The Oxidation of Diarylmethylpyridine and Pyrimidine Carbanions. Some Steric Requirements

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Our interest in the preparation of diaryl heterocyclic carbinols led us to consider their synthesis from the corresponding methane derivatives (1). Russell and co-workers (2,3) have shown that aryl carbinols are obtained by the reaction of oxygen gas with carbanions generated in solutions of dimethylsulfoxide (DMSO) and *t*-butyl alcohol containing potassium *t*-butoxide. The use of DMSO alone as a solvent with potassium *t*-butoxide and oxygen gas was reported to be unsatisfactory because this base catalyzes DMSO decomposition to dimethylsulfone and methanesulfonic acid (4).

In this communication we wish to describe the use of a single solvent system which affords high yields of tertiary heterocyclic alcohols in a very short time. The diaryl heterocyclic carbinols (Table I) were prepared using DMSO alone in the presence of powdered sodium hydroxide and oxygen gas with no apparent complicating side reactions. The reaction was found to be very rapid, generally requiring only 20-30 minutes for completion and was moderately exothermic, usually giving a 40-50° temperature rise. The rate of disappearance of starting material and the degree of exotherm were dependent on the surface area of the sodium hydroxide. These data were in general agreement with the mechanism proposed by Russel (Eq. 1-3) in which the rate controlling step was demonstrated to be the ionization of hydrocarbon (Eq. 1), although in our case this step may be at least in part heterogeneous.

Eq. 1 $Ar_3CH + :B \xrightarrow{\text{slow}} Ar_3C:^- + H:B$

Eq. 2 $Ar_3C:^- + O_2 \xrightarrow{\text{fast}} Ar_3COO:^-$

Eq. 3 $Ar_3COO:^- \xrightarrow[\text{decomp.}]{\text{radical}} Ar_3COH$

By carrying out this reaction under our conditions on a series of compounds, it was shown that the conversion to the carbinol was dependent on the number of *ortho* substituents on the aromatic rings adjacent to the central methine carbon atom. However, all of the solutions formed deep red to amber colors on exposure to sodium hydroxide, indicative of carbanion formation. The unsubstituted compounds (**1** through **4**) gave excellent yields (87-97%) of carbinol while only a fair yield (72%) was obtained with one *ortho* group present (compound **5**). Surprisingly, the presence of two *ortho* halogen atoms completely inhibited the oxidation, regardless of whether the two substituents were in the same ring (compound **6**) or in adjacent rings (compounds **7**, **8**, and **9**). These results are summarized in Table I. The chemical inertness of these *ortho*-dichloroarylpyrimidyl methanes (**6**, **7**, **8** and **9**) could be attributed to several factors: (a) a shift in equilibrium in Eq. 1 toward the left due to decreased resonance stabilization of the resulting carbanion. This explanation has been suggested to explain the weaker acidity of triptycene (5), and tri-*o*-tolymethane (6) as compared with triphenylmethane (7). (b) The approach of an oxygen atom to the α-carbon is sterically hindered and bond formation cannot occur.

Recently, αH-perchlorotriphenylmethane was shown to be quantitatively converted into the perchlorocarbanion in DMSO-ether solution using sodium hydroxide as the base, and was completely inert toward attacking species such as oxygen and iodine (8). The inertness of the perchlorocarbanion was attributed to steric shielding of the α-carbon by the surrounding chlorine atoms. Thus, explanation "a" was not tenable with our less hindered aryl methanes.

These data provide compelling evidence that the carbanions from compounds **6**, **7**, **8** and **9** are stable species under our conditions and have ample opportunity to react with oxygen. Therefore, we conclude that the steric shielding imposed on the central carbon atom of the carbanion intermediate by two axially opposed chlorine atoms is sufficient to inhibit an effective collision with an oxygen atom.

Further studies on the selectivity of this oxidation on other *o*-substituted diaryl-heterocyclic methanes are planned to elucidate the steric requirements of this reaction.

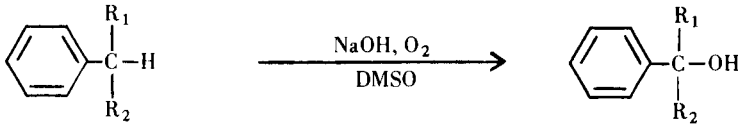
EXPERIMENTAL (9)

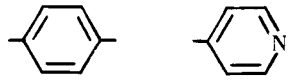
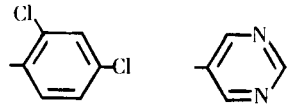
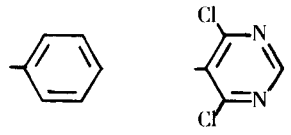
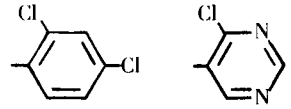
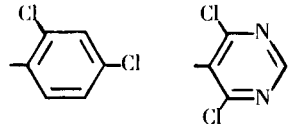
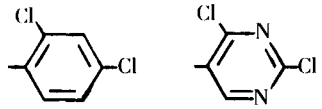
General Oxidation Procedure.

To a 250 ml. wide-mouth Erlenmeyer flask containing 0.05 mole of methane derivative (this amount was used unless otherwise stated), 100 ml. of DMSO, and 2.0 g. (0.05 mole) of powdered sodium hydroxide was passed a vigorous stream of

TABLE I

The Oxidation of Diarlymethylpyridines and Pyrimidines with Sodium Hydroxide and Oxygen in DMSO (a).



No.	Compound	Reaction Color	Product	% Yield Carbinol	Reaction Time (Minutes)
	R_1 R_2				
1		amber	10	94	30
2		amber	11	87	38
3		red-orange	12	97	20
4		red	13	96	30
5		red	14	72	14
6		amber	----	0	90 (b)
7		red	----	0	90 (b)
8		red	----	0	120 (b)
9		red	----	0	120 (b)

(a) All reactions were monitored by thin layer and gas chromatography. (b) The recovery of starting material was generally 85-90%.

oxygen gas through a glass frit addition tube beneath the surface. The mixture was stirred rapidly until the exotherm ceased (generally 20-30 minutes), then poured into 300 ml. of cold water with swirling, and the aqueous solution adjusted to *p*H 7 with concentrated hydrochloric acid. The solid was collected, washed with water and dried. In several instances a gum was obtained on neutralization and the aqueous phase was extracted with chloroform (3 x 100 ml.). The combined chloroform layers were washed with 5 x 100 ml. of water to remove the DMSO, dried over anhydrous magnesium sulfate and evaporated affording the product.

When whole pellets were used in place of powdered sodium

hydroxide, no exotherm occurred on exposure to oxygen gas. However, the oxidation was complete in 5-6 hours.

Diphenylmethylpyridines (**1**, **2**, and **3**).

The three isomeric diphenylmethylpyridines were purchased from the Aldrich Chemical Co., Inc. and were used as received.

Diphenyl-2-pyridyl Carbinol (**10**).

Filtration of the neutral aqueous phase from the oxidation reaction with 12.2 g. (0.05 mole) of **1**, gave a white solid which was dried *in vacuo* at 40° for 12 hours affording 12.3 g. (94%), m.p. 100-103° (lit. value (9) 105°) of crude **10**; ir (chloroform) 3350 cm^{-1}; pmr (deuteriochloroform) τ 3.73 (singlet, hydroxyl proton, exchangeable with deuterium oxide).

Diphenyl-3-pyridyl Carbinol (**11**).

The amount of starting methane (**2**) used was 12.2 g. (0.05 mole). The resulting gum upon isolation by extraction afforded 12.2 g. of a clear glassy liquid which crystallized on addition of pentane. Recrystallization from ethylacetate-hexane gave 11.0 g., m.p. 120-121° (lit. value (11) 115°). A second crop gave a total of 11.4 g. (87%); ir (chloroform) 3100-3400 cm^{-1} br.; pmr (DMSO-d_6) τ 2.23 (singlet, 1H, hydroxyl proton exchangeable with deuterium oxide).

Diphenyl-4-pyridyl Carbinol (**12**).

Diphenyl-4-pyridylmethane, 12.2 g. (0.05 mole) was used as starting material. The crude product was dried at 90° *in vacuo* for 3 hours affording 12.7 g. (97%) of a white powder, m.p. 233-235° (lit. value (10) 235°). This substance was insoluble in most organic solvents; ir (mull) 2300-2400 cm^{-1} br.; pmr (DTFAA) τ 1.17 and 1.70 (two doublets, 4H, $J_{2,3}$ and $J_{5,6}$ 6.0 cps. pyridine ring protons), τ 2.59 (multiplet, 10H, phenyl protons).

Diphenyl-5-pyrimidyl Carbinol (**13**).

Diphenyl-5-pyrimidylmethane (**4**) 12.3 g. (0.05 mole) was treated as described in the general procedure. The water washed solid was dried *in vacuo* at 60° for 2 hours affording a cream colored solid, 12.6 g. (96.3%), m.p. 166-169°; ir (mull) 3150-3400 cm^{-1} br.; pmr (DMSO-d_6) τ 1.10 (singlet, 1H, H-2 of pyrimidine ring), 1.40 (singlet, 2H, H-4 and H-6 on pyrimidine ring), τ 2.83 (multiplet, 10H, phenyl protons), τ 3.45 (singlet, 1H, hydroxyl proton, exchangeable on D_2O shake). A portion was crystallized from ethyl acetate for an analytical sample, m.p. 171-173°.

Anal. Calcd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68. Found: C, 77.59; H, 5.65; N, 10.49.

2,4-Dichlorodiphenyl-5-pyrimidyl Carbinol (**14**).

The pyrimidyl methane (**6**) 14.3 g. (0.045 mole) afforded a tan solid on filtration. After several water washes, the substance was dried *in vacuo* at 40° for 5 hours giving 13.7 g., m.p. 65-70° of crude **14**. Recrystallization from cyclohexane gave 10.9 g., m.p. 97-98° (72%), as a white powder.

Anal. Calcd. for $C_{17}H_{12}N_2Cl_2O$: C, 61.64; H, 3.65; N, 8.46. Found: C, 61.55; H, 3.72; N, 8.61.

Attempted Oxidation of 5-(Diphenylmethyl)-4,6-dichloropyrimidine (**5**).

This pyrimidine (**5**) under the general oxidation procedure and extraction workup gave 85% recovery of starting material, identical with an authentic sample, m.p. 76-78°, tlc, r_f 0.83; pmr (deuteriochloroform) τ 1.32 (singlet, 1H, H-2, pyrimidine ring proton), τ 2.75 (multiplet, 10H, phenyl protons), τ 3.68 (singlet, 1H, methine proton, non-exchangeable with deuterium oxide).

Anal. Calcd. for $C_{17}H_{12}N_2Cl_2$: C, 64.77; H, 3.83; N, 8.89. Found: C, 65.03; H, 4.02; N, 8.43.

Attempted Oxidation of 5-(2,4-Dichlorodiphenylmethyl)-4-chloropyrimidine (**7**).

The product was isolated by the extraction technique and afforded a gum (95% recovery of starting material). Vpc showed only one component (r_t 4.8 minutes) identical with **7**, tlc r_f 0.74. Crystallization from hexane gave cubes, m.p. 105.5-107°; pmr (deuteriochloroform) τ 1.07 (singlet, 1H, H-2 of pyrimidine ring), τ 1.75 (singlet, 1H, H-4 of pyrimidine ring), τ 2.50-3.17 (multiplet, 8H, phenyl protons), τ 3.90 (singlet, 1H, methine proton).

Anal. Calcd. for $C_{17}H_{11}N_2Cl_3$: C, 58.39; H, 3.17; N, 8.01. Found: C, 58.60; H, 3.19; N, 8.07.

Attempted Oxidation of 5-(2,4-Dichlorodiphenylmethyl)-4,6-dichloropyrimidine (**8**).

The reaction of **8** under the general procedure afforded a white solid which was shown to be identical with the starting material (the recovery was 86%). The sample was shown by tlc (r_f 0.85) to be one main component with a trace spot of r_f 0.41 (**12**). Crystallization from isopropyl alcohol gave clear cubes, m.p. 136-138°; pmr (deuteriochloroform) τ 1.34 (singlet, 1H, H-2 of pyrimidine ring), τ 3.07-3.32 (multiplet, 8H, phenyl protons), τ 3.82 (singlet, 1H, methine proton).

Anal. Calcd. for $C_{17}H_{10}N_2Cl_4$: C, 53.16; H, 2.62; N, 7.29. Found: C, 53.08; H, 2.84; N, 7.45.

Attempted Oxidation of 5-(2,4-Dichlorodiphenylmethyl)-2,4-dichloropyrimidine (**9**).

Thin layer chromatography on the crude solid product isolated under the general conditions showed it to be one component (r_f 0.82), of unchanged **9** (92% recovery). Crystallization of the crude product from isopropyl alcohol gave clear white cubes, m.p. 112-114°; pmr (deuteriochloroform) τ 1.99 (singlet, 1H, H-6 of pyrimidine ring) τ 2.50-3.20 (multiplet, 8H, phenyl protons), τ 3.95 (singlet, 1H, methine proton).

Anal. Calcd. for $C_{17}H_{10}N_2Cl_4$: C, 53.16; H, 2.62; N, 7.29. Found: C, 52.95; H, 2.49; N, 7.03.

Acknowledgment.

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