= 7.5 Hz, H-8). This spectrum is in excellent agreement with that reported.[3]

**3-*n*-Butylisocoumarin (Dihydroartemidin) (7).** A solution of *o*-iodobenzoic acid (20 g) in dimethylformamide (250 mL) was added to a suspension of cuprous *n*-butylacetylide (12.73 g) in the same solvent (250 mL), and the mixture was refluxed and worked up as in the previous experiment to yield dihydroartemidin as an oil, which crystallized from ether–light petroleum as colorless cubes (7.14 g): mp 49.5–50.5 °C (lit.[8] mp 45–46 °C); NMR δ 0.94 (t, *J* = 7.5 Hz, H-4'), 1.19–2.05 (m, H-2' and 3'), 2.50 (t, *J* = 7.5 Hz, H-1'), 6.23 (s, H-4), 7.36 (br d, *J* = 8 Hz, H-5), 7.38 (ddd, *J* = 7.5, 7.5, 1.5 Hz, H-7), 7.66 (ddd, *J* = 7.5, 7.5, 1.5 Hz, H-6), and 8.21 (br d, *J* = 7.5 Hz, H-8). Saponification as described[8] gave the keto acid, mp 89–90 °C (lit.[8] 85–86 °C), which yielded the 2,4-dinitrophenylhydrazone, mp 179–180 °C (lit.[8] 174–175 °C).

**1'-Bromo-3-*n*-butylisocoumarin (8).** *N*-Bromosuccinimide (7.14 g) was added to a solution of dihydroartemidin (7.14 g) in carbon tetrachloride (150 mL) and the mixture heated under reflux for 10 h, then cooled, filtered, and evaporated. A solution of the residue was filtered first through a short column of alumina and then through silica gel. Crystallization of the eluted product from methanol or light petroleum gave 1'-bromo-3-*n*-butylisocoumarin as rectangular prisms (4.65 g): mp 69.5–70 °C; NMR δ 0.97 (t, *J* = 7 Hz, Me), 1.3–1.75 (m, H-3'), 2.21 (q, *J* = 7.5 Hz, H-2'), 4.71 (t, *J* = 7.5 Hz, H-1'), 6.55 (s, H-4), 7.42 (br d, *J* = 7.5 Hz, H-5), 7.52 (ddd, *J* = 7.5, 7.5, 1.5 Hz, H-7), 7.73 (ddd, *J* = 7.5, 7.5, 1.5 Hz, H-6), and 8.28 (dd, *J* = 7.5, 1.5 Hz, H-8). Anal. Calcd for $C_{13}H_{13}O_2Br$: C, 55.53; H, 4.66. Found: C, 55.84; H, 4.61.

**Artemidin (6).** A solution of 1,5-diazabicyclo[5.4.0]undec-5-ene (1.75 g) in benzene (75 mL) was added to a solution of the 1'-bromoartemidin (8) (3.23 g) in the same solvent (75 mL) and the mixture heated under reflux under nitrogen for 10 h. It was diluted with ether, washed with dilute sulfuric acid and water, and dried ($MgSO_4$). The residue obtained on evaporation was dissolved in benzene and filtered through a short column of alumina, and the product crystallized from light petroleum to give artemidin (3-but-1'-*trans*-enylisocoumarin) as prisms: mp 49.5–50.5 °C (lit.[8] mp 49–50 °C); NMR δ 1.09 (t, *J* = 7.5 Hz, Me), 2.25 (m, H-3'), 6.01 (dt, *J* = 15.5, 1.5 Hz, H-1'), 6.25 (s, H-4), 6.68 (dt, *J* = 15.5, 6.5 Hz, H-2'), 7.35 (br d, *J* = 8 Hz, H-5), 7.40 (ddd, *J* = 7.5, 7.5, 1.5 Hz, H-7), 7.65 (ddd, *J* = 7.5, 7.5, 1.5 Hz, H-6), and 8.22 (br d, *J* = 7.5 Hz, H-8).

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**Registry No.** 1, 88-67-5; 4, 13141-35-0; 5, 72917-31-8; 6, 29428-84-0; 7, 30531-69-2; 8, 72917-32-9; 2-(2-oxohexyl)benzoic acid, 30531-71-6; 2-(2-oxohexyl)benzoic acid 2,4-dinitrophenylhydrazone, 30650-58-9; CuC≡CPr, 19093-51-7; CuC≡CBu, 33589-44-5.

# *Communications*

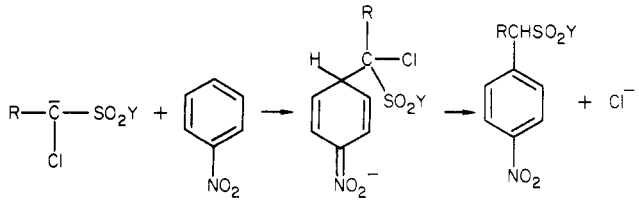
## Vicarious Substitution of Hydrogen in Aromatic Nitro Compounds with Acetonitrile Derivatives[1]

*Summary:* Carbanions of α-phenoxy and thioalkoxy nitriles substitute hydrogen in the para or ortho position of aromatic nitro compounds, giving nitroarylacetonitriles in a process in which phenolate or thiolate anions are vicarious leaving groups.

*Sir:* In a preceding paper[2] we described the general principle of "vicarious" nucleophilic substitution of hydrogen in aromatic nitro compounds by carbanions derived from 1-haloalkylphenyl sulfones and *N,N*-dialkyl-1-haloalkanesulfonamides. The main feature of this process is that the α-halocarbanions attack an unsubstituted carbon atom of an aromatic nitro compound, giving an intermediate σ complex. The latter, upon loss of halide anion, gives rise to the product (Scheme I).

One could expect that this novel substitution could proceed with other C–H acids containing leaving groups in the α position. However, such C–H acids are usually active electrophiles. Therefore, the success of the vicarious substitution process would depend on the relative rates of the reactions of the carbanions with aromatic nitro compounds and with the starting C–H acid–carbanion precursors. α-Chloroalkanenitriles would be suitable reactants providing the rate of the reaction with aromatic nitro compounds is sufficiently high. Indeed, chloroacetonitrile in the presence of NaOH in $Me_2SO$ reacts with 1-nitronaphthalene and 4-chloronitrobenzene, affording

Scheme I




Y = Ph, $NR_2$

the corresponding α-nitroarylacetonitriles in fair yields. With nitrobenzene or 4-nitrobiphenyl the substitution process does not occur; instead, chloroacetonitrile is completely destroyed, and the nitro compounds are essentially unaffected.

As is shown in Scheme I, vicarious substitution involves departure of the leaving group from an anionic σ complex. Hence, one could assume that α substituents such as phenoxy, alkoxy, and their corresponding thio analogues should also be able to serve as leaving groups in this process. This possibility would be of interest since these groups cannot be easily displaced via $S_N2$ type processes; yet they are good leaving groups from anionic intermediates, as, for example, in the case of transesterification or substitution of the methoxy group in *p*-nitroanisole.

Accordingly we investigated the reactions of aryloxy and alkoxy derivatives of acetonitrile and their thio analogues with aromatic nitro compounds in the presence of strong bases. In accord with our expectations, these nitriles indeed reacted with a variety of nitroarenes by vicarious substitution and yielded nitroarylated derivatives of acetonitrile or phenylacetonitrile, respectively.

The products of the substitution contain nitroaryl sub-

(1) Paper 96 in the series "Reaction of Organic Anions". Part 95: A. Jończyk, M. Ludwikow, and M. Makosza, *Org. Prep. Proced. Int.*, in press.

(2) J. Goliński and M. Makosza, *Tetrahedron Lett.*, 3495 (1978).

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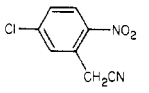
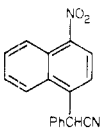
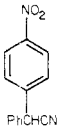
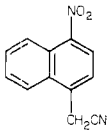
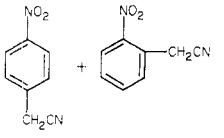
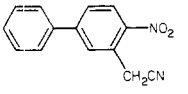
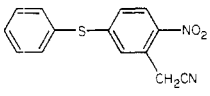
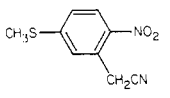
Table I

$$RCHXCN + O_2NArH \xrightarrow[(2)\ HCl,\ H_2O]{(1)\ NaOH/Me_2SO} O_2NArCHRCN + XH$$

| R | X | $O_2N-Ar-CH(R)-CN$ | yield,[a] % | mp, °C |
|---|---|---|---|---|
| H | Cl |  | 40 | 94-95.5 |
| Ph | PhO |  | 77 | 117-121 |
| Ph | $2,4\text{-}Cl_2C_6H_3O$ |  | 57 | 69-71[b] |
| H | Cl |  | 75 | |
| H | $CH_3S$ | | 75 | 118-121 |
| H | PhS | | 80 | |
| H | PhS |  | 50[c] *p*<br>18 *o* | 114-116[d]<br>82-83[d] |
| H | PhS |  | 74 | 123-124 |
| H | PhS |  | 74 | 104-105 |
| H | $(CH_3)_2NCS_2$ |  | 40 | 90-93 |

[a] All new compounds gave satisfactory microanalyses. These structures were established by IR and NMR spectra. Yields are given for isolated compounds. [b] Lit. mp 70-72 °C (R. B. Davis, L. C. Pizzini, *J. Org. Chem.*, 25, 1884 (1960). [c] Determined by GLC. [d] Lit. mp *p* 116 °C, *o* 81.5-82.5 °C (J. R. Knowles, R. Norman, *J. Chem. Soc.*, 2938 (1961).

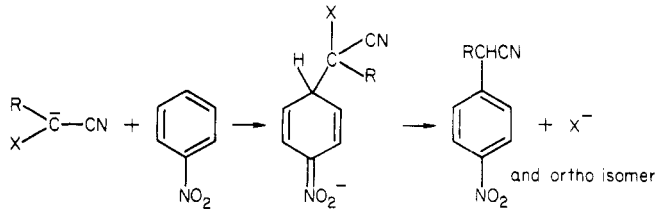
stituents; hence, they are much stronger C–H acids than the starting nitriles. In the reaction mixture they exist as corresponding carbanions; hence, the process should be carried out in the presence of at least 2 equiv of base (Scheme II).

Thus, when *S*-phenylthioglycolonitrile and nitrobenzene in $Me_2SO$ solution were treated with an excess of powdered NaOH, an exothermic reaction accompanied by strong coloration of the mixture occurred. The reaction was carried out at 30 °C for 1.5 h; then dilution with water and acidification yielded a mixture of ortho and para isomers of nitrophenylacetonitrile, total yield 68%. Similarly from α-(2,4-dichlorophenoxy)phenylacetonitrile, phenyl(*p*-nitrophenyl)acetonitrile was obtained in 57% yield. No ortho isomer was observed in this case.

The examples of vicarious substitution of hydrogen by various α-substituted acetonitrile derivatives are given in Table I.

Vicarious substitution of hydrogen in aromatic nitro compounds with acetonitrile derivatives, besides being of mechanistic interest, offers a very practical synthetic approach of considerable utility. Although some of these products are easily prepared by other routes (e.g., nitration or nitroarylation of phenylacetonitrile), there are many compounds, particularly those containing a cyanomethyl group ortho to the nitro group, which cannot be easily prepared in other ways. The utility of these compounds as versatile starting materials in the synthesis of heterocycles is well established.[3]

Scheme II




R = H; X = PhS, MeS, $(CH_3)_2NCS_2$
R = Ph; X = PhO

Finally, we wish to comment on the probable mechanism of this reaction. Since we investigated these reactions with a preconception of the probable reaction pathway, we suppose that the transformation of the intermediate σ complex into the product proceeds via migration of the hydride anion to the carbon atom from which the "vicarious" leaving group departs (as shown in Scheme II). This general scheme illustrates our preconceivable mechanism; clearly, this is a tentative but consistent explanation of the reaction course. There are of course alternative mechanisms of worthy consideration; particularly, E2 type elimination from the intermediate would also be reasonable. A detailed mechanistic study is presently under way in our laboratory and will be reported in the future.

**Acknowledgment.** We express our thanks to the National Science Foundation for support of this research (Grant INT-14966).

**Registry No.** Chloroacetonitrile, 107-14-2; phenoxyphenylacetonitrile, 32121-27-0; α-(2,4-dichlorophenoxy)phenylacetonitrile, 72301-64-5; *S*-methylthioglycolonitrile, 35120-10-6; *S*-phenylthioglycolonitrile, 5219-61-4; *S*-(dimethylthiocarbamoyl)thioglycolonitrile, 61540-35-0; α-(5-chloro-2-nitrophenyl)acetonitrile, 72301-65-6; α-(4-nitro-1-naphthalenyl)phenylacetonitrile, 72301-66-7; phenyl(*p*-nitrophenyl)acetonitrile, 7599-05-5; 4-nitro-1-naphthaleneacetonitrile, 72301-67-8; *p*-nitrophenylacetonitrile, 555-21-5; *o*-nitrophenylacetonitrile, 610-66-2; 4-nitro-3-biphenylacetonitrile, 72301-68-9; α-[2-nitro-5-(phenylthio)phenyl]acetonitrile, 72301-69-0; α-[2-nitro-5-(methylthio)phenyl]acetonitrile, 72301-70-3; 1-nitronaphthalene, 86-57-7; 4-chloronitrobenzene, 100-00-5; nitrobenzene, 98-95-3; 4-nitrobiphenyl, 92-93-3.

(3) I. D. London and G. Tennant, *Q. Rev., Chem. Soc.*, 18, 389 (1964). P. N. Preston and G. Tennant, *Chem. Rev.*, 72, 627 (1972).

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## Transition-State-Stabilized Macrolide Closures

*Summary:* Thiol-functionalized crown ethers serve as reagents for macrolide closures. The thioesters derived from these crown ethers and ω-hydroxy carboxylic acids yield macrolides when treated with potassium *tert*-butoxide. The reaction proceeds via a templated conformation in which the ω-alkoxide is held proximate to the thioester

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