

corresponding coupling constant ($J = 13$ Hz): S. Torii, K. Uneyama, and M. Kuyama, *Tetrahedron Lett.*, 1513 (1976), and ref 1. The α isomer on C-11 may arise from epimerization at C-11 under the reaction conditions because of the steric repulsion between the phenylsulfonyl group and methyl at C-10.

- (10) R. M. Carman and H. Deeth, *Aust. J. Chem.*, **24**, 1099 (1971). The authors are grateful to Professor R. M. Carman, Department of Chemistry, University of Queensland, Australia, for a kind gift of the IR and ^1H NMR spectra of

13,14,15,16-tetranorlabd-7-en-12-oic acid.

- (11) The product **2b** was homogeneous on ^1H NMR, and the stereochemistry of the phenylsulfonyl group at C-11 was assigned on the basis of the coupling constant between H-8 and H-11 ($J = 2$ Hz).
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 (13) (a) M. Julia and J. M. Paris, *Tetrahedron Lett.*, 4833 (1973); (b) B. M. Trost and Y. Matsumura, *J. Org. Chem.*, **42**, 2036 (1977).

Communications

Sodium and Potassium Carbonates: Efficient Strong Bases in Solid-Liquid Two-Phase Systems¹

Summary: Anhydrous potassium and sodium carbonates in the presence of catalysts—tetraalkylammonium salts or crown ethers were found to be efficient strong bases for generation and reactions of a variety of carbanions.

Sir: A recent paper by White,² in which the alkylation of diethyl malonate, ethyl cyanoacetate, and some other compounds in the presence of potassium carbonate in DMF was reported, prompts us to publish a preliminary communication describing some of our results concerning the application of alkali metal carbonates as efficient strong bases.

Among the variety of basic agents employed for the generation of carbanions, concentrated aqueous sodium hydroxide in the presence of catalysts such as tetraalkylammonium salts or crown ethers is of particular value.³ Such reactions take place in a liquid-liquid two-phase system in which both phases, aqueous sodium hydroxide and organic reactants (neat or in nonpolar solvent) are mutually immiscible. This catalytic two-phase (CTP) system offers numerous advantages over other bases such as NaH, NaNH_2 , and *t*-BuOK, inter alia elimination of hazardous and expensive reactants, anhydrous organic solvents, etc.

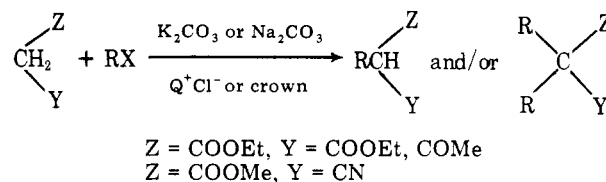
Despite many advantages, the CTP system has some limitations, one of them being the hydrolytic activity of concentrated aqueous alkali. Although due to the mutual immiscibility of the phases, hydrolysis of starting materials and/or products interferes much less than one would expect; carboxy and carbomethoxy groups are hydrolyzed in this system to a considerable extent. As a consequence alkylation of diethyl malonate, methyl cyanoacetate, and similar compounds cannot be performed efficiently in the CTP system.

We have found that many reactions proceeding via carbanions can be efficiently carried out using anhydrous sodium or potassium carbonates as bases. In these cases the reactions proceed in liquid-solid two-phase systems. Organic reactants neat (if liquids) or in aprotic solvents form the organic phase in which solid sodium or potassium carbonate is suspended. In this system reactions are catalyzed by tetraalkylammonium salts or crown ethers. The catalysts are unable to transfer carbonate anions (CO_3^{2-}) into the organic phase,⁴ thus solid-liquid phase-transfer phenomena are probably not involved here. It is more plausible that the first step, namely proton abstraction, takes place on the surface of the solid carbonate. The anions formed then migrate into the organic phase as ion pairs with tetraalkylammonium cations or crown ether complexed alkali metal cations. Since anhydrous alkali carbonates form fine powders with well-developed surfaces and also show no tendency to form lumps, the speed of stirring is not of crucial importance. When K_2CO_3 or Na_2CO_3 are used as bases the reactions should be carried out at higher temperatures than if aqueous NaOH is used in the CTP system.

This normally does not cause any difficulties, since the carbonates are rather mild bases.

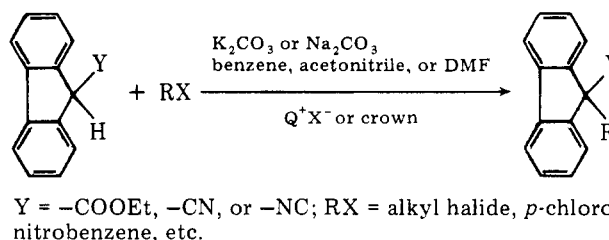
Up to now the following reactions have been found to proceed efficiently in the presence of alkali carbonates.

1. Alkylation of diethyl malonate, methyl cyanoacetate, and ethyl acetoacetate.



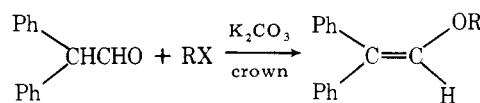
These reactions are conducted between 50 and 100 °C depending on the alkylating agent used. In the case of diethyl malonate the process is highly selective in the sense of mono- vs. dialkylation. Methyl cyanoacetate is much more prone to undergo dialkylation. Nevertheless in both cases, mono- and dialkylated products can be prepared in high yields.

2. Alkylation and nitroarylation of 9-substituted fluorene derivatives.



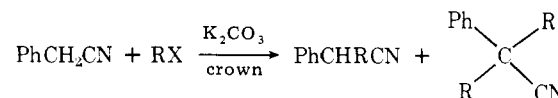
Since the starting compounds are solids, small amounts of solvents are necessary.

3. Alkylation and nitroarylation of diphenylacetaldehyde.



Exclusively O-alkylated derivatives are formed in high yields.

4. Alkylation of phenylacetonitrile.



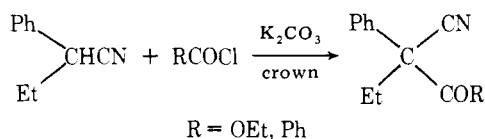
Although phenylacetonitrile is a quite weak carbon acid it can still be deprotonated and subsequently alkylated using the potassium carbonate system at elevated temperatures. Since phenylacetonitrile is efficiently alkylated under CTP conditions,⁵ this method is advantageous only for alkylation with compounds sensitive toward alkaline hydrolysis (e.g., ethyl chloroacetate).

Table I

no.	starting compds	molar ratio	base and catalyst ^g	temp and time	product	% yield
1	ethyl malonate butyl bromide	1:1	K ₂ CO ₃ TBAB	110 °C 1 h	ethyl <i>n</i> -butylmalonate	93
2	ethyl malonate allyl chloride	1:1	K ₂ CO ₃ 18-c-6	90 °C 1 h	ethyl allylmalonate	94
3	methyl cyanoacetate benzyl chloride	1:2	Na ₂ CO ₃ TEBA	90 °C 3 h	methyl dibenzylcyanoacetate	87
4	9-carboethoxyfluorene phenacyl chloride	1:1	K ₂ CO ₃ ^a 18-c-6	40 °C 0.5 h	9-carboethoxy-9-phenacylfluorene ^d	89
5	9-isocyanofluorene <i>p</i> -chloronitrobenzene	1:1	K ₂ CO ₃ ^c 18-c-6	80 °C 6 h	9-isocyano-9-nitrophenylfluorene ^e	70
6	diphenylacetaldehyde 2,4-dinitrochlorobenzene	1:1	K ₂ CO ₃ ^b 18-c-6	55 °C 3 h	1,1-diphenyl-2-(2,4-dinitrophenoxy)ethylene ^f	77
7	phenylacetonitrile ethyl chloroacetate	1:1	K ₂ CO ₃ 18-c-6	120 °C 8 h	ethyl 3-cyano-3-phenylpropionate	45
8	2-phenylbutyronitrile ethyl chloroformate	1:3	K ₂ CO ₃ DB-18-c-6	150 °C 1 h	ethyl phenylcyanoacetate	43
9	2-phenylbutyronitrile benzoyl chloride	1:1	K ₂ CO ₃ ^b DB-18-c-6	150 °C 40 min	2-benzoyl-2-phenylbutyronitrile	35
10	diethyl phosphite benzyl chloride	1:1.2	Na ₂ CO ₃ TBAB	100 °C 3 h	diethyl benzylphosphonate	66
11	butanol butyl bromide	1:1	K ₂ CO ₃ 18-c-6	100 °C 3 h	dibutyl ether	70
12	ethyl chloroacetate benzaldehyde	1.5:1	K ₂ CO ₃ 18-c-6	130 °C 0.5 h	ethyl 2-phenylglycidate	72
13	bromoform α -methylstyrene	1.5:1	K ₂ CO ₃ 18-c-6	140 °C 4 h	2-methyl-2-phenyl-1,1-dibromocyclopropane	68

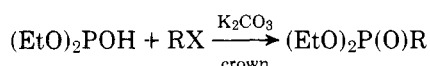
^a The reaction was carried out in acetonitrile. ^b Benzene was used as a solvent. ^c The reaction was carried out in DMF. ^{d-f} New compounds, satisfactory analyses were obtained: ^d mp 177 °C, ^e mp 137 °C, ^f mp 173–174 °C. ^g TEBA, benzyltriethylammonium chloride; TBAB, tetra-*n*-butylammonium bromide; 18-c-6, 18-crown-6; DB-18-c-6, dibenzo-18-crown-6.

5. Acylation of 2-phenylalkenenitriles.



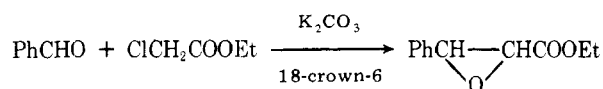
This is the simplest procedure for acylation of the 2-phenylalkenenitriles.

6. The Michaelis–Becker alkylation of diethyl phosphite.



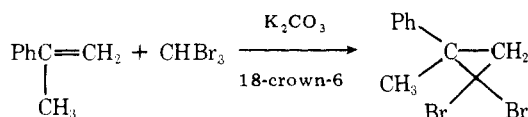
The known procedure⁶ requires the preparation of sodium or potassium diethyl phosphite (using NaH or K metal) and their subsequent alkylation in an anhydrous solvent. We have found that diethyl phosphite can be directly alkylated in the presence of potassium carbonate, without an organic solvent.

7. The Darzens condensation.

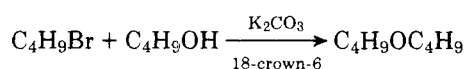


This is a valuable improvement, since the Darzens condensation with ethyl chloroacetate cannot be carried out under the CTP conditions using aqueous NaOH.

8. Dibromocarbene generation.



9. The Williamson ether synthesis.



Some examples of above mentioned processes are shown in Table I. The procedure is very simple; below are described

three typical preparations.

It is difficult to anticipate presently how widely these simple bases can be employed in other processes. On the basis of the examples presented it is beyond any doubts that these possibilities were overlooked by chemists being usually attracted by more complicated and “elegant” yet less efficient base–solvent systems.

Experimental. 1. Methyl Dibenzylcyanoacetate. Methyl cyanoacetate (19.8 g, 0.2 mol), benzyl chloride (53.1 g, 0.42 mol), sodium carbonate (44.5 g, 0.42 mol) and triethylbenzylammonium chloride (0.9 g, 0.004 mol) were stirred at 90 °C for 3 h. Then the mixture was cooled and diluted with water, the organic phase was separated, and after ordinary workup methyl dibenzylcyanoacetate was isolated by distillation in vacuo [bp 130–140 °C at (0.1 mmHg)] and purified by recrystallization from ether–ligroin: mp 78 °C; yield 48.5 g, 87%.

2. 2-Benzoyl-2-phenylbutyronitrile. 2-Phenylbutyronitrile (14.5 g, 0.1 mol), potassium carbonate (14.5 g, 0.105 mol), dibenzo-18-crown-6 (0.4 g, 0.001 mol), and benzene (20 mL) were heated with stirring in a flask equipped with a short distillation column. When the temperature of the mixture reached 150 °C (benzene was partially distilled off) benzoyl chloride (14.1 g, 0.1 mol) in benzene (20 mL) was added dropwise during 0.5 h and the reaction was continued 10 min after the addition was completed. A temperature of 150 °C was maintained throughout the reaction. The mixture was cooled and diluted with water. Vacuum distillation gave 2-benzoyl-2-phenylbutyronitrile [bp 145–150 °C at (0.2 mmHg); yield 9 g, 35%] and starting 2-phenylbutyronitrile (10 g, 65% of recovery).

3. Ethyl 2-Phenylglycidate. Benzaldehyde (10.6 g, 0.1 mol), potassium carbonate (16.6 g, 0.12 mol), and 18-crown-6 (0.26 g, 1 mmol) were stirred and heated to 125–130 °C. While this temperature was maintained, 18.4 g (0.15 mol) of ethyl chloroacetate was added dropwise (0.5 h). After the addition was completed the mixture was stirred at 130 °C for 10 min, cooled to room temperature, and diluted with water. After

ordinary workup, ethyl 2-phenylglycidate was isolated by distillation in vacuo [99–107 °C (0.5 mmHg)] as a mixture of *E* and *Z* isomers (1:1 by GLC): yield 13.9 g, 72%.

References and Notes

- (1) Paper 86 in the series Reactions of Organic Anions. Part 85 A. Jończyk, Z. Ochal, and M. Mąkosza, *Synthesis*, in press.
- (2) D. A. White, *Synth. Commun.*, **7**, 559 (1977), and references cited therein. One should also mention a paper by R. M. Boden [*Synthesis*, 784 (1975)] describing the use of potassium carbonate for generation of phosphonium ylides and subsequently the Wittig condensation.
- (3) M. Mąkosza, *Pure Appl. Chem.*, **43**, 439 (1975); W. P. Weber and G. W. Gokel, "Phase Transfer Catalysis in Organic Synthesis", Springer Verlag, West Berlin, 1977.
- (4) We have found that CO_3^{2-} anions (determined as total alkalinity) are not transferred into acetonitrile on benzene solution from the solid phase of K_2CO_3 either by 18-crown-6 or by tetrabutylammonium bromide.
- (5) M. Mąkosza and A. Jończyk, *Org. Synth.*, **55**, 91 (1975).
- (6) A. F. Grapov, *Reakts. Metody Issled. Org. Soedin.*, **15**, 41 (1966).

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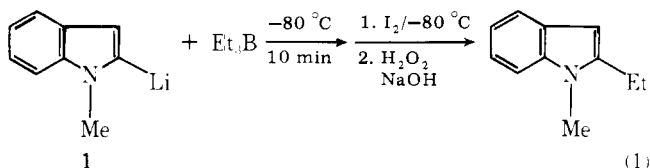
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Aromatic Substitution via Organoboranes. Regiospecific Formation of 2-Alkylindoles

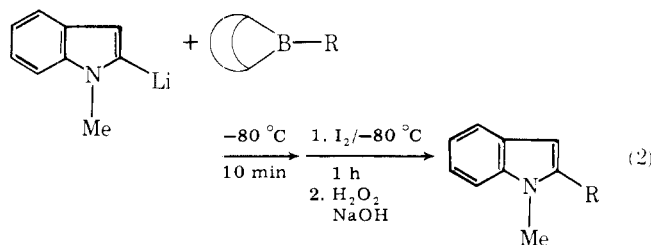
Summary: *N*-Substituted 2-lithioindoles react with trialkylboranes or *B*-alkyl-9-BBN derivatives to give, after iodination, 2-alkylindoles in yields ranging from 60 to 96%.

Sir: The pioneering work of Gilman¹ and others² has demonstrated that many aryllithium derivatives are available via either halogen–lithium exchange or proton abstraction. In particular, in heterocycles, many aryllithiums are available with the lithium attached at positions not easily substituted via electrophilic substitution reactions. Our recent interest in alkenyltrialkylborate salts³ and their use in organic synthesis has led us to begin an investigation of the related aryltrialkylborate salts. We now wish to report our results on the iodination of the aryltrialkylborate salts⁴ derived from *N*-substituted 2-lithioindoles.

When *N*-methyl-2-lithioindole⁵ (1) is treated at –80 °C with 1 equiv of triethylborane followed by iodination and the usual oxidative workup, a 79% yield of *N*-methyl-2-ethylindole⁶ is obtained (eq 1). Furthermore, treatment of 1 with



B-alkyl-9-BBN derivatives⁷ gives selective transfer of the alkyl group to the indole nucleus (eq 2).



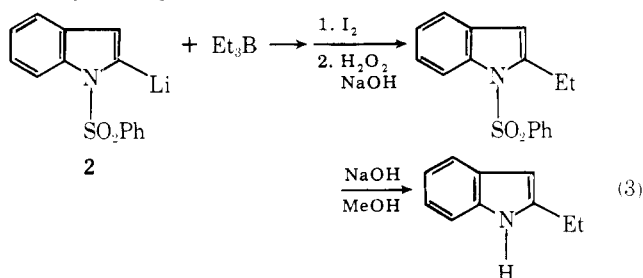
In general, electrophilic functionalization of the indole nucleus leads to regioselective formation of 3-substituted indoles.⁸ We have therefore undertaken an investigation of the scope of this reaction using a variety of organoboranes. The results are summarized in Table I.

Table I. The Reaction of the "Ate" Complex Derived from 1-Methyl-2-lithioindole^a and Trialkylboranes^b with Iodine^c for the Synthesis of *N*-Methyl-2-alkylindoles⁶

Organoborane	product	% yield ^e
triethylborane	<i>N</i> -methyl-2-ethylindole	79
triisobutylborane	<i>N</i> -methyl-2-isobutylindole	71
<i>B</i> -isobutyl-9-BBN ^d		85
tri- <i>sec</i> -butylborane	<i>N</i> -methyl-2- <i>sec</i> -butylindole	71
<i>B</i> - <i>sec</i> -butyl-9-BBN ^d		78
tricyclopentylborane	<i>N</i> -methyl-2-cyclopentylindole	79
<i>B</i> -cyclopentyl-9-BBN ^d		60
tricyclohexylborane	<i>N</i> -methyl-2-cyclohexylindole	96
<i>B</i> -cyclohexyl-9-BBN ^d		78

^a 5 mmol in 10 mL of ether. ^b 5 mmol added neat or as a 0.5–1.0 M solution in THF at –80 °C. ^c 5.25 mmol added in 5 mmol of THF. ^d Reactions involving *B*-alkyl-9-BBN derivatives were run on a 2.5-mmol scale. ^e Analysis by GLC vs. an internal standard.

While *N*-methylindoles include many biologically important indole alkaloids,⁹ any general methodology must allow for the direct substitution of the indole nucleus itself. The recent preparation of 2-lithio-*N*-benzenesulfonylindole (2)¹⁰ provides a potentially useful substrate. Thus, treatment of 2 with triethylborane and iodine leads to the 2-alkylated indole in 57% isolated yield. Subsequent hydrolysis with methanol/2 *N* NaOH (5:1, reflux, 48 h)¹⁰ gives 2-ethylindole in 85% isolated yield (eq 3).



Presumably, the mechanism of this reaction is analogous to the iodination of alkenylborate salts. Initial complexation of the lithium derivative with the borane leads to an "ate" complex (eq 4). Subsequent formation of an iodonium ion, followed by migration of an alkyl group from boron to carbon, leads to 4. β -Haloboranes similar to 4 are known to eliminate R_2BX under a variety of conditions.¹¹ Thus, a thermal syn elimination³ of R_2BI leads directly to the 2-alkylindole (eq 5).

In summary, the present development allows the regio-specific functionalization of the 2 position of the indole nu-

