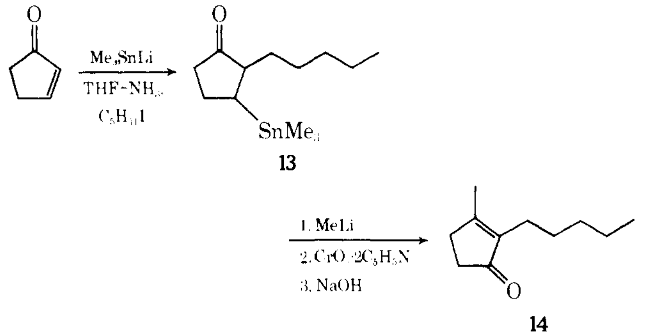
To illustrate this transformation, we have prepared dihydrojasmone by a simple four-step procedure from 2-cyclopentenone. First, addition of trimethylstannyllithium in 1:2 THF-NH_3 and *n*-pentyl iodide gave (−33 °C, 6 h) the alkylated stannyl ketone **13** (IR (neat) 1740, 770 cm^{-1}) in 90% yield. Methyllithium (Et_2O, −78 °C) added to the carbonyl and chromic anhydride/pyridine (15 equiv, 23 °C, 16 h) oxidized the trimethyltin moiety to yield a hydroxy cyclopentanone. Basic dehydration[17] then gave dihydrojasmone[18] **14** in 71% overall yield from **13** (89% conversion).



13

14

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References and Notes

(1) Other synthetic applications of organotin compounds include E. J. Corey and R. H. Wollenberg, *J. Am. Chem. Soc.*, **96**, 5581 (1974); *J. Org. Chem.*, **40**, 2265, 3788 (1975); E. J. Corey, P. Ulrich, and J. M. Fitzpatrick, *J. Am. Chem. Soc.*, **98**, 222 (1976). For a short review see A. J. Bloodworth and A. G. Davies, *Chem. Ind.* (*London*), 490 (1972); P. J. Smith, *ibid.*, 1025 (1976).

(2) (a) Professor H. G. Kuivila of the State University of New York at Albany has independently observed conjugate addition of trimethylstannyllithium to representative α,β-unsaturated ketones: personal communication. (b) Tributylstannylmagnesium bromide reacts with enones to give either 1,2 or 1,4 addition depending on the substitution of the substrate: J.-C. Lahournere and J. Valade, *J. Organomet. Chem.*, **33**, C7 (1971). (c) Stannyl cuprate addition: J. Hudec, *J. Chem. Soc., Perkin Trans 1*, 1020 (1975).

(3) W. C. Still, *J. Org. Chem.*, **41**, 3061 (1976).

(4) Other preparations of R_3SnLi have been reported but are less efficient that the ones described here. These include (a) RLi + $SnCl_2$ (H. Gilman and S. D. Rosenberg, *J. Am. Chem. Soc.*, **75**, 2507 (1953); D. Blake, G. E. Coates, and J. M. Tate, *J. Chem. Soc.*, 618 (1961); W. L. Wells and T. L. Brown, *J. Organomet. Chem.*, **11**, 271 (1968)); (b) R_3SnX or R_6Sn_2 + Li (C. Tamborski, F. E. Ford, and E. J. Soloski, *J. Org. Chem.*, **28**, 237 (1963); H. Gilman, F. K. Cartledge, and S.-Y. Sim, *J. Organomet. Chem.*, **1**, 8 (1963); A. T. Weibel and J. P. Oliver, *ibid.*, **82**, 281 (1974)).

(5) Yields of R_3SnLi were estimated by reaction with 2-cyclohexenone and VPC analysis against an internal standard. These reactions should be conducted with care in an efficient hood since volatile organotin compounds (e.g., Me_4Sn) are toxic.

(6) R_3SnNa has been prepared previously by this method: C. H. W. Jones, R. G. Jones, P. Parington, and R. M. G. Roberts, *J. Organomet. Chem.*, **32**, 201 (1971).

(7) Yields of numbered compounds refer to isolated material after chromatography, distillation or recrystallization.

(8) All new compounds gave satisfactory IR, NMR, and C, H analyses.

(9) Sterochemistry follows from the half-height peak width ($W_{1/2}$ only 0.3 Hz wider than TMS) of the C-3 methyl and the chemical shift (δ 0.03) of protons on the $-SnMe_3$ grouping. Examination of shifts of a large number of 3-trimethylstannylcyclohexanones shows that equatorial $-SnMe_3$ groups absorb at lower field (δ 0.11–0.06); cf. R. K. Boeckman and S. M. Silver, *J. Org. Chem.*, **40**, 1755 (1975). See also G. S. Koermer, M. L. Hall, and T. G. Traylor, *J. Am. Chem. Soc.*, **94**, 7205 (1972).

(10) Prepared by addition of MeLi to Me_6Sn_2 in Et_2O (20 °C, 30 min).

(11) Compound **7** underwent substantial decomposition on standing and on silica gel chromatography. Immediate NMR and TLC analysis of the crude product showed **7** to be the major product.

(12) Cf. J. W. Patterson, Jr., and J. H. Fried, *J. Org. Chem.*, **39**, 2506 (1974); E. S. Binkley and C. H. Heathcock, *ibid.*, **40**, 2156 (1975).

(13) Other chromic acid oxidants (Jones reagent, chromic acid/acetic acid) were less effective. Pyridinium chlorochromate may be used, but the rate of oxidation is slower. Chromic acid/acetic acid oxidation of simple alkylstannanes has been studied previously: C. Deblandre, M. Gielen, and J. Nasielski, *Bull. Soc. Chim. Belg.*, **73**, 214 (1964).

(14) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).

(15) Other halide → ketone transformations include W. Pritzkow and H. Schaefer, *Chem. Ber.*, **93**, 2151 (1960); V. Franzen and S. Otto, *ibid.*, **94**, 1360 (1961); H. J. Bestmann and O. Kratzer, *ibid.*, **96**, 1899 (1963); D. M. Lemal and A. J. Fry, *Tetrahedron Lett.*, 775 (1961); B. Ganem and R. K. Boeckman, *ibid.*, 719 (1974); K. Baum, C. D. Beard, and V. Grakauskas, *J. Am. Chem. Soc.*, **97**, 267 (1975).

(16) Monoalkylative enone transpositions: B. M. Trost, and J. L. Stanton, *J. Am. Chem. Soc.*, **97**, 4018 (1975); B. M. Trost, K. Hiroi, and N. Holy, *ibid.*, **97**, 5873 (1975); W. Oppolzer, T. Sarkar, and K. K. Mahalanabis, *Helv. Chim. Acta*, **59**, 2012 (1976).

(17) H. Hundsdiecker, *Chem. Ber.*, **75**, 460 (1942).

(18) Jasmone syntheses have been reviewed: T.-L. Ho, *Synth. Commun.*, **4**, 265 (1974).

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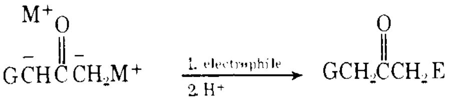
Unusual Mode of Alkylation of Certain Ketone Dianions

Sir:

It has been amply demonstrated[1] that dianions of the general formula **1** react with a variety of electrophiles to give products of structure **2**, resulting from *exclusive* attack at the terminal methylene position. These results have been explained by arguing that the methylene position should bear a higher electron density than the methine site and therefore it should be more reactive.[1,2]

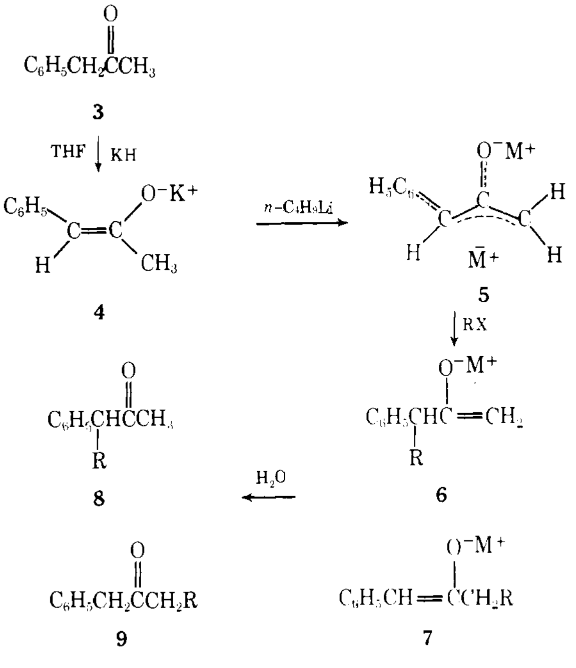


$$\mathrm{G\overset{-}{C}H\overset{\overset{M^+O}{\|}}{C}\overset{-}{C}H_2M^+} \xrightarrow[2.\ H^+]{1.\ \text{electrophile}} \mathrm{GCH_2\overset{\overset{O}{\|}}{C}CH_2E}$$

1 2

In the present communication, we wish to report the first examples of electrophilic reactions of ketone dianions which lead to carbon-carbon bond formation *at the methine rather than the methylene site.* Thus, we have observed that reaction of the 1-phenyl-2-propanone dianion **5**, generated as shown in Scheme I, with a variety of alkyl halides led predominately, and in many cases exclusively, to alkylation products at C_1 (structure **8**) rather than at C_3 (structure **9**).

Scheme I



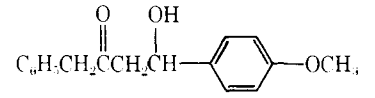
3 4 5 6 7 8 9

$M^+ = K^+, Li^+$

Similar results were observed during the alkylation reactions of the 1,1-diphenyl-2-propanone dianion, although generally larger quantities of terminal (C_3) alkylation products were obtained in this case.

Dianion **5** was generated by sequentially treating 1-phenyl-2-propanone with potassium hydride and *n*-butyllithium as shown in Scheme I.[3] The presence of enolate **4** was ascertained by treating the reaction mixture with a number of alkyl halides to produce the expected C_1 alkylation products in good yield. Enolate **4** was considered to possess the trans rather than the cis geometry on the basis of its ^1H NMR spectrum (in THF), which displayed, in addition to the aromatic absorptions, a sharp singlet at δ 4.5 ppm for the proton at C_1. The cis isomer has been shown to display ^1H NMR absorption for H_1 at a considerably lower field.[4]

The presence of dianion **5** was confirmed in a number of ways. First, treatment of the reaction mixture with 2.5 equiv of methyl iodide afforded the expected dimethylation product 2-phenyl-3-pentanone.[5] Second, dianion **5** was reacted with 1 equiv of *p*-anisaldehyde to produce the terminal aldol condensation product **10**, in 44% yield, mp 78-79 °C from benzene-ligroin.[6] Upon dehydration alcohol **10** gave the corresponding α,β-unsaturated ketone, previously reported by Hauser.[1c]



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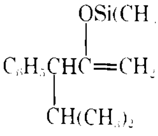

$C_6H_5\underset{CH(CH_3)_2}{CH}\overset{OSi(CH_3)_3}{C}{=}CH_2$

11

Finally dianion **5** was generated in THF-d_8–hexane and its ^1H NMR spectrum was recorded on a 60-MHz instrument, using tetramethylsilane (TMS) as an external standard. The absorptions displayed in the NMR spectrum of **5** and their corresponding assignments were as follows: broad multiplet at δ 6.33 (4 H), assigned to the ortho and meta protons of the benzene ring; broad multiplet at 5.47 (1 H), assigned to the para proton; broad singlet at 3.82 (1 H), assigned to the proton at C_1; partially resolved doublet centered at 2.60 (2 H), assigned to the protons at C_3.

In addition to lending additional support for the presence of dianion **5**, the NMR spectrum provides substantial information about the structure and charge distribution of this intermediate. The most important observation, in our view, is that the overall appearance of the spectrum of dianion **5** is remarkably similar to that of the allylbenzene anion, reported earlier by Freedman and his coworkers.[7] The close resemblance of their NMR spectra strongly implies a close structural similarity between the two systems. Indeed, if one of the negative charges in dianion **5** is considered to be largely localized on oxygen,[8] the lower portion of the intermediate would constitute a system essentially identical with the allylbenzene anion, with the second negative charge highly delocalized over C_1, C_2, C_3, and the benzene ring.

A further observation of interest in connection with the NMR spectra of the two intermediates is that, at comparable temperatures, the spectrum of dianion **5** displayed less sharply defined absorptions than the allylbenzene anion, indicating that the barrier of rotation around the C_6H_5–C_1, C_1–C_2, and C_2–C_3 bonds in the former intermediate is lower than in the latter.

The course of the alkylation reactions of dianion **5** was found to depend substantially on the reactivity of the alkyl halide used. For example, reaction of **5** with a variety of secondary alkyl halides afforded essentially exclusively C_1 alkylation products, while reaction of dianion **5** with a number of primary alkyl and allyl halides afforded mixtures of C_1 and C_3 alkylation products (Table I).

Table I. Alkylations of Dianions

Alkyl halide	1-Phenyl-2-propanone dianion,[a] C_1:C_3 alkylation[c] (% overall yield)	1,1-Diphenyl-2-propanone dianion,[b] C_1:C_3 alkylation (% overall yield)
$(CH_3)_2CHCl$		4.3:1.0[d] (60)
$(CH_3)_2CHBr$	Only C_1 alkylation[e] (63)	1.8:1.0[d] (54)
$(CH_3)_2CHCH_2Br$	Only C_1 alkylation[e] (57)	
Cyclohexyl bromide	Only C_1 alkylation[f] (61)	
Cyclopentyl bromide	Only C_1 alkylation[g] (65)	
n-C_4H_9Br	19:1[h] (72)	
n-C_4H_9I	9:1[h] (57)	
n-C_3H_7Cl		0.9:1.0[i] (87)
C_2H_5Br	>99% C_1 alkylation[e] (55)	0.64:1.0[i] (87)
C_2H_5I	5:1[h] (65)	0.1:1.0[i,j] (76)
CH_3I	5.5:4.5[h] (62)	
$CH_2{=}CHCH_2Cl$	8:1[k] (66)	

[a] Alkylations were performed by treating the 1-phenyl-2-propanone dianion with 1.2–1.5 equiv of the alkyl halide at ~5 °C. The reaction mixture was then allowed to reach room temperature and stirring was continued for 2–4 h. Water was then added, the organic layer collected and dried, and the alkylation product(s) isolated by vacuum distillation. [b] Alkylations were performed by treating the 1,1-diphenyl-2-propanone dianion with 1.5 equiv of the alkyl halide at ~10 °C. The reaction mixture was then allowed to stir at room temperature for 24 h. Water was then added, the organic layer was collected and dried, and the alkylation products were isolated by means of high pressure liquid chromatography using methylene chloride as the eluting solvent. [c] The C_1 alkylation products were identified by comparing their physical and spectral properties with those resulting from corresponding alkylations of the enolate monoanion **4**. The latter products were all known compounds. Identification of the products resulting from terminal alkylation (C_3) was accomplished by preparing authentic samples of these compounds as described in the literature. [d] The C_1 alkylation product, mp 92.5–94.0 °C from ethanol-water, was a new compound; satisfactory C, H analysis and spectra were obtained. The C_3 alkylation product displayed properties identical with those reported in the literature: R. Huisgen and L. Feiler, *Chem. Ber.*, **102**, 3391 (1969). [e] E. M. Schultz, J. B. Bicking, S. Mickey, and F. S. Crossley, *J. Am. Chem. Soc.*, **75**, 1072 (1953). [f] C. A. Buehler, H. A. Smith, K. V. Nayak, and T. A. Magee, *J. Org. Chem.*, **26**, 1573 (1961). [g] G. N. Walker and D. Alkalay, *ibid.*, **36**, 491 (1971). [h] For C_1 alkylation product, see ref *e*; for C_3 alkylation product see E. H. Sund and H. R. Henze, *J. Chem. Eng. Data*, **15**, 200 (1970). [i] Both the C_1 and C_3 alkylation products were known compounds; see E. M. Schultz, J. B. Bicking, S. Mickey, and F. S. Brossley, *J. Am. Chem. Soc.*, **75**, 1072 (1953), and F. Billiard, *Bull. Soc. Chim. Fr.*, **29**, 429 (1921). [j] In addition to monoalkylation at C_1 and C_3 this reaction afforded a sizable amount of the 1,3-dialkylation product 3,3-diphenyl-4-heptanone. The latter was characterized on the basis of its ^1H NMR spectrum and its high resolution mass spectrum: calcd for $C_{19}H_{22}O$, *m/e* 266.1671; found, *m/e* 266.1651. [k] The C_1 alkylation product was identified as described earlier in ref *c* and *e*; the minor (C_3) product was identified on the basis of its mass spectrum which displayed diagnostic peaks at *m/e* 174 (M^+), 119, 91, 83, and 55.

To ascertain that alkylation at C_1 did indeed occur through the dianion intermediate **5** to give the enolate monoanion **6** as shown in Scheme I, an experiment was performed where dianion **5** was treated with 1.2 equiv of isopropyl bromide, the reaction mixture was allowed to stir at room temperature for 1 h, and 1.5 equiv of trimethylchlorosilane was then added. Gas chromatographic analysis of the crude reaction mixture showed the presence of a single product. This product was subsequently isolated by vacuum distillation (78% yield) and characterized as the trimethylsilyl enol ether **11**.[9]

In addition to the alkylations of dianion **5**, we have also examined its protonation by means of water and deuterium oxide.

Thus, dianion **5** was titrated with 1 equiv of water in THF-hexane and the ^1H NMR of the resulting reaction mixture was recorded on a 60-MHz spectrometer using TMS as an external standard. Interestingly, the resulting spectrum was found to be identical with that of the enolate monoanion **4** (Scheme I) described earlier. These results strongly suggest that, while alkylations of the 1-phenyl-2-propanone dianion **5** occur predominately at the methine site, protonation occurs exclusively at the terminal methylene position.

The alkylation reactions of the 1,1-diphenyl-2-propanone dianion were next examined. This dianion was generated from the corresponding ketone by the method described earlier in connection with the 1-phenyl-2-propanone dianion **5** (Scheme I).

Treatment of the 1,1-diphenyl-2-propanone dianion with a variety of alkyl halides again showed that the site of electrophilic attack was substantially dependent upon the reactivity of the alkylating agent (Table I).

The mode of alkylation of the 1-phenyl-2-propanone dianion **5** outlined in the present communication closely parallels that described in the literature for the allylbenzene anion. Thus, numerous studies[10] have shown that alkylations of this anion, under a variety of experimental conditions, occurred largely at the carbon adjacent to the benzene ring. Terminal alkylation products were also formed during these reactions, but in smaller quantities.[10b,c] It was further shown that the amount of terminal alkylation products formed was largely dependent upon the reactivity of the alkyl halide used, the more reactive halides producing larger quantities of terminal alkylation products.[10c]

The close similarity in the alkylation patterns of dianion **5** and the allylbenzene anion is very much in line with the close structural similarity of these two intermediates suggested earlier on the basis of their NMR spectra.

The higher reactivity of the carbon atom adjacent to the benzene ring in both intermediates can be best explained by recognizing that the presence of the benzene ring will cause the accumulation of a higher electron density on C_1 relative to C_3.[10d,11-13] As a result of this, even though C_1 is more sterically hindered than C_3, alkyl halides of low reactivity (high selectivity) will preferentially react at the more reactive methine site. On the other hand as the reactivity of the alkyl halides is made increasingly higher, their selectivity will be lowered, and steric effects will begin to favor alkylation at the less hindered terminal site.

Reaction of dianion **5** with *p*-anisaldehyde at the terminal position rather than the site adjacent to the benzene ring also parallels the reaction patterns observed earlier in connection with the allylbenzene anion and related systems. Steric effects have been considered to be at least partly responsible for the observed regioselectivity of these reactions,[14] although a number of alternative mechanisms have also been proposed to explain the reactions of allylic anions with carbonyl compounds.[15]

The mode of protonation of dianion **5** is not entirely understood at this point. Initial proton attack at C_1 to give the less stable terminal enolate intermediate, followed by fast equilibration of the latter to the more stable enolate **4**, seems unlikely in view of the results of the alkylation-silylation experiment described earlier. It is noteworthy to mention that protonation of the allylbenzene anion is also not entirely understood.[10d] In the latter case the site of proton attack appears to be highly dependent on the reaction solvent. Thus, protonation under *kinetically controlled conditions* with a variety of proton donors in liquid ammonia, afforded propenylbenzene in excess of 90%,[10c,d] while protonation in less polar solvents gave largely allylbenzene.[10c,d]

Inspection of Table I clearly shows that the alkylation reactions of the 1,1-diphenyl-2-propanone dianion follow a pattern quite similar to that observed in the case of dianion **5**. In the former case, however, more severe steric crowding around C_1 has caused an increase in terminal alkylation.

A more detailed investigation of the two dianions described herein and related systems is currently underway.

Acknowledgments. The authors wish to thank Professor B. M. Trost, Department of Chemistry, University of Wisconsin, Madison, Wis., for suggesting the alkylation-silylation experiment, and R. Cutler, Western Michigan University, for running some of the allyl halide alkylations. R. TenBrink wishes to thank the Upjohn Co., Kalamazoo, Mich., for providing laboratory space and equipment necessary for the work involving the 1,1-diphenyl-2-propanone dianion.

References and Notes

(1) (a) C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958); (b) T. M. Harris and C. R. Hauser, *ibid.*, **84**, 1750 (1962); (c) J. F. Wolfe, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3249 (1964); (d) W. I. O'Sullivan, D. F. Travares, and C. R. Hauser, *J. Am. Chem. Soc.*, **83**, 3453 (1961); (e) C. L. Mao, C. R. Hauser, and M. L. Miles, *ibid.*, **89**, 5303 (1967); (f) L. Weiler, *ibid.*, **92**, 6702 (1970); (g) S. N. Huckin and L. Weiler, *ibid.*, **96**, 1082 (1974); (h) J. S. Griffiths, Ph.D. Dissertation, Duke University, 1971, pp 102–107; *Diss. Abstr. Int. B*, **32**, 5103 (1972); (i) P. A. Grieco and C. S. Pogonowski, *J. Am. Chem. Soc.*, **95**, 3071 (1973); (j) P. A. Grieco and C. S. Pogonowski, *J. Org. Chem.*, **39**, 732 (1974); (k) E. A. Sancaktar, J. D. Taylor, J. V. Hay, and J. F. Wolfe, *ibid.*, **41**, 509 (1976); (l) for recent reviews of the reactions of ketone dianions with electrophilic reagents, see T. M. Harris and C. M. Harris, *Org. React.*, **17**, 155 (1969), and E. M. Kaiser and D. W. Slocum in "Organic Reactive Intermediates", S. P. McManus, Ed., Academic Press, New York, N.Y., 1973, pp 366–369.

(2) For a discussion involving chemical reactivity as a function of charge density, see M. J. S. Dewar, *Adv. Chem. Phys.*, **8**, 102 (1965).

(3) The generation of dianion **5** by methods similar to that shown in Scheme I have been previously reported by Hauser and his coworkers[1e] and by Griffiths.[1h]

(4) H. O. House, R. A. Auerbach, M. Gall, and N. P. Peet, *J. Org. Chem.*, **38**, 514 (1973).

(5) W. W. Leake and R. Levine, *J. Am. Chem. Soc.*, **81**, 1169 (1959).

(6) Satisfactory C, H analysis and spectra were obtained for this new compound.

(7) V. R. Sandel, S. V. McKinley, and H. H. Freedman, *J. Am. Chem. Soc.*, **90**, 495 (1968).

(8) For studies showing that the negative charge in enolate anions resides largely on the oxygen atom, see (a) G. J. Heiszwolf and H. Kloosterziel, *Recl. Trav. Chim., Pays-Bas*, **86**, 807 (1967); (b) *ibid.*, **89**, 1153 (1970).

(9) A satisfactory elemental analysis was obtained for this new compound and $n^{19}{}_D$ 1.4830; ^1H NMR (CCl_4) δ 0.00 (s, 9 H), 0.70 (d, 3 H), 1.05 (d, 3 H), 2.25 (m, 1 H), 2.74 (d, 1 H), 4.04 (d of d, 2 H), 7.10 (m, 5 H); mass spectrum: *m/e* 248 (M^+).

(10) (a) H. Levy and A. C. Cope, *J. Am. Chem. Soc.*, **66**, 1684 (1944); (b) W. G. Young, M. Kosmin, R. Y. Mixer, and T. W. Campbell, *ibid.*, **74**, 608 (1952); (c) R. Y. Mixer and W. G. Young, *ibid.*, **78**, 3379 (1956); (d) H. F. Herbrandson and D. S. Mooney, *ibid.*, **79**, 5809 (1957); (e) T. Ando and N. Tokura, *Bull. Chem. Soc. Jpn.*, **31**, 1026 (1958).

(11) For a discussion of the effect of substituents on electron density distribution in allylic anions, see (a) C. D. Broaddus, *Acc. Chem. Res.*, 1, 231 (1968); (b) D. H. Hunter in "Isotopes in Organic Chemistry", Vol. 1, E. Buncel and C. C. Lee, Ed., Elsevier, Amsterdam, 1975, pp 153–157.

(12) For a theoretical treatment of the electron density distribution in allylic anions, see (a) H. C. Longuet-Higgins, *J. Chem. Phys.*, **18**, 265 (1950); (b) M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3345 (1952).

(13) For a general discussion concerning the reactions of unsymmetrically substituted allylic anions with electrophilic reagents, see W. C. Still and T. L. Macdonald, *J. Org. Chem.*, **41**, 3620 (1976), and references sited therein.

(14) (a) T. W. Campbell and W. G. Young, *J. Am. Chem. Soc.*, **69**, 3066 (1947); (b) R. H. DeWolfe, D. E. Johnson, R. I. Wagner, and W. G. Young, *ibid.*, **79**, 4798 (1957).

(15) V. Rautenstrauch, *Helv. Chim. Acta*, **57**, 496 (1974).

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An Approach to Biradical-like Species. Spectroscopy of *o*-Xylylene in Argon Matrix

Sir:

The reactive intermediate, *o*-xylylene (**1**), and its simple derivatives have been the subject of considerable interest.[1]