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Base-Promoted Rearrangement of Arenesulfonamides of N-Substituted Anilines to N-Substituted 2-Aminodiaryl Sulfones[1]

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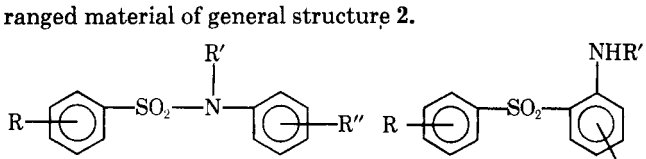
Arenesulfonamides of N-substituted aromatic amines react readily with lithium bases (e.g., methyllithium) in ether solvents to give N-substituted 2-aminodiaryl sulfones in quite respectable yield. The reaction is probably intramolecular, and involves formation of a dianion from the sulfonamide before rearrangement occurs. The immediate product of the rearrangement is a dianion with a carbanionic carbon ortho to the sulfonyl group in the nonamino ring. The reaction would appear to be the method of choice for synthesizing such amino sulfones, particularly when electron-donating groups are present. The NMR spectra of these amino sulfones indicate that the N–H proton is hydrogen bonded to a sulfone oxygen.

While previous work indicated that treatment of arenesulfonamides of unsubstituted anilines or of dialkylamines with strong bases (phenyl- or butyllithium) in THF resulted only in metalation ortho to the sulfonyl group[2] (or, in the case of *o*-toluenesulfonamides, at the *o*-methyl group),[3] we have observed that treatment of sulfonamides of general structure **1** with excess alkyl- or aryllithium in THF, followed by quenching with water, yields a rearranged material of general structure **2**.



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2

a, R = R″ = H; R′ = CH_3
b, R = *p*-CH_3; R′ = CH_3; R″ = *p*-CH_3O
c, R = R″ = H; R′ = CH_3CH_2
d, R = *p*-CH_3; R′ = CH_3CH_2; R″ = H
e, R = *p*-CH_3O; R′ = CH_3CH_2; R″ = H
f, R = R″ = H; R′ = C_6H_5
g, R = *p*-$(CH_3)_2N$; R′ = CH_3; R″ = H
h, R = *p*-CH_3O; R′ = CH_3; R″ = H
i, R = *p*-CH_3O; R′ = CH_3; R″ = *p*-CH_3O
j, R = *o*-CH_3; R′ = CH_3; R″ = H
k, R = *p*-CH_3; R′ = CH_3; R″ = H

Initially, reactions were carried out by injecting a 2.5- to threefold excess of *n*-butyllithium (in hexane) into a solution of the sulfonamide in THF at 0°, allowing the mixture to stir for 5–15 min, and then quenching with water. Under these conditions **1a** gave about a 50% yield of **2a** as well as ca. 40% of *N*-methylaniline, presumably resulting from direct attack of the lithium alkyl on the sulfonamide sulfonyl group. Further investigation showed that methyl-, phenyl-, and *tert*-butyllithium, as well as the hindered bases derived from butyllithium and dicyclohexyl- and diisopropylamine, all brought about the rearrangement. Bases examined which did not cause rearrangement were sodium and lithium hydride, sodium amide, lithium metal, and methylmagnesium iodide. Phenylsodium caused very small amounts of rearrangement but its use was not examined in detail. Methyllithium proved to be the most economical and efficient reagent, a 97% yield (by gc) of **2a** being obtainable.

Table I
Yields and Properties of 2-Aminodiaryl Sulfones[a]

Sulfone	Base	Yield, %	Mp, °C	Registry no.
2a	CH_3Li	89	136–137	53973-76-5
2b	CH_3Li	61	150–151	53973-77-6
2c	CH_3Li	40	106–107	53973-78-7
2d	CH_3Li	81	87–88	53973-79-8
2e	CH_3Li	57	110–111	53973-80-1
2f	n-C_4H_9Li	86	79–80	52914-17-7
2g	n-C_4H_9Li	54	152–153	53973-81-2
2h	n-C_4H_9Li	45	144–145	53973-82-3
2i	n-C_4H_9Li	53	164–165	53973-83-4
2j[b]	CH_3Li	50	103–104	53973-84-5
2k	n-C_4H_9Li	52	134–135	53973-85-6

[a] Satisfactory analytical data (±0.4% for C, H) were reported for all compounds in the table. [b] Prepared by methylating dianion of **2a** with methyl iodide.

In Table I are given isolated yields and physical properties of the aminosulfones. The reactions with methyllithium were most conveniently carried out at 25°, allowing about 2 hr for reaction before quencing. The sulfones were easily isolated by recrystallization and the progress of the reaction could readily be followed by TLC, all of the aminosulfones exhibiting a characteristic blue fluorescence on excitation by uv. Several of the entries in Table I involve use of butyllithium. The yields in these cases could probably be improved through use of methyllithium.

The major structural requirement of the sulfonamide for rearrangement was that the nitrogen be completely substituted. Sulfonamides of primary anilines merely formed the normal salt and were recovered unchanged. Halogen substituents did not survive, as would be expected, and alkyl groups ortho to the sulfonyl seriously interfered (vide infra).[3]

Proof of the structures of the aminosulfones was established by several means. The least substituted sulfone, **2a**,

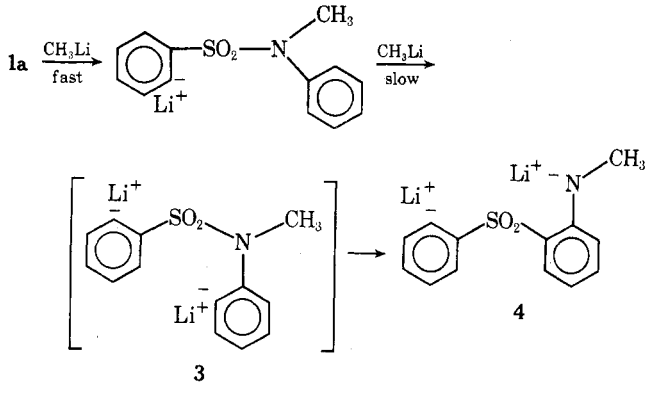
was identical with material prepared after the manner of Halberkann.[4] An NMR study of the **1b–2b** system strongly implied that the sulfonyl group had migrated to an ortho position in the amino ring; **1b** exhibited two AB quartets in the aromatic region, one for the sulfonyl ring centered at 7.22 and 7.48 ppm (J = 8.0 Hz) and one for the amino ring centered at 6.76 and 6.97 ppm (J = 9.0 Hz), while **2b** showed only one AB quartet centered at 7.29 and 7.78 ppm (J = 8.0 Hz) clearly corresponding to a para-substituted sulfonyl ring. The aromatic protons of the amino ring of **2b** appeared as an ABX system, ν_A = 6.60 ppm, ν_B = 7.00 ppm, and ν_X = 7.43 ppm (J_{AB} = 9.0, $J_{AX} \approx 0$, J_{BX} = 3.0 Hz). Finally, all of the sulfones bearing an alkyl group on nitrogen exhibited in the NMR a rather strong coupling ($J \approx 5$ Hz) between the amino proton and the α protons of the alkyl group. This has been noted as being characteristic of alkylamino groups that are intramolecularly hydrogen bonded to nitro groups in the ortho position.[5] For example, in **2a** the methyl group comes at 2.83 ppm (J = 4.9 Hz), while in *N*-methyl-*o*-nitroaniline it comes at 2.93 ppm (J = 5.1 Hz).[5] Exchange of the amino proton of **2a** with acidic D_2O collapses the doublet.

Other methods of effecting the rearrangement of arenesulfonanilides to aminosulfones have usually involved treatment with concentrated sulfuric acid at relatively high temperatures.[4,6] A photochemical rearrangement of *p*-toluenesulfonanilide to 4-methyl 4′-aminodiphenyl sulfone in relatively low yield has also been noted.[7] It would seem that this regiospecific, base-promoted technique for preparing 2-aminodiaryl sulfones from the readily available sulfonamides might have considerably synthetic value.

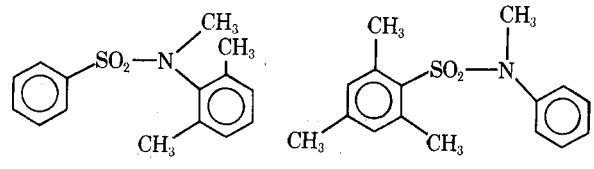
The mechanism of the reaction was shown probably to be intramolecular by treating a mixture of sulfonamides **1i** and **1k** with butyllithium at 25°. Only the expected sulfones, **2i** and **2k**, could be isolated. The possible "cross products", **2b** and **2h**, would have been easily detected by GC and were clearly shown to be absent. Such an experiment does not absolutely rule out an intermolecular pathway, particularly if the rates of reaction of **1i** and **1k** were quite different. However, considering that the two sulfonamides are fairly similar in structure and that the butyllithium reaction is quite rapid at 25° and thus probably not very selective, we feel that the probability that it is intramolecular is quite high.

More information on the mechanism was obtained by observing that 1 equiv or less of alkyllithium did not cause any rearrangement at all even though a rapid reaction, as evidenced by gas evolution (butane or methane) and development of a bright yellow color, ensued. Treatment of such solutions with water or methanol yielded unrearranged sulfonamide (ca. 90% yield) and no trace of rearrangement product. Treatment of the yellow solution so obtained from **1a** with methyl iodide yielded, after work-up, the ortho-methylated sulfonamide, **1j**. Thus, the first stage of the reaction is simple ortho metalation as observed previously.[2] Treatment with larger ratios of alkyllithium resulted in rapid formation of yellow color (quenching at this stage again yielded unrearranged sulfonamide) followed by much slower formation of a red-brown solution. (When **1a** was treated with 3 equiv of methyllithium at 25°, formation of the yellow species was apparently complete in ca. 5 min, while complete rearrangement required about 90 min). Quenching of the red-brown solution with water yielded the corresponding amino sulfone. Quenching of the red-brown solution so obtained from **1a** with methyl iodide yielded a new amino sulfone, mp 103–104°, to which, on the basis of evidence described below, we assign structure **2j**. (Alkylation of the amino anion in these amino sulfones is

Scheme I



apparently very difficult. See Experimental Section.) The overall sequence of steps is depicted in Scheme I. Whether or not dianion **3** has a finite existence is not clear. The proposed second metalation ortho to the amino group seems reasonable on several grounds. First, it is the position to which the sulfonyl group migrates. Second, if these positions are blocked by methyl groups, as in *N*-methyl-*N*-2,6-dimethylphenylbenzenesulfonamide (**5**), rearrangement

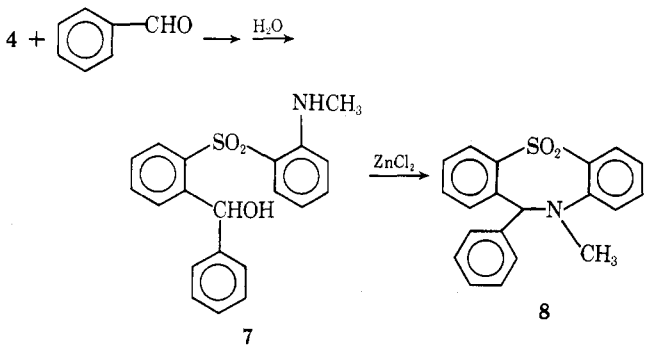


fails. (Instead, a variety of cleavage reactions apparently occur.) Thirdly, chelation of the lithium cation by one of the sulfonyl oxygens via a six-membered ring is feasible at this site,[8] as well as the well-known directing effect of a heteroatom at the adjacent ortho position.[9]

An attempt was made to see whether metalation ortho to the sulfonyl group was a prerequisite for rearrangement by treating *N*-methyl-*N*-phenylmesitylenesulfonamide (**6**) with methyllithium in THF. As in the case of **5**, no rearrangement but rather a variety of cleavage reactions ensued, as inferred from the large number of unidentified, low molecular weight peaks observed on GC analysis of the product mixture. Even one *o*-methyl group in the sulfonyl ring diverted the course of the reaction, as sulfonamide **1j** also yielded only low molecular weight products on treatment with methyllithium rather than the expected **2j**. While no firm evidence is at hand, we suspect that the metalation of the ortho benzylic positions is occurring rapidly,[3] followed by unknown side reactions.

The location of the carbanion in species **4** (Scheme I) was determined as follows. A solution of **4**, obtained by rearrangement of **1a** in usual fashion, was treated with an excess of benzaldehyde. Usual work-up of the mixture yielded a solid product to which, on the basis of ir and NMR evidence, and the result of the next reaction, we assign structure **7**. Refluxing **7** in benzene with toluenesulfonic acid failed to effect any change, but heating it at 110° with zinc chloride for several minutes caused cyclization to 10-methyl-11-phenyldibenzo[*b*,*f*][1,4]thiazepin 5,5-dioxide (**8**), whose structure was readily confirmed by spectroscopic data. In particular, the *N*-methyl group had collapsed to a singlet in the nmr (δ 2.95 ppm) and the parent peak in the mass spectrum was at *m/e* 335. The sequence of reactions is shown in Scheme II. Barring any unusual rearrangement in the zinc chloride reaction, formation of **8** from **4** conclusive-

Scheme II



7 8

ly locates the position of the carbanionic center ortho to the sulfonyl group in the nonamino ring.

Experimental Section

Materials and Equipment. Alkyllithium and phenyllithium solutions were obtained from commercial sources. Tetrahydrofuran (THF) was Matheson Coleman and Bell reagent grade and was dried by distillation from potassium benzophenone ketyl and stored under nitrogen. Elemental analyses were performed by Instranal Laboratory, Inc., Rensselaer, N.Y. Melting points were determined on a Mel-Temp apparatus and are reported uncorrected. Gas chromatographic analyses were performed on a Hewlett-Packard Model 5750 instrument equipped with flame ionization detectors, using a 6 ft × 0.125 in., 10% silicone rubber (UC-W98) on Chromosorb W column. Yields by GC were determined using internal standards and measuring peak areas by cutting and weighing. The NMR spectra were recorded using either a Varian A-60A instrument or an HA-100-D instrument modified by a Digilab FTS-3 Fourier transform system.[10]

Sulfonamides were prepared by standard techniques from commercially available sulfonyl chlorides and amines except in the cases noted. Their physical properties are described in Table II.

***N*-Methyl-*N*-2,6-dimethylphenylbenzenesulfonamide (5).** To 150 ml of water were added 2.0 g of sodium hydroxide, 4.84 g (0.04 mol) of 2,6-dimethylaniline, and 7.48 g (0.04 mol) of benzenesulfonyl chloride and the resulting mixture was stirred for 9 hr. After acidification and usual work-up 1.51 g (15% yield) of white crystals of *N*-2,6-dimethylphenylbenzenesulfonamide was obtained, mp 152–153° (methanol). To 100 ml of water were added 1.43 g (5.5 mmol) of this material, 0.4 g (10 mmol) of sodium hydroxide, and 1.64 g (13 mmol) of dimethyl sulfate.

The mixture was heated at reflux for 45 min, cooled, and the product extracted with ether. After removal of ether the product was recrystallized from methanol, yielding 1.20 g (79%) of **5.**

***N'*-Methyl-*N'*-phenyl-*p*-dimethylaminobenzenesulfonamide (1g).** *N'*-Methyl-*N'*-phenyl-*p*-aminobenzenesulfonamide was prepared by acid hydrolysis of the corresponding *p*-acetamidobenzenesulfonamide, yielding material of mp 141–141.5° (benzene) (lit. mp 138–140°).[11] To 0.524 g (2.0 mmol) of this material in 20 ml of dry THF at 0° was added dropwise 1.25 ml of 1.6 *M* butyllithium in hexane. After stirring for 5 min the red-brown solution was then treated (dropwise) with 0.284 g (0.13 ml, 2.0 mmol) of methyl iodide. After stirring for another 10 min, another 2.0-mmol portion of butyllithium was added slowly as previously. After 5 min another 2.0-mmol portion of methyl iodide was added, and the mixture was stirred for 15 min and then quenched with water. After normal work-up the crude solid was recrystallized from methanol, yielding 0.406 g (70%) of **1g.**

Rearrangement of Sulfonamides with Lithium Bases. The general procedure was to dissolve 1 g of sulfonamide (ca. 4 mmol) in 10 ml of dry THF under a nitrogen atmosphere and then rapidly add, with stirring, ca. 8.5 mmol of lithium base. A water bath was often essential to absorb the heat of the reaction. After stirring for 70–100 min, water was added, and products were separated by ether extraction and isolated in usual fashion. The resulting aminosulfones were recrystallized from methanol or methanol–water mixtures.

Rearrangement of *N*-Methyl-*N*-phenylbenzenesulfonamide (1a) with Sulfuric Acid. The method followed is essentially that of Halberkann.[4] To 5.0 g (0.02 mmol) of **1a** was added 15 g of 98% sulfuric acid and the mixture was stirred and heated at 100° for 2 hr. After cooling, the mixture was poured into ice water and the resulting brown solid was separated by filtration. Two recrystallizations from methanol yielded 0.355 g (7% yield) of white needles, mp 136–137°, of **2a**, identical in all respects (ir, NMR, mass spectrum) with **2a** obtained by reaction of **1a** with methyllithium.

Table II
Properties of Sulfonamides

Sulfonamide	Mp, °C	Lit. mp, °C
1a	79–79.5	79[a]
1b	61–62°	68–69[b]
1c	Liquid[a]	
1d	86–87	88[c]
1e	67–68[d]	
1f	122–123	124[a]
1g	132–133[d]	
1h	106.5–107	109–110[e]
1i	76–77	77[f]
1j	Liquid[g]	
1k	92.5–93.5	94[a]
5	111–112[d]	
6	94–95	95–96[h]

[a] Z. Rappaport, "Handbook of Tables for Organic Compound Identification", 3rd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1967, Table XVIII. [b] J. Halberkann, *Ber.*, **54**, 1669 (1921). [c] A. I. Vogel, "Practical Organic Chemistry", Longmans, Green and Co., New York, N.Y., 1948, p 627. [d] Satisfactory analytical data (±0.4% for C, H) were reported for these new compounds. [e] S. Ji, L. B. Gortler, A. Waring, A. Battisti, S. Bank, W. D. Closson, and P. Wriede, *J. Am. Chem. Soc.*, **89**, 5311 (1967). [f] Y. Osawa, *Nippon Kagaku Zasshi*, **84**, 134 (1963). [g] Reaction with an excess of sodium naphthalene in THF resulted in production of 98% of the calculated amount (determined by GC) of *N*-methylaniline. See W. D. Closson, S. Ji, and S. Schulenberg, *J. Am. Chem. Soc.*, **92**, 650 (1970). [h] M. Pezold, R. S. Schreiber, and R. L. Shriner, ibid., **56**, 696 (1934).

Preparation of 2-(*N*-Methylamino)diphenyl Sulfone by Alkylation of 2-Aminodiphenyl Sulfone. 2-Aminodiphenyl sulfone was prepared by the method of Ullman and Pasdermadjian,[12] mp 120–121° (lit.[12] mp 121°). To a stirred solution of 0.233 g (1.0 mmol) of this material in 10 ml of THF at −30° was added 1.3 ml of 1.0 *M* *n*-butyllithium in hexane. This was immediately followed by addition of 0.12 g (1.3 mmol) of dimethyl sulfate, and the reaction mixture was warmed quickly to 50° and stirred at this temperature for 3 min. After quenching with water and usual work-up a brown oil was obtained which was purified by column chromatography, using 40–140 mesh silica gel and chloroform eluent. A pale yellow oil was obtained which crystallized on standing. Several recrystallizations from methanol yielded 0.010 g (4% yield) of white solid, mp 135–137°, which had ir and NMR spectra identical with those of **2a** obtained by the rearrangement reactions. Attempts at alkylation with butyllithium–methyl iodide, or by refluxing the sulfone in trimethyl phosphate, failed to yield any detectable amount of **2a.**

Reaction of *N*-Methyl-*N*-phenylbenzenesulfonamide (1a) with 1 Equiv of Butyllithium. To a stirred solution of 1.0 g (4 mmol) of **1a** in 10 ml of dry THF (at 25°) was slowly added 2.5 ml of 1.6 *M* *n*-butyllithium in hexane. The bright yellow solution was stirred for 5 min and then quenched with water. Analysis by GC showed the presence of only **1a** and no trace of **2a.** Usual work-up resulted in recovery of 0.91 g (91%) of **1a.**

To a similarly prepared solution of the anion derived from **1a** was added 0.61 g (4.3 mmol) of methyl iodide. After stirring for 5 min after disappearance of the yellow color, water was added and the product was isolated by extraction in the usual way, yielding a viscous liquid. This was purified by column chromatography on 40–140 mesh silica gel, using methylene chloride as eluent. The resulting oil, 0.715 g (68%), was identical in spectral properties (ir, NMR) with *N*-methyl-*N*-phenyl-*o*-toluenesulfonamide (**1j**) prepared by the Schotten–Baumann reaction of *o*-toluenesulfonyl chloride and *N*-methylaniline.

Reaction of *N*-Methyl-*N*-phenylbenzenesulfonamide (1a) with 2.5 Equiv of Methyllithium. To a stirred solution of 1.0 g (4.0 mmol) of **1a** in 10 ml of dry THF at 25° was added 5.5 ml (9.2 mmol) of 1.67 *M* methyllithium in ether. The solution was then

stirred for 90 min and then 0.71 g (5 mmol) of methyl iodide was added slowly. After another 5 min of stirring, 50 ml of water was added and the product was isolated in usual fashion. Recrystallization from aqueous methanol yielded 0.515 g (50%) of white crystals: mp 103–104°; NMR ($CDCl_3$) δ 2.49 (s, 3 H, CH_3), 2.79 (d, 3 H, J = 5.0 Hz, NCH_3), 5.9–6.2 (m, 1 H, NH), 6.5–8.1 (m, 8 H, aromatic).

On the basis of this and other evidence the compound is tentatively identified as 2-(*N*-methylamino)-2′-methyldiphenyl sulfone (**2j**).

A similar solution of dianion was prepared from 1.7 g (6.9 mmol) of **1a** in 15 ml of dry THF and treated dropwise with 1.05 g (10 mmol) of benzaldehyde. After stirring for another 15 min the mixture was quenched with water and the product was isolated. The resulting viscous oil was purified by chromatography on silica gel, eluting with carbon tetrachloride–chloroform. This yielded 2.07 g (85%) of clear oil which crystallized on standing: mp 115–116°; NMR ($CDCl_3$) δ 2.63 (d, 3 H, J = 5.0 Hz, NCH_3), 3.57 (broadened d, 1 H, J = 4.0 Hz, OH), 6.05 (broadened d, 1 H, J = 4.0 Hz, C-H), 6.4–7.9 (m, 14 H, aromatic and NH).

On the basis of this and subsequent evidence, the material is tentatively assigned structure **7**.

Preparation of 10-Methyl-11-phenyldibenzo[*b,f*][1,4]thiazepin 5,5-Dioxide (8). To 2.07 g (5.86 mmol) of alcohol **7** was added 150 mg of anhydrous zinc chloride. The neat mixture was then heated at 115–120° under a nitrogen atmosphere for 40 min. At this point the mixture had solidified. After cooling, 50 ml of water was added and the mixture was extracted with chloroform. After drying with magnesium sulfate, removal of solvent, and recrystallization from aqueous ethanol, 1.45 g (73%) of a white solid was obtained: mp 211–212°; NMR ($CDCl_3$) δ 2.95 (s, 3 H, NCH_3), 6.02 (broadened s, 1 H, CH), 6.67–7.55 (m, 13 H, aromatic); mass spectrum *m/e* 335 (parent), 306, 270.

Anal. Calcd for $C_{20}H_{16}NO_2S$: C, 71.62; H, 5.11. Found: C, 71.31; H, 5.12.

Registry No.—**1a**, 90-10-8; **1e**, 35088-88-1; **1g**, 53973-86-7; **5**, 53973-87-8; **7**, 53973-88-9; **8**, 53973-89-0; 2,6-dimethylaniline, 87-62-7; benzenesulfonyl chloride, 98-09-9.

References and Notes

(1) (a) Supported in part by the U.S. Public Health Service (Research Grant No. R01-AM11419 from the National Institute of Arthritis and Metabolic Diseases), and by the Alfred P. Sloan Foundation. (b) Presented in part at the 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973, Abstract ORGN 093. (c) Some similar results have been since reported by D. Hellwinkel and M. Supp, *Angew. Chem.*, **86**, 273 (1974).
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(10) We would like to thank the National Science Foundation for Grant No. GP-28061 for the purchase of the FTS-3 system.
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A Novel and Efficient Route to 5-Arylated γ-Lactones

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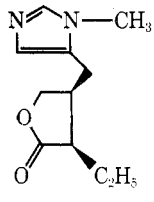
Title compounds (IV) were prepared by oxidation of lactols I with Ag_2CO_3 on Celite in refluxing xylene. Lactols I were obtained from reaction of ketones II with organomagnesium compound III and subsequent hydrolysis of the products V in 10% sulfuric acid. Prepared were the following compounds IV (R_1, R_2 given): H, 3-pyridyl; H, 4-pyridyl; H, 1-benzylimidazol-2-yl; H, 1-methylimidazol-2-yl; H, 1-benzyl-2-methylimidazol-5-yl; H, 1-benzyl-2-isopropylimidazol-5-yl; H, 1,2-dimethylimidazol-5-yl; phenyl, phenyl.

In our current research program we were interested in lactones of type I, bearing an imidazole or pyridine moiety at the 5 position, in order to examine their anticholinergic activities compared to pilocarpine (1). A survey of the literature revealed that there are no convenient methods to synthesize lactones of this particular type, because of the difficult availability of the required starting materials or inconvenient experimental conditions of the documented methods.



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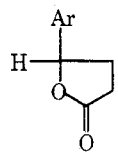

I

However, in a recent report,[2] benzimidazoles could be synthesized by reaction of readily available carboxaldehydes with the Grignard derivative of 2-(2-bromoethyl)-dioxolane-1,3 (**3**)[3] and subsequent cyclization in alcoholic medium. It was established that these reactions proceed *via* lactols as intermediates, which in fact could be isolated. With this consideration in mind, it was obvious that oxidation of the lactols might afford the required lactones.

Reaction of the aldehyde **2d** with Grignard derivative **3** in tetrahydrofuran gave **4d**, which upon refluxing in 10% sulfuric acid afforded lactol **5d**. Oxidation of this lactol with convenient reagents such as permanganate, chromous trioxide, manganese dioxide, and silver oxide did not provide the desired lactone **6d**.

At that stage our attention was focussed to the work of Fetizon, *et al.*,[4] who reported that lactones should be generated from 1,5-diols in one simple oxidative conversion by silver carbonate on Celite.

There is much evidence that this reaction proceeds *via* the lactol stage.[5] Indeed, on refluxing lactol **5d** with silver carbonate on Celite, in xylene as solvent, lactone **6d** could be obtained in a 51% yield. Treatment of lactols **5a–c** and **5e,f** under similar conditions gave in moderate to good yields lactones **6a–c** and **6e,f**.

Further elucidation of this reaction showed that this method is not restricted to heterocyclic compounds. So, on