$$\gamma_{R,G} = \frac{\beta_G}{\beta_{G^\circ}} = \frac{mq_G}{mq_{G^\circ}} \qquad (6)$$

The β values were obtained under the same reaction conditions. Choosing the p-phenylene group as G°

$$\gamma_{R,G} = q_G/0.143 = 7q_G \qquad (7)$$

For a comparison of values of γ_R calculated from eq 7 with observed values of γ_R see paragraph at end of paper. The results obtained show that eq 7 is only a crude approximation; calculation of β values is best accomplished by eq 2.

In the calculation of q by the method of Dewar, the carbon atoms in the species -GCH$_2$:- are divided into two sets of $n + 1$ and n atoms. The value of q at the atoms of the n set is zero. Examples are m-phenylene, and 6-substituted 1-naphthylene groups. Sets such as these do show significant values of q, however. We have previously attempted[9] to predict β values for such sets from the equation

$$\beta = m'\sum q_{\mathrm{adj}} + c \qquad (8)$$

where $\sum q_{\mathrm{adj}}$ is the sum of the q's on the carbon atoms adjacent to that carbon atom which bears the reaction site. To determine the validity of eq 8, values of β_G for the ionization of carboxylic acids in 50% v/v EtOH-H$_2$O and the ionization of azaarenes in H$_2$O at 20° were correlated with it. The correlations obtained were not significant. We may reject eq 8 as a means of predicting β values.

We propose that q values for groups such as m-phenylene and 6-substituted 1-naphthylene may be calculated from some reference series for which good values of m and c are available. Values of q for other types of groups for which calculation by the method of Dewar is not possible may also be obtained from eq 2 when β, m, and c are known. Such groups are those which contain triple bonds, and those in which a saturated side chain intervenes between reaction site and ring. For values of q calculated in this manner, see paragraph at end of paper.

It is interesting to note that for the -C≡C-, 4-C$_6$H$_4$C≡C-, and 4-C$_6$H$_4$C≡CC$_6$H$_4$-4- groups a linear relationship exists between their q values and the q values of the corresponding groups with double bonds in place of the triple bonds. Thus

$$q_{C\equiv C-} = nq_{C=C} + d \qquad (9)$$

For a comparison of β values calculated from the q values obtained from eq 2 with observed β values see paragraph at end of paper.

Supplementary Material Available. Data used in correlations with eq 1, results of these correlations, values of γ_R, q values calculated from eq 2, and values calculated from these q values will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $4.00 for photocopy or $2.00 for microfiche, referring to code number JOC-74 -2797.

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Oxidative Decyanation of Arylacetonitriles. A Synthesis of Ligusticumic Acid

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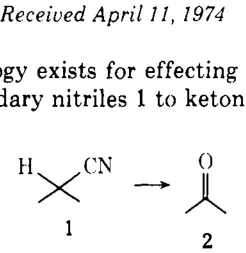
Little methodology exists for effecting the oxidative decyanation of secondary nitriles 1 to ketones 2.[1] As primary nitriles can be monoalkylated to afford secondary nitriles,[2] a procedure capable of effecting this transformation (1 → 2) would render nitriles a member of the class of synthetic intermediates called acyl carbanion equivalents.[3] We now wish to report a convenient synthesis of aryl alkyl ketones and diaryl ketones from substituted arylacetonitriles.

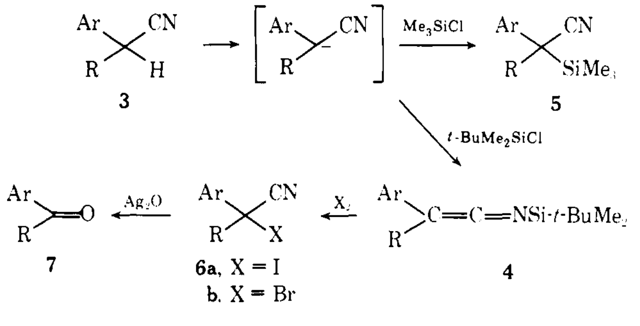


Anions derived from the reaction of secondary arylacetonitriles 3 underwent regioselective N-silylation with *tert*-butyldimethylchlorosilane[4] to provide N-*tert*-butyldimethylsilyl ketenimines 4 in good yield (see Table I) and C-silylation with trimethylchlorosilane to provide α-trimethylsilyl nitriles 5.[5] On bromination or iodination of 4,

Table I
Silylation and Oxidative Decyanation of Arylacetonitriles ArCHRCN

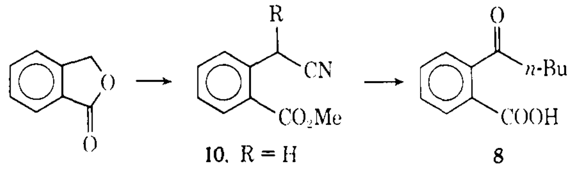
ArCHRCN registry no.	Ar	R	Yield[a] of ketenimine 4, %	Yield of ketone 7, %
1823-91-2	Ph	Me	89	71[b]
51965-61-8	p-FPh	Me	72	79[b]
2184-88-5	p-ClPh	Me	71	61[b]
769-68-6	Ph	Et	73	81[b]
5558-29-2	Ph	i-Pr	78	82[c]
15601-30-6	Ph	n-Oc	76	77[c]
86-29-3	Ph	Ph	90	63[c]
24168-42-1	α-Np	Me	71	63[b]

[a] Isolated by distillation at reduced pressure. [b] Isolated using Girard T reagent. [c] Isolated by thick layer chromatography on Merck silica gel F254.



α-halonitriles **6** are obtained.[6] The treatment of α-iodonitriles **6a** but not the inert α-bromonitriles **6b** with silver oxide in tetrahydrofuran afforded aryl alkyl ketones **7** or diaryl ketones **7** (R = Ar) in good yield (see Table I). Unfortunately, dialkyl ketones could not be made by this procedure.

The use of nitriles as acyl carbanion equivalents was illustrated in a synthesis of the acetogenin,[7] ligusticumic acid (**8**).[8] Phthalide (**9**) was converted to the nitrile ester **10** *via* sequential treatment with sodium cyanide and diazomethane. Alkylation of **10** with *n*-butyl bromide afforded the nitrile **11** in 79% yield. Application of the oxidative decyanation procedure described above and subsequent saponification of the carboxylic ester provided ligusticumic acid (**8**).



9

10, R = H

11, R = *n*-Bu

8

Experimental Section

Infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer. Nmr spectra were determined on a Varian A-60A spectrophotometer. Mass spectra were determined on a Varian MAT CH5 mass spectrometer. Melting points were determined using a Thomas-Hoover apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, Ga.

The following is a representative example of the oxidative decyanation procedure.

***N*-(*tert*-Butyldimethylsilyl)ethylphenylketenimine (4).** To 111 mg (1.1 mmol, 1.1 equiv) of diisopropylamine in 2.5 ml of anhydrous tetrahydrofuran at −78° under a nitrogen atmosphere was added 0.48 ml (1.1 mmol) of 2.29 *M* *n*-butyllithium in hexane. The solution was stirred for 10 min. To the lithium diisopropylamide solution was added 145 mg (1.0 mmol) of 2-phenylbutyronitrile in 1.0 ml of anhydrous tetrahydrofuran. The solution was stirred for 10 min. To the lithionitrile solution was added 316 mg (2.1 mmol, 2.1 equiv) of *tert*-butyldimethylchlorosilane in 1.0 ml of anhydrous tetrahydrofuran. The solution was stirred for 30 min at −78° and 60 min at 25°. The solvents were evaporated at reduced pressure, and the product was evaporatively distilled at 135–140° (oven temperature) (0.25 mm) to afford 244 mg (94%) of yellow ketenimine **4** (R = Et; Ar = Ph). Repetition of this experiment using 3.32 g of 2-phenylbutyronitrile afforded 4.13 g (73%) of **4**: bp 95–99° (0.15 mm); ir (TF) 4.98 (C=C=N) and 6.31 μ (Ar); nmr (CCl_4) δ 0.25 [s, 6, $Si(CH_3)_2$], 1.00 [s, 9, $SiC(CH_3)_3$], 1.17 (t, *J* = 7 Hz, 3, $CH_2\mathbf{CH_3}$), 2.31 (q, *J* = 7 Hz, 2, $\mathbf{CH_2}CH_3$) and 6.8–7.4 (m, 5, ArH).

Propiophenone. To 259 mg (1.0 mmol) of ketenimine **4** (R = Et; Ar = Ph) in 1.0 ml of tetrahydrofuran at 0° was added 280 mg (1.1 mmol, 1.1 equiv) of iodine in tetrahydrofuran. The dark brown solution was stirred for 15 min at 0°. To this solution was added 1160 mg (5.0 mmol, 2.5 equiv) of freshly prepared,[9] moist silver oxide. The mixture was refluxed for 30 min, cooled, and filtered through a pad of Celite 545. The Celite pad was thoroughly washed with three 20-ml portions of ether. The ethereal solutions were combined, washed with 20 ml of brine, and dried over anhydrous magnesium sulfate. The solvents were evaporated to afford 590 mg of yellow oil. Girard "T" reagent[10] was utilized to effect the isolation of 108.2 mg (81%) of propiophenone which was identical with an authentic sample.

Methyl 2-Cyanomethylbenzoate (10). To 174 mg (1.0 mmol) of *o*-carboxyphenylacetonitrile[11] (Aldrich) in 10 ml of anhydrous ether at 0° was distilled diazomethane[12] in ether until nitrogen evolution ceased. The solution was stirred for 2 hr at 25°. The excess diazomethane was destroyed by the dropwise addition of acetic acid. The ethereal solution was washed with 20 ml of water, 20 ml of saturated sodium bicarbonate solution, and 20 ml of brine and dried over anhydrous magnesium sulfate. The solvent was evaporated to afford 185 mg (98%) of **10** as a tan solid: mp 48.5–49.5° (lit.[13] mp 48°); ir ($CHCl_3$) 4.44 (C≡N), 5.79 (C=O), 6.26, and 6.34 μ (Ar); nmr ($CDCl_3$) δ 3.92 (s, 3, OCH_3), 4.19 (s, 2, CH_2CN), and 7.2–8.2 (m, 4, ArH).

Anal. Calcd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18. Found: C, 68.60; H, 5.27.

Methyl 2-(1-Cyanopentyl)benzoate (11). The alkylation[2e] of **10** afforded 256.5 mg of oil which was chromatographed on two 20 × 20 cm thick layer Merck silica gel F254 plates in 1:3 ether–hexane to afford 181 mg (79%) of **11**: ir (TF) 4.47 (C≡N) and 5.81 μ (C=O); nmr (CCl_4) δ 0.93 (t, 3, CH_2CH_3), 1.1–2.0 (m, 6, CH_2), 3.90 (s, 3, OCH_3), 5.05 (d of d, *J* = 6 and 8 Hz, 1, CHCN), and 7.1–8.1 (m, 4, ArH); mass spectrum (70 ev) *m/e* (rel intensity) 231 (27) and 188 (100).

An analytical sample was prepared by evaporative distillation at 140–145° (oven temperature) (0.2 mm).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.85; H, 7.42.

Ligusticumic Acid (8). Repetition of the silylation procedure described above using 231 mg (1.0 mmol) of **11** afforded 284 mg (82%) of ketenimine **4** (R = *n*-Bu; Ar = *o*-CO_2MePh), ir (TF) 4.87 (C=C=N) and 5.79 μ (C=O). Repetition of the iodine–silver oxide procedure described above using 282 mg of this ketenimine afforded 428 mg of crude yellow oil. The crude keto ester was refluxed in 1 ml of methanol and 3 ml of 2 *M* aqueous potassium hydroxide for 1 hr. The product was diluted with 50 ml of water and extracted with two 20-ml portions of ether. The ethereal solutions were washed with 10 ml of water. The combined aqueous solutions were acidified with 10 ml of 3 *M* hydrochloric acid and extracted with two 20-ml portions of ether. The ethereal solutions were washed and dried as described previously. The solvent was evaporated to afford 128.7 mg (77%) of ligusticumic acid (**8**) a a viscous oil. The purity of this material was estimated to exceed 90% according to tlc (silica gel, 1:3:3 methanol–ether–hexane). The propensity of **8** to suffer lactonization–dehydration[14]precluded crystallization and required characterization of **8** as the phthalazone,[15] mp 150–153° (lit.[16] mp 153–154°).

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Registry No.—**3** (R = H; Ar = *o*-CO_2HPh), 6627-91-4; **4** (R = Et; Ar = Ph), 51965-62-9; **4** (R = *n*-Bu; Ar = *o*-CO_2MePh), 28060-41-5; **8**, 550-37-8; **10**, 5597-04-6; **11**, 28060-41-5; *tert*-butyldimethylchlorosilane, 18162-48-6.

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