Association (C.R.), and Grant BG-42247-X from the National Science Foundation (K.R.H.). We would like to thank Dr. H. Bleich for the Jeol ^{1}H NMR spectrum.

Registry No.—**2**, 6911-23-0; **4**, 140-10-3; **6**, 58836-15-0; propiolaldehyde, 624-67-9; 1,3-butadiene, 106-99-0; malonic acid, 141-82-2.

References and Notes

(1) Abbreviations and nomenclature: (*E,E*)-hexa-2,4-dienoic acid, sorbic acid, **5**; (*E*)-3-(1,4-cyclohexadienyl)-2-propenoic acid, *trans*-3-(1,4-cyclohexadienyl)acrylic acid, or 2,5-dihydrophenylacrylic acid, **2**; *trans*-3-phenylacrylic acid, *trans*-cinnamic acid, **4**.
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Impregnated Cyanide Reagents. Convenient Synthesis of Nitriles[1]

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We wish to report a convenient method for carrying out cyanide displacement on organic halides. Our approach is based on an impregnation technique and requires only two steps for product isolation, filtration and solvent evaporation.[2]

Attempted reaction of sodium cyanide with 1-bromooctane in toluene at 130 °C (sealed tube) produced a negligible yield of the corresponding displacement product.[3,5] In contrast, similar reactions carried out in which the salt was first impregnated onto certain inorganic solids resulted in considerable substitution. Empirical testing of 15 supports revealed that neutral alumina was most effective in activating cyanide (Table I).

An optimal procedure for impregnating NaCN onto alumina (reagent **1**) is presented in the Experimental Section. Reaction of **1** with a series of organic halides gave yields of nitrile product which are summarized in Table II. The convenience afforded with the use of **1** is exemplified by the conversion of 1-bromododecane to 1-cyanododecane. After a toluene solution of 1-bromododecane was stirred at 90 °C for 45 h in the presence of **1**, the spent and unused insoluble reagent were removed under reduced pressure, leaving a 100% yield of 1-cyanododecane which was spectroscopically identical with an authentic sample.

Table I. Impregnated Cyanide Reagents[a]

support	reactive cyanide, mmol/g
LMS 3A ($^1/_{16}$-in. pellets)	0.1
LMS 4A ($^1/_{16}$-in. pellets)	trace
LMS 5A ($^1/_{16}$-in. pellets)	trace
LMS 13X ($^1/_{16}$-in. pellets)	1.0
LMS 4A (powder)	0.1
LMS 5A (powder)	trace
LMS 13X (powder)	1.4
LMS 4A (8–12 mesh)	0.2
K-10 Montmorillonite clay (powder)	trace
K-306 Montmorillonite clay (powder)	0.4
K-306 Montmorillonite clay (spheres)	0.1
graphite	trace
Celite	0.1
silica gel (100–200 mesh)	trace
neutral alumina	1.8
none	trace

[a] All impregnated reagents were prepared using the following standard procedure. A 2.0-g amount of support was added to 20 mL of an aqueous solution containing 0.5 g of sodium cyanide. Water was removed by rotary evaporation (bath temperature was kept below 65 °C), and the resulting reagent was dried under reduced pressure [4 h, 110 °C (0.05 mm)]. No effort was made to physically separate nonadsorbed cyanide. The quantity of reactive cyanide was determined by reaction of 0.5 g of impregnated reagent with 2.5 mmol of 1-bromooctane in 3 mL of toluene at 130 °C for 24 h. Reaction mixtures were unstirred and analyzed by GLC using internal standard techniques. Material balance and reproducibility were excellent. Values reported above are in millimoles of 1-cyanooctane per gram of reagent.

Table II. Nitrile Synthesis Using Sodium Cyanide Coated Alumina[a]

reactant	product	time, h	yield, %[b]
1-bromobutane	1-cyanobutane	24	93
1-chlorobutane	1-cyanobutane	40	42
1-iodooctane[7]	1-cyanooctane	40	37
1-bromooctane	1-cyanooctane	24	97[c]
1-chlorooctane	1-cyanooctane	40	52
1-bromododecane	1-cyanododecane	24	100[c]
1-chlorododecane	1-cyanododecane	40	33
2-bromooctane	2-cyanooctane	40	27

[a] Unless noted otherwise, displacement on 1.0 mmol of the indicated organic halide was carried out in 4.0 mL of toluene using 1.49 g of **1** at 90 °C. Reaction mixtures were stirred with a Teflon-coated magnetic stirring bar. [b] Yields were determined by GLC using internal standard techniques. Material balance was >95% in all cases. Control experiments carried out under identical conditions using nonimpregnated sodium cyanide showed no reaction. [c] Isolated yield from a preparative reaction (45 h) using procedures described in the Experimental Section.

The advantage of this procedure for the preparation of nitriles lies in its simplicity, its avoidance of aqueous workup and extraction steps,[4] and also its avoidance of highly toxic solvents (e.g., hexamethylphosphoramide) required in procedures currently used;[6] its principal disadvantage is the relatively slow rate of reaction. Nonetheless, this method serves as a useful synthetic alternative for small-scale conversions.

Experimental Section

General Methods. Unless stated otherwise, all reagents and chemicals were obtained commercially and were used without further

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purification. Linde molecular sieves were purchased from Alpha Chemicals, Danvers, Mass. Neutral alumina was purchased from Bio-Rad Laboratories (AG-7, 100–200 mesh) and used as obtained. Toluene was dried by distillation from sodium and benzophenone under a nitrogen atmosphere. All ^{1}H NMR and IR spectra were recorded using Varian A-60 and Beckman Acculab 7 spectrometers, respectively. Product mixtures were analyzed by GLC on a Hewlett Packard Model 5830A flame ionization instrument. Culture tubes were used as reaction vessels (25 × 150 mm Corning no. 9826 tubes) and were equipped with a Teflon-lined screw cap and a Teflon-coated magnetic stirring bar.

Impregnation of NaCN on Alumina (Reagent 1). A 50-mL round-bottom flask was charged with 2.0 g (40.8 mmol) of sodium cyanide dissolved in 5 mL of distilled water, and 4.0 g of neutral alumina was added to it in one portion. The flask was transferred to a rotary evaporator, and water was removed under reduced pressure, keeping the bath temperature below 65 °C. Impregnated alumina was then dried [4 h, 110 °C (0.05 mm)].

General Procedure for Small-Scale Reactions. Procedures similar to that described for the conversion of 1-bromooctane to 1-cyanooctane were followed for all of the small-scale reactions described in Table II. A mixture of 0.19 g (1.0 mmol) of 1-bromooctane, 1.49 g of 1, 4.0 mL of toluene, and an internal standard was placed in a 25 × 150 mm Corning no. 9826 culture tube equipped with a Teflon-coated magnetic stirring bar. The flask was placed in an oil bath (90 °C), stirred for 24 h, withdrawn, and cooled to room temperature. The liquid phase was analyzed using a UCW-982 on Chromosorb W column.

Conversion of 1-Bromododecane to 1-Cyanododecane. A mixture of 2.5 g (10.0 mmol) of 1-bromododecane, 15.0 g of 1, and 30 mL of toluene was placed in a 100-mL round-bottom flask and stirred with a Teflon-coated magnetic stirring bar for 45 h at 90 °C. The nitrile product was isolated by filtering the mixture, washing the spent and unused reagent with 100 mL of toluene, and removing the solvent from the combined filtrate under reduced pressure to yield 1.96 g (100%) of 1-cyanododecane, obtained as a colorless liquid. The infrared and NMR spectra were identical with those of an authentic sample.

Registry No.—1-Bromobutane, 109-65-9; 1-chlorobutane, 109-69-3; 1-iodooctane, 629-27-6; 1-bromooctane, 111-83-1; 1-chlorooctane, 111-85-3; 1-bromododecane, 143-15-7; 1-chlorododecane, 112-52-7; 2-bromooctane, 557-35-7; 1-cyanobutane, 110-59-8; 1-cyanooctane, 2243-27-8; 1-cyanododecane, 629-60-7; 2-cyanooctane, 2570-96-9; NaCN, 143-33-9; alumina, 1344-28-1.

References and Notes

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(3) Acetonitrile has also been examined as a solvent and found to give greater reaction rates. However, we have observed significant displacement using sodium cyanide in the absence of alumina with this more polar solvent.[4]

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(5) A control experiment carried out in which reagent **1** was replaced by finely ground NaCN plus nonimpregnated alumina (used as obtained or dried prior to reaction [4 h, 110 °C (0.05 mm)]) did show significant displacement. However, the yield of nitrile was consistently low, and, in contrast to **1**, the experiment gave substantial amounts of 1-octanol plus an unidentified side product. A further control experiment in which **1** was replaced by an aqueous sodium cyanide solution plus nonimpregnated alumina showed no evidence of displacement after heating for 24 h at 90 °C.

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(7) Surprisingly, 1-iodooctane was much less reactive toward **1** than 1-bromooctane. The origin of this unusual selectivity is not clear at present and is under investigation.

Indole Syntheses with *o*-Tolyl Isocyanide. 3-Acylindoles and 2-Substituted Indoles

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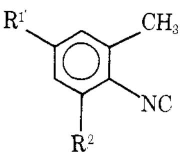
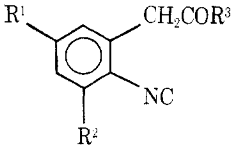
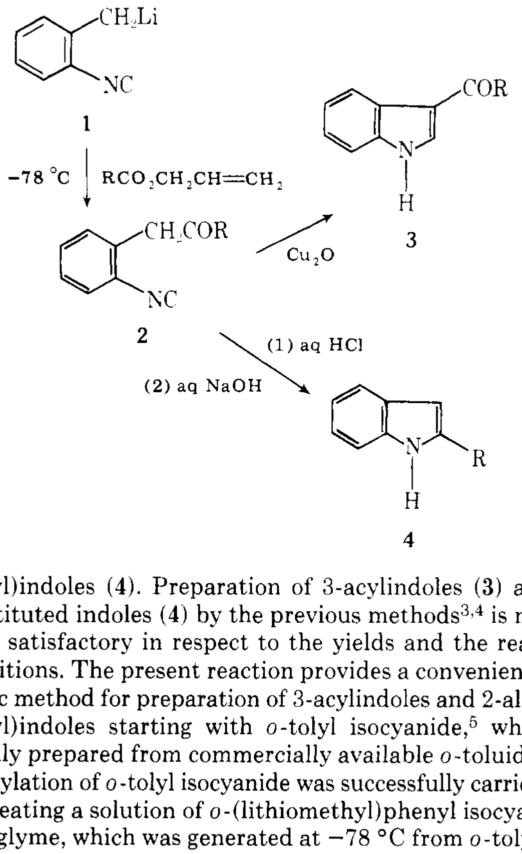
In the preceding paper we described syntheses of some indole derivatives by elaboration of *o*-(lithiomethyl)phenyl isocyanide (1) with electrophiles such as alkyl halides,[1] alkylene oxides,[1] and isocyanates,[2] followed by cyclization. Herein, we wish to report that acylation of the ortho methyl group of *o*-tolyl isocyanide can be best performed by treating *o*-(lithiomethyl)phenyl isocyanide (1) with allyl carboxylates and that *o*-(acylmethyl)phenyl isocyanides (2) thus prepared were readily converted to 3-acylindoles (3) and 2-alkyl(or 2-aryl)indoles (4). Preparation of 3-acylindoles (3) and 2-substituted indoles (4) by the previous methods[3,4] is not always satisfactory in respect to the yields and the reaction conditions. The present reaction provides a convenient synthetic method for preparation of 3-acylindoles and 2-alkyl(or 2-aryl)indoles starting with *o*-tolyl isocyanide,[5] which is readily prepared from commercially available *o*-toluidine.

Table I. Acylations of the Ortho Methyl Group of *o*-Methylphenyl Isocyanides

	$R^3CO_2CH_2$-$CH{=}CH_2$	 %^{a} (product)
R^1 = H, R^2 = H	R^3 = CH_3	48 (**2-i**)
R^1 = H, R^2 = H	R^3 = n-C_3H_7	57 (**2-ii**)
R^1 = H, R^2 = H	R^3 = i-C_4H_9	55 (**2-iii**)
R^1 = H, R^2 = H	R^3 = t-C_4H_9	57 (**2-iv**)
R^1 = H, R^2 = H	R^3 = n-C_7H_{15}	71 (**2-v**)
R^1 = H, R^2 = H	R^3 = Ph	95 (**2-vi**)
R^1 = Cl, R^2 = H	R^3 = t-C_4H_9	48 (**2-vii**)
R^1 = CH_3, R^2 = H	R^3 = i-C_4H_9	62 (**2-viii**)
R^1 = CH_3, R^2 = H	R^3 = t-C_4H_9	50 (**2-ix**)
R^1 = CH_3, R^2 = H	R^3 = Ph	72 (**2-x**)
R^1 = H, R^2 = CH_3	R^3 = t-C_4H_9	63 (**2-xi**)

^{a}Isolated yields.



Acylation of *o*-tolyl isocyanide was successfully carried out by treating a solution of *o*-(lithiomethyl)phenyl isocyanide[1] in diglyme, which was generated at −78 °C from *o*-tolyl isocyanide and 2 equiv of lithium diisopropylamide (LDA), with 2 equiv of allyl carboxylate. Use of an acyl halide instead of an allyl carboxylate gave unsatisfactory results. Acylations of the ortho methyl group of 4-chloro-2-methylphenyl isocyanide, 2,4-dimethylphenyl isocyanide, and 2,6-dimethylphenyl isocyanide could be similarly carried out, producing the corresponding *o*-(acylmethyl)phenyl isocyanides **2** in moderate yields. Some results on the acylations of *o*-methylphenyl isocyanides are summarized in Table I.

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