-Bis(dimethylamino)-1,8-dicyano-1,8-diphenyloctane (4a). By use of the same procedure, the reaction of α-(dimethylamino)-α-phenylacetonitrile (**1a**; 1.282 g, 8 mmol) with 1,6-dibromohexane (0.976 g, 4 mmol) was carried out to give 1.419 g (88% yield) of **4a**: mp 98–100 °C; IR (KBr) ν_{CN} 2230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (br s, 8 H), 1.50–2.0 (br m, 4 H), 2.25 (s, 12 H), 7.40 (s-like, 10 H). Anal. Calcd for $C_{26}H_{34}N_4$: C, 77.57; H, 8.51; N, 13.92. Found: C, 77.62; H, 8.50; N, 13.94.

1,12-Bis(dimethylamino)-1,12-dicyano-1,12-diphenyldodecane (5a). By use of the same procedure, the reaction of α-(dimethylamino)-α-phenylacetonitrile (**1a**; 1.282 g, 8 mmol) with 1,10-dibromodecane (1.2 g, 4 mmol) was carried out to give ca. 2.0 g of crude **5a** (above 90% yield). The compound **5a** was hydrolyzed in a silica gel column, and a mixture of **5a** and the corresponding diketone (**9**) was obtained. The mixture was not purified and directly led to the diketone **9** by subsequent hydrolysis.

2,5-Bis(dimethylamino)-2,5-bis(4-methoxyphenyl)adiponitrile (13a). By use of the same procedure, the reaction of α-(dimethylamino)-α-(4-methoxyphenyl)acetonitrile (**10a**; 1.522 g, 8 mmol) with 1,2-dibromoethane (0.752 g, 4 mmol) was carried out to give 0.602 g (37% yield) of **13a**: mp 137–139 °C; IR (KBr) ν_{CN} 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.78 (s, 4 H), 2.16 (s, 12 H), 3.85 (s, 6 H), 6.90 (d, 4 H, J = 9 Hz), 7.38 (d, 4 H, J = 9 Hz). Anal. Calcd for $C_{24}H_{30}N_4O_2$: C, 70.91; H, 7.44; N, 13.78. Found: C, 70.73; H, 7.59; N, 13.57.

2,5-Bis(dimethylamino)-2,5-bis(4-chlorophenyl)adiponitrile (14a). By use of the same procedure, the reaction of α-(4-chlorophenyl)-α-(dimethylamino)acetonitrile (**11a**; 0.752 g, 4 mmol) was carried out to give 0.602 g (59% yield) of **14a**: mp 160–162 °C; IR (KBr) ν_{CN} 2230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.78 (s, 4 H), 2.19 (s, 12 H), 7.44 (s, 8 H); MS, *m/e* 359 ($M^{+\cdot}$ – 2HCN). Anal. Calcd for $C_{22}H_{24}N_4Cl_2$: C, 63.62; H, 5.79; N, 13.49. Found: C, 63.42; H, 5.90; N, 13.61.

2,5-Bis(dimethylamino)-2,5-bis(2-thienyl)adiponitrile (15a). By use of the same procedure, the reaction of α-(dimethylamino)-α-(2-thienyl)acetonitrile (**12a**; 1.33 g, 8 mmol) and 1,2-dibromoethane (0.752 g, 4 mmol) was carried out to give 0.344 g (24% yield) of **15a**: mp 120–122 °C; IR (KBr) ν_{CN} 2220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.95 (s, 4 H), 2.30 (s, 12 H), 7.01 (t, 2 H, J = 4 Hz), 7.25–7.55 (m, 4 H). Anal. Calcd for $C_{18}H_{22}N_4S_2$: C, 60.30; H, 6.18; N, 15.63. Found: C, 60.17; H, 6.31; N, 15.52.

1,5-Bis(dimethylamino)-1,5-dicyano-1,5-bis(2-thienyl)pentane (16a). By use of the same procedure, the reaction of α-(dimethylamino)-α-(2-thienyl)acetonitrile (**12a**; 1.33 g, 8 mmol) with 1,3-dibromopropane (0.808 g, 4 mmol) was carried out to give 1.162 g (78% yield) of **16a**: mp 122–124 °C; IR (KBr) ν_{CN} 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.58 (t-like, 4 H, J = 6 Hz), 1.80–2.20 (m, 2 H), 2.28 (s, 12 H), 6. 90 (t, 2 H, J = 5 Hz), 7.18 (d, 2 H, J = 5 Hz), 7.32 (d, 2 H, J = 5 Hz). Anal. Calcd for $C_{19}H_{24}N_4S_2$: C, 61.26; H, 6.49; N, 15.04. Found: C, 61.18; H, 6.47; N, 15.19.

2,3-Dimorpholino-2,3-diphenylsuccinonitrile (21) and 2-Morpholino-2-phenyl-3-butenenitrile (23). By use of the same procedure, the reaction of α-morpholino-α-phenylacetonitrile (**1d**; 1.618 g, 8 mmol) with 1,2-dibromoethane (0.752 g, 4 mmol) was carried out to give 290 mg (18% yield) of **21**, 36 mg (4% yield) of **23**, and a substantial amount of unreacted **1d**. Physical properties of **21** are as follows: mp 153–154 °C; IR (KBr) ν_{CN} 2260 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.62 (d, 8 H, J = 9 Hz), 3.72 (d, 8 H, J = 9 Hz), 7.40 (s, 10 H); MS, *m/e* 402 ($M^{+\cdot}$). Anal. Calcd for $C_{24}H_{26}N_4O_2$: C, 71.62; H, 5.51; N, 13.92. Found: C, 71.30; H, 5.39; N, 13.74.

Physical properties of **23** are as follows: viscous oil; IR (KBr) ν_{CN} 2260 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.55 (t, 2 H, J = 4 Hz), 2.64 (t, 4 H, J = 4 Hz), 3.75 (t, 4 H, J = 4 Hz), 5.30 (dd, 1 H, J = 8,3 Hz), 5.80 (d, 1 H, J = 3 Hz), 5.85 (d, 1 H, J = 8 Hz), 7.3–7.8 (m, 5 H); MS, *m/e* 228 ($M^{+\cdot}$). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.41; H, 6.89; N, 12.49.

(III) Preparation of Symmetrical Diketones by Hydrolysis. The hydrolysis was carried out according to the procedure reported in the literature.[7] The typical procedure is as follows: a mixture of **2a** (150 mg, 0.4 mmol) dissolved in a solution of 3 mL each of THF and 30% aqueous oxalic acid was gently refluxed for 90 min and then extracted with diethyl ether (3 × 15 mL). The ether layer was washed with brine and dried with anhydrous sodium sulfate. After the solvent was distilled off, 1,4-diphenyl-1,4-butanedione (**6**) was recrystallized from ethanol and obtained in 92% yield (95 mg); mp 143–145 °C (lit.[8] mp 144–145 °C).

1,5-Diphenyl-1,5-pentanedione (7). By use of the same procedure, the hydrolysis of **3a** (150 mg, 0.4 mmol) was carried out to give **7**: 105 mg (84% yield); mp 64–66 °C (lit.[11] mp 65–66 °C).

1,8-Diphenyl-1,8-octanedione (8). By use of the same procedure, the hydrolysis of **4a** (202 mg, 0.5 mmol) was carried out to give **8**: 147 mg (98% yield); mp 86–87 °C (lit.[16] mp 85–87 °C).

1,12-Diphenyl-1,12-dodecanedione (9). By use of the same procedure, crude **5a**, which was not purified, was directly hydrolyzed to give **9**: 84% overall yield from 1a; mp 94–96 °C (lit.[12] mp 96–97 °C).

1,4-Bis(4-methoxyphenyl)-1,4-butanedione (17). By use of the same procedure, the hydrolysis of **13a** (162 mg, 0.4 mmol) was carried out to give **17**: 90 mg (76% yield); mp 153–155 °C (lit.[9] mp 154–155 °C).

1,4-Bis(4-chlorophenyl)-1,4-butanedione (18). By use of the same procedure, the hydrolysis of **14a** (200 mg, 0.5 mmol) was carried out to give **18**: 116 mg (78% yield); mp 148–149 °C (lit.[13] mp 150 °C).

1,4-Bis(2-thienyl)-1,4-butanedione (19). By use of the same procedure, the hydrolysis of **15a** (108 mg, 0.3 mmol) was carried out to give **19**: 70 mg (93% yield); mp 130–132 °C (lit.[11] mp 131–132 °C).

1,5-Bis(2-thienyl)-1,5-pentanedione (20). By use of the same procedure, the hydrolysis of **16a** (112 mg, 0.3 mmol) was carried out to give **20**: 79 mg (86% yield); mp 88–89 °C (lit.[11] mp 88–89 °C).

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Benzil (22) and Vinyl Phenyl Ketone (24). By use of the same procedure, the hydrolyses of **21** (161 mg, 0.4 mmol) and **23** (114 mg, 0.5 mmol) were carried out to give **22**: [45 mg (53% yield); mp 92–93 °C (lit.[14] mp 93–95 °C)] and **24**: 42 mg (64% yield); bp 98–100 °C (10 mmHg) [lit.[15] bp 114–115 °C (17 mmHg)].

Registry No. **1a**, 827-36-1; **1b**, 5097-99-4; **1c**, 31466-31-6; **1d**, 15190-10-0; **1e**, 15190-67-7; **2a**, 85356-09-8; **2b**, 85356-10-1; **2c**, 85356-11-2; **2d**, 85356-12-3; **3a**, 85356-13-4; **4a**, 85356-14-5; **5a**, 85356-15-6; **6**, 495-71-6; **7**, 6263-83-8; **8**, 6268-58-2; **9**, 66901-95-9; **10a**, 15190-05-3; **11a**, 15190-08-6; **12a**, 15190-02-0; **13a**, 85356-16-7; **14a**, 85356-17-8; **15a**, 85356-18-9; **16a**, 85356-19-0; **17**, 15982-64-6; **18**, 24314-35-0; **19**, 13669-05-1; **20**, 37709-57-2; **21**, 85356-20-3; **22**, 134-81-6; **23**, 85356-21-4; **24**, 768-03-6; $TsOCH_2CH_2OTs$, 6315-52-2; 1,2-dibromoethane, 106-93-4; 1,3-dibromopropane, 109-64-8; 1,6-dibromohexane, 629-03-8; 1,10-dibromodecane, 4101-68-2.

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Cross-Coupling Reaction of 1,3-Butadien-2-ylmagnesium Chloride with Alkyl or Aryl Halides by Lithium Chloride-Cupric Chloride (Li_2CuCl_4), a Superior Catalyst

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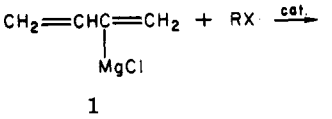
Cross-coupling reactions of Grignard reagents have been reported with alkyl, allyl, alkenyl, and aryl halides in the presence of various kinds of transition-metal catalysts.[1-8] The authors also reported that copper(I) iodide (CuI), and tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) were effective catalysts in the cross-coupling reactions of 1,3-butadien-2-ylmagnesium chloride (**1**) with alkyl and aryl iodides, respectively.[9]

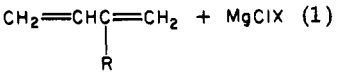
In the course of our studies in exploring more efficient and selective catalyst systems, Li_2CuCl_4, initially reported by Tamura and Kochi,[2] was found to be a very effective and selective catalyst for the coupling reactions of **1** with primary alkyl iodides or bromides. In the cross-coupling reactions of Grignard reagent, Li_2CuCl_4 generally appears to be quite a good catalyst. Fouquet[10] and Chapman[11] improved the yields by the use of tosylate as a leaving group. Selective coupling of ω-bromo acid was also reported by Baer.[12]

In this note, we report the syntheses of 2-substituted 1,3-butadienes and selective cross-coupling reactions of mixed halides taking advantage of the high reactivity of primary alkyl iodide and bromide.

Cross-Coupling Reactions of 1 with Octyl Halides. The results of the cross-coupling reactions of Grignard reagents with octyl halides are shown in Table I.



1



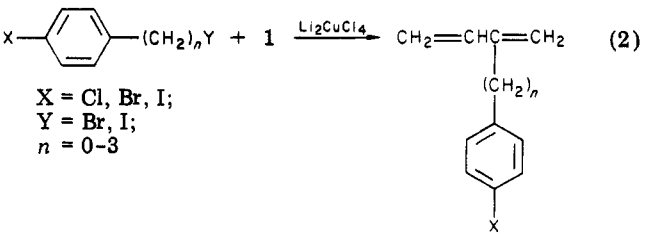
The reactions with CuI as catalyst gave only reasonable yields. Even with the iodide (no. 1, 2) considerably large amounts of the catalyst were required. On the contrary, good to excellent yields could be obtained even with the bromide by employing only small amounts of Li_2CuCl_4 as catalyst (no. 6, 7).

Although a little longer reaction time is required, the Li_2CuCl_4 system has several advantages over the CuI system: namely, moderate reaction temperature, smaller amounts of catalyst, higher yield of the product, and easiness of the separation of the product.

The order of reactivity of the halides was I > Br ≫ Cl, and secondary halides showed much lower reactivity than primary halides.

Cross-Coupling Reactions of 1 with Aryl Halides. The results of the cross-coupling with aryl halides are shown in Table II. Despite the relatively lower reactivities of aryl halides, reasonable yields of the cross-coupled product could still be obtained from aryl iodide substrate (no. 17). The bromide showed considerably lower reactivity than iodides.

Taking advantage of the differences in reactivity, the selective cross-coupling reactions of the aromatic dihalides were investigated (no. 18–22).



(2)

X = Cl, Br, I;
Y = Br, I;
n = 0-3

In the cross-coupling reactions of **1** with halides having both aromatic and aliphatic halogens, yields as high as 87% of the selectively coupled product, namely, 2-halogenoaromatic-substituted butadienes, could be obtained. It was interesting to note that the aromatic halogen was not affected at all in the reaction.

However, with $Pd(PPh_3)_4$ as catalyst, the aromatic iodide preferentially reacted (no. 23).

Cross-Coupling Reactions of 1 with Functional Halides. The cross-coupling reactions of **1** with halides containing other functional groups were also investigated, and the results are given in Table III. The cross-coupling

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