data on nucleotides. These studies and enzymatic studies are in progress.

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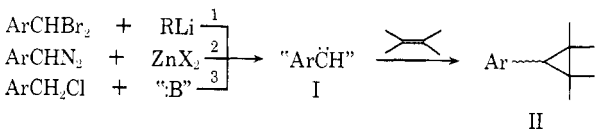
Communications to the Editor

A Useful Synthesis of Arylcyclopropanes

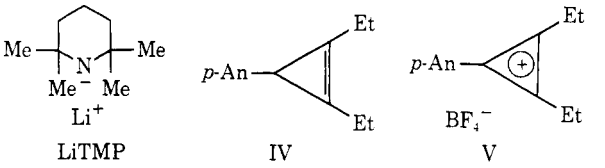
Sir:

In the best published general methods[1,2] for the preparation of arylcyclopropanes (II) by routes involving the reaction of phenyl carbenes or carbenoids (I) with alkenes, the intermediate I is generated: (1) by treatment of the costly and often unstable benzal bromides (but not $ArCHCl_2$[3]) with organolithium reagents,[1] or (2) by zinc halide induced decomposition of the unstable and detonation prone aryldiazomethanes.[2,4] A



high-yield synthesis of II from I formed (3) by reaction of a base with a benzyl chloride (usually commercially available, inexpensive) is thus attractive both economically and from a safety standpoint. Numerous past attempts to develop such a method have been unsuccessful.[5-8] With organometallic bases, the products obtained include substances which may be visualized as derived from metal–halogen exchange reactions and from processes involving deprotonation of the alkene trap to an allyl anion. Generally, however, the base is just benzylated. Even when initial α-proton abstraction occurs, the $ArCHCl$ generated does not fragment but is instead alkylated by more $ArCH_2Cl$. The only published exception is the reaction of $PhCH_2Cl$ with *n*-BuLi in cyclohexene from which 7-phenylnorcarane (III) was isolated in a disappointing 14% yield.[6] We have confirmed this result (13%) and have found that MeLi (<9%), PhLi (<5%), and *t*-BuLi (0%) are even less satisfactory for the production of III. In other new tests, no III was isolated with KO-*t*-Bu or with the Schlenk–Hauser base, sodium triphenylmethide,[9] and only traces of III were obtained with lithium bistrimethylsilylamide[10] or with another Hauser base, bromomagnesium diisopropylamide.[11] Calculated yields in these eight experiments using a radioisotope dilution assay to ensure the stability of III in the reaction media and to correct for loss during the sometimes complex isolation schemes required still were only 13, 9, 8, 2, 1–2,[12] 2, 3, and 7%, respectively. The last four reagents above have previously been recommended specifically for their excellence as very strong proton-specific bases.[8-11]

We now report here the successful use of lithium 2,2,-6,6-tetramethylpiperidide (LiTMP) as the base[13] in a practical synthesis of II from $ArCH_2Cl$. In the optimum experimental procedure, a rapidly stirred, concentrated solution (under N_2) of 1 equiv of $ArCH_2Cl$ and the alkene (large excess) in ether is slowly titrated with 1 equiv of a *ca.* 1 *M* solution of LiTMP in ether. The reaction temperature and base addition rate are



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(2) S. H. Goh, L. E. Closs, and G. L. Closs, *J. Org. Chem.*, **34**, 25 (1969).
(3) Which reacts to give $ArCCl$: R. A. Moss, *ibid.*, **27**, 2683 (1962).
(4) Simple photochemical or thermal decomposition of $ArCHN_2$ is a much less satisfactory source of I.[1,2] Also: C. D. Gutsche, G. L. Bachman, and R. S. Coffey, *Tetrahedron*, **18**, 617 (1962).
(5) Bases studied include KOH, LiOMe, NaOEt, KO-*t*-Bu, HCONHNa in $HCONH_2$, $LiNH_2$ or $NaNH_2$ in NH_3, ether, THF, hydrocarbon, or $(Me_2N)_3PO$, MeLi, EtLi, *n*-BuLi, Na in NH_3, NaH in THF or $(Me_2N)_3PO$, and "active NaH" in THF. For review of material prior to 1960 see ref 6. For more recent results see ref 7 and S. Bank and M. C. Prislopski, *Chem. Commun.*, 1624 (1970); P. Caubére, *Bull. Soc. Chim. Fr.*, 1293 (1966); P. Caubére and J. Moreau, *ibid.*, 1986 (1970); *Tetrahedron*, **25**, 2469 (1969); J. F. Bunnett and J. D. Reinheimer, *J. Amer. Chem. Soc.*, **84**, 3284 (1962); P. E. Verkade, K. S. deVries, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **82**, 637 (1963). For new data see ref 8.
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(7) But note also that the reaction of $PhCH_2Cl$ with *n*-BuLi by a different pathway (similar conditions minus cyclohexene) is used as a quantitative assay for these RLi reagents: H. Gilman and A. H. Haubein, *J. Amer. Chem. Soc.*, **66**, 1515 (1944); D. H. Hoeg and D. I. Lusk, *ibid.*, **86**, 928 (1964); R. West and W. H. Glaze, *J. Chem. Phys.*, **34**, 685 (1961).
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(9) B. E. Hudson and C. R. Hauser, *ibid.*, **63**, 3156, 3163 (1941); D. F. Thompson, P. L. Bayless, and C. R. Hauser, *J. Org. Chem.*, **19**, 1490 (1954); W. Schlenk, H. Hillemann, and I. Rodloff, *Justus Liebigs Ann. Chem.*, **487**, 135 (1931).
(10) C. R. Krüger and E. G. Rochow, *J. Organometal. Chem.*, **1**, 476 (1964), and references therein; D. H. R. Barton, R. H. Hesse, G. Tarzia, and M. M. Pechet, *Chem. Commun.*, 1497 (1969); M. Tanabe and D. F. Crowe, *ibid.*, 1498 (1969); M. W. Rathke, *J. Amer. Chem. Soc.*, **92**, 3222 (1970).
(11) F. C. Frostick and C. R. Hauser, *ibid.*, **71**, 1350 (1949); C. R. Hauser and H. G. Walker, *ibid.*, **69**, 295 (1947).
(12) Depending on reaction solvent: *t*-BuOH, ether, or cyclohexene.
(13) Since 2,2,6,6-tetramethylpiperidine (HTMP) is readily prepared by reduction of 2,2,6,6-tetramethylpiperidone-4 (≡ triacetonamine (i); from acetone, ammonia, and $CaCl_2$), it is potentially inexpensive enough for most synthetic purposes. Because of the value of the derived nitroxides as spin labeled diagnostic reagents in spectroscopy, both HTMP and i are already available from several sources. The unfortunate impurities (*ca.* 10%) in commercial samples are easily removed by distillation. Treatment of HTMP with a commercial RLi (R = Me, *n*-Bu) solution provides a convenient small scale source of LiTMP. The reaction is best performed in the addition funnel just before use.

chosen so that the exothermic process causes the alkene (or ether) to reflux gently. Representative reactions are listed in Table I. With only one exception the cyclopropane yields are better—sometimes two or three times better—than published yields based on the less satisfactory $ArCHBr_2$ and $ArCHN_2$ precursors of I.

Table I. Preparation of Arylcyclopropanes from $ArCH_2X$, Alkenes, and LiTMP

Reactants	Yield,[a] % (syn/anti ratio)	Lit. yield,[b] % A	B
$PhCH_2Cl$ + *cis*-butene	78 (2.1)	21	70
$PhCH_2Cl$ + *trans*-butene	50	14	
$PhCH_2Cl$ + cyclohexene	53 (2.2)		90
p-$MeOPhCH_2Cl$ + *cis*-butene	87 (~18)	55	37
p-$MeOPhCH_2Cl$ + cyclohexene	82 (10)		37
p-$MeOPhCH_2Cl$ + butadiene	74[c] (2.3)		50
p-$ClPhCH_2Cl$ + isobutene	65	19	
o-$MePhCH_2Br$ + *cis*-butene	69[d,e] (3.5)	*f*	*f*
α-$C_{10}H_7CH_2Cl$ + isobutene	69[d,g]		
p-$MePhCH_2Cl$ + H_2C=CHOEt	78[d,h] (2.0)		
p-$MeOPhCH_2Cl$ + H_2C=$C(OMe)_2$	87[d,i]		

[a] Of pure product after isolation by vacuum distillation; syn/anti ratio determined by vpc–nmr combination. [b] A, from $ArCHBr_2$;[1] B, from $ArCHN_2$ + ZnX_2.[2] [c] Of 1-*p*-anisyl-2-vinylcyclopropane. [d] New compound; satisfactory combustion analysis and corroborative spectral data have been obtained. [e] Vpc on a 5 ft × 1/4 in. 20% SE-30 on 60–80 Chromosorb W column; temperature 175°; flow rate 75 cm³/min; retention times: anti isomer, 5.4 min; syn, 6.6 min. [f] Production of the *p*-tolyl isomer in 22% yield by route A[1] and 60% yield by route B[2] has been reported. [g] Bp 89.5–91° (0.2 Torr). [h] Vpc on column in footnote *e*; 165°; 50 cm³/min; retention times: syn, 10.3 min; anti, 11.7 min. Isomer assignment based on comparison with vpc–nmr data for 1-MeO-2-Ph-cyclopropanes: W. Kirmse and H. Schütte, *Chem. Ber.*, **101**, 1674 (1968). The published assignment is not definitive. [i] Bp 92–93° (0.4 Torr).

In the preparation of III from $PhCH_2Cl$, LiTMP, and cyclohexene, substitution of tetrahydrofuran (at 35°) for ether did not change the product yield, but with cyclohexane as solvent the yield decreased to 32%. Other evidence for the significance of ion pairing and aggregation phenomena in determining the reaction course was obtained by including 1 equiv of tetramethylethylenediamine, a complexing agent for Li^+,[14] in the ether reaction. Under these conditions, the yield was only 14%.[15] In all reactions studied, the cyclopropanes were formed by stereospecific cis additions, and when epimer pairs were possible, the thermodynamically less stable syn isomer was the predominant product. The high syn/anti ratios in Table I are similar to those generally found for reactions previously characterized as carbenoid.[1,2,16,17] The base-catalyzed isomerization normally used[1,16,18] for the conversion of *syn*-arylcyclopropanes to the corresponding anti isomers is not significant under the reaction conditions: even after 3 days in 0.5 *M* LiTMP in ether at 25°, *syn*-1-*p*-anisyl-*cis*-2,3-dimethylcyclopropane is not appreciably contaminated by the anti isomer (the equilibrium mixture from reaction with KO-*t*-Bu–DMSO has a syn/anti ratio of <0.1). The variation of III yield with $LiNR_2$ structure is discussed in the accompanying paper.[8]

Of special note in Table I is the fact that no methyl insertion product was found using *o*-$MePhCH_2Br$ as the reaction substrate (expected carbenoid selectivity) and the discovery (especially in view of the data in the following communication[8]) that benzyne formation was not a competitive process in the *p*-$ClPhCH_2Cl$ reaction when 1 equiv LiTMP was used as the base. An attempt to extend the cyclopropane synthesis to secondary benzylic halides (*e.g.*, α-chloroethylbenzene) failed; only styrene derived (β elimination) products were found. However, Traylor and Brown[19] have recently obtained *cis*-1,2-ethylenedioxy-3-phenylcyclopropane from 1,4-dioxene, $PhCH_2Cl$, and LiTMP, and we have similarly isolated a monooxygen functionalized cyclopropane using commercial H_2C=CHOEt as the alkene component (78%, Table I). The further elaboration of this discovery to a superior preparation of arylcyclopropanone acetals from ketene acetals has also been achieved. The previously favored route to this interesting class of compounds—reductive dehalogenation of the Cl-substituted derivative (from an ArC̈Cl or ClC̈Cl reaction)[20]—failed when the three-membered ring was substituted by hydrogen.[20] The 87% yield in the example in Table I signifies the removal of this restriction.

By use of nonterminal acetylenes in place of the alkene substrates, 3-arylcyclopropenes are also available by the present method. An example is the isolation of 1,2-diethyl-3-*p*-anisylcyclopropene (IV, 60%; bp 87–88.5° (0.4 Torr); ir 5.32 μ[21]) after addition of LiTMP to a 3-hexyne–ether solution of *p*-$MeOPhCH_2Cl$. As part of the structure proof for IV, it was converted (81%) to V (mp 72–72.5°, pK_{R^+} = 6.8[21]) by treatment with trityl fluoroborate in CH_2Cl_2. This last reaction also illustrates the utility of the overall scheme as a source of cyclopropenium cations.

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(18) F. R. Jensen and D. B. Patterson, *Tetrahedron Lett.*, 3837 (1966).
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(21) For comparison data see: R. Breslow, H. Höver, and H. W. Chang, *ibid.*, **84**, 3168 (1962).

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Lithium 2,2,6,6-Tetramethylpiperidide and Related, Strong, Proton-Specific Bases. Evaluation in Synthesis

Sir:

The immense utility in synthesis and rarity of bases which selectively abstract protons from substrates containing intrinsically more reactive sites toward nucleophilic attack is recognized in the fact that superior rea-