

positions much more resistant to solvent exchange than in those compounds previously labeled by gas chromatographic means. It also provides access to labeling possibilities for those compounds which cannot be volatilized or which would be damaged by the tempera-

tures of the gas chromatographic column. Perhaps the greatest immediate advantage over gas chromatographic labeling techniques is the sample capacity of liquid-solid adsorption columns which extends to gram quantities without special equipment.

Electron Paramagnetic Resonance Studies on Chelation of Alkali Cations by the *o*-Dimesitylbenzene Radical Anion

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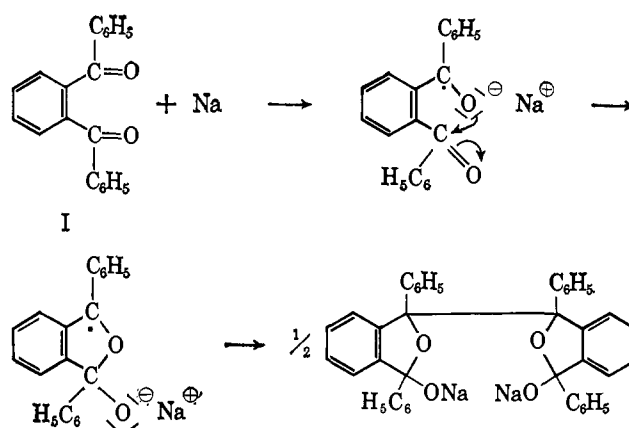
The stable radicals obtained by addition of alkali metals to *o*-dimesitylbenzene in 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were studied by electron paramagnetic resonance (e.p.r.). A spectrum arising from the interaction of the unpaired electron with one alkali metal nucleus (quadruplet for Li, Na, and K and octuplet for Cs) and from two equivalent protons was observed. In the system *o*-dimesitylbenzenepotassium in THF, finer structure from the mesityl groups consistent with considerable noncoplanarity was resolved. The unusually high splittings a_M due to the alkali metal are interpreted in terms of the formation of a chelate with partially covalent bonding. The fraction a_M/a (in which a is the hyperfine splitting constant for the free atom in the fundamental state) is shown to be a linear function of $r^{-1/2}$, r being the ionic radius of the metal. This correlation can be used to predict the alkali metal splitting and shows that the covalent character of the bond increases in the order $Cs < K < Na < Li$. For this type of complex in which the ligand is a radical the e.p.r. is shown to be a highly satisfactory method to reveal covalency of the bond to the metal.

Introduction

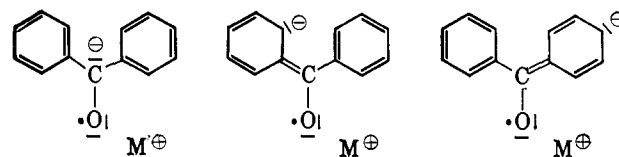
In previous studies of the 1:1 addition of sodium to *o*-dibenzoylbenzene (I) in ether (in dry nitrogen atmosphere)³ it was found that a dimerization occurs. A previous cyclization was postulated.

Although the present investigation does not answer the question as to whether this mechanism is correct, it was undertaken as a first approach to this problem. In the reaction of alkali metals with similar ketones in which the phenyl groups are substituted by bulkier groups, steric hindrance is expected to lessen the equilibrium constant for the dimerization of the radical.

Earlier research in this field has given experimental evidence that the alkali metal chosen is also one of the factors that influence the stability of the ketyls. In terms of resonance theory,⁴ in the case, e.g., of benzo-



phenone ketyl, the following structures contribute to the stabilization.



Such structures should have an increasing contribution when the covalent character of the OM bond decreases, which is to be expected in the case of the series Li, Na, K, Rb, and Cs, according to the views of Fajans⁵ on the polarizing abilities of ions of different radii. This explains the observation of E. Müller, *et al.*,⁶ and Mikhailov⁷ that the equilibrium constant for the dimerization of a ketyl decreases in such a series.

Variations in the stability of the ketyl, however, are only an indirect approach to the study of the character of the ligand-metal bond.

(4) G. W. Wheland, "Advanced Organic Chemistry," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1960, p. 796.

(5) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," Interscience Publishers, Inc., Division of John Wiley and Sons, Inc., New York, N. Y., 1962, p. 157.

(6) E. Müller and W. Janke, *Z. Elektrochem.*, **45**, 380 (1939).

(7) B. M. Mikhailov and N. G. Chernova, *Dokl. Akad. Nauk SSSR*, **85**, 341 (1952).

(1) Supported in part by the NATO Research Grants Program (182).

(2) From the University of Coimbra, Portugal.

(3) B. J. Herold, *Tetrahedron Letters*, **2**, 75 (1962).

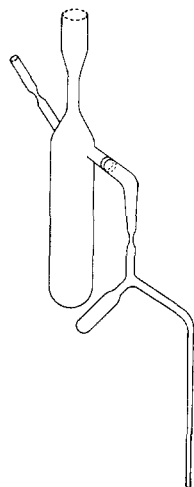
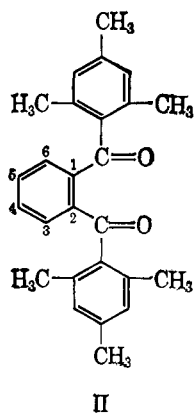


Figure 1.

In this investigation a more direct proof was attempted by the examination of the ketyl itself by e.p.r.

Alkali metal complexes of organic radicals have been a fruitful field of study using this technique,⁸⁻¹³ but to our knowledge no correlation between the fundamental properties of the metal and its splitting constants in the complex has yet been reported. This seems to be caused partly by the existence of more than one class of these complexes.

We will show that those cases where chelation is to be expected may form a class which is susceptible to a general interpretation. *o*-Dimesitylbenzene (II) was found to be a convenient substrate when 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were used as solvents.



II

Experimental

The preparation of samples was made in a modified Schlenk tube provided with a sintered disk (Figure 1).

The *o*-dimesitylbenzene used was synthesized according to Fuson, *et al.*,¹⁴ and recrystallized up to

(8) N. M. Atherton, and S. I. Weissmann, *J. Am. Chem. Soc.*, **83**, 1330 (1961).

(9) R. L. Ward, *J. Chem. Phys.*, **36**, 1405 (1962).

(10) G. R. Luckhurst and L. W. Orgel, *Mol. Phys.*, **7**, 297 (1963).

(11) E. de Boer and E. Mackor, *J. Am. Chem. Soc.*, **86**, 1513 (1964).

(12) H. Nishiguchi, Y. Nakai, K. Nakamura, K. Ishizu, Y. Degushi, and H. Takaki, *J. Chem. Phys.*, **40**, 241 (1964).

(13) N. Hirota, and S. I. Weissmann, *J. Am. Chem. Soc.*, **86**, 2537 (1964).

(14) R. C. Fuson, S. B. Speck, and W. R. Hatchard, *J. Org. Chem.*, **10**, 55 (1945).

constant melting point. The solvents were boiled over sodium wire to blue reaction with benzophenone¹⁵ and distilled, either directly into the Schlenk tube under purified nitrogen, or used immediately after distillation.

Lithium was cut and weighed in a weighing flask under dry ligroin; sodium, potassium, and cesium were used in thin-walled, sealed ampoules containing *ca.* 100 mg. and filled as described by Zintl, Goubeau, and Dullenkopf.¹⁶

In the preparation of the sample itself the technique was as follows. A magnetic stirring rod (and also some pieces of broken glass in the case of lithium) and a weighed quantity of *o*-dimesitylbenzene (stoichiometrically equivalent to the alkali metal) were introduced into the Schlenk tube which was evacuated to *ca.* 10 mm. The tube was heated for some minutes with the reducing flame of a torch in order to dry its walls. The tube was filled with nitrogen purified in an apparatus already described¹⁷ but using the BTS catalyst.^{18,19} This operation was repeated twice. Afterwards the solvent (either THF or DME) was introduced, and, finally, the alkali metal. In the case of sodium and potassium the ampoule was broken over the opening of the neck of the apparatus under a current of nitrogen; in the case of cesium this had to be done inside the enlarged neck of the apparatus. The tube was cooled in acetone-Dry Ice and sealed under reduced pressure (*ca.* 10 mm.).

The contents was stirred with a magnetic rod until all the alkali metal had disappeared. Part of the solution was filtered into the quartz tube to wash its walls and returned to the main tube; this operation was repeated, and finally the sample tube was filled and sealed off.

All measurements were made in a Varian V-4502-04 e.p.r. spectrometer using a 12-in. magnet.²⁰ The samples are stable for several months which is an interesting feature.

E.p.r. Spectra and Their Analysis

The e.p.r. spectra of the ketyl solutions prepared by a reaction of the diketone with lithium, sodium, potassium, and cesium, respectively, are reproduced in Figures 2a-d. The quartet structures in the first three cases and the octet in the last case are due to the interaction of the unpaired electron with the magnetic nuclei of the metals. The additional triplet structure results from the interaction of the free electron with two equivalent protons which appear to be those bonded to C-4 and C-5 of the phenylene ring, according to our calculations.²¹

For a better visualization we include the reconstructions based on the constants of Table I.

(15) K. Ziegler, F. Crössmann, H. Kleiner, and O. Schäfer, *Ann. Chem.*, **473**, 20 (1929).

(16) G. Brauer, "Handbuch der Präparativen Anorganischen Chemie," 2nd Ed., Ferdinand Enke Verlag, Stuttgart, 1960.

(17) E. Müller, "Methoden der Organischen Chemie," Houben-Weyl, Ed., Georg Thieme Verlag, Stuttgart, 1959.

(18) M. Schütze (to Badische Anilin- und Soda-Fabrik A.G.), German Patent 965,634 (1955).

(19) To BASF, Ludwigshafen, we are grateful for a generous quantity of this catalyst.

(20) The first measurement of this series was made for B. J. H. by courtesy of Professor Dr. K. H. Hausser, Heidelberg; B. J. Herold, Dissertation, Heidelberg, 1961.

(21) A. F. Neiva Correia and J. dos Santos Veiga, to be published.

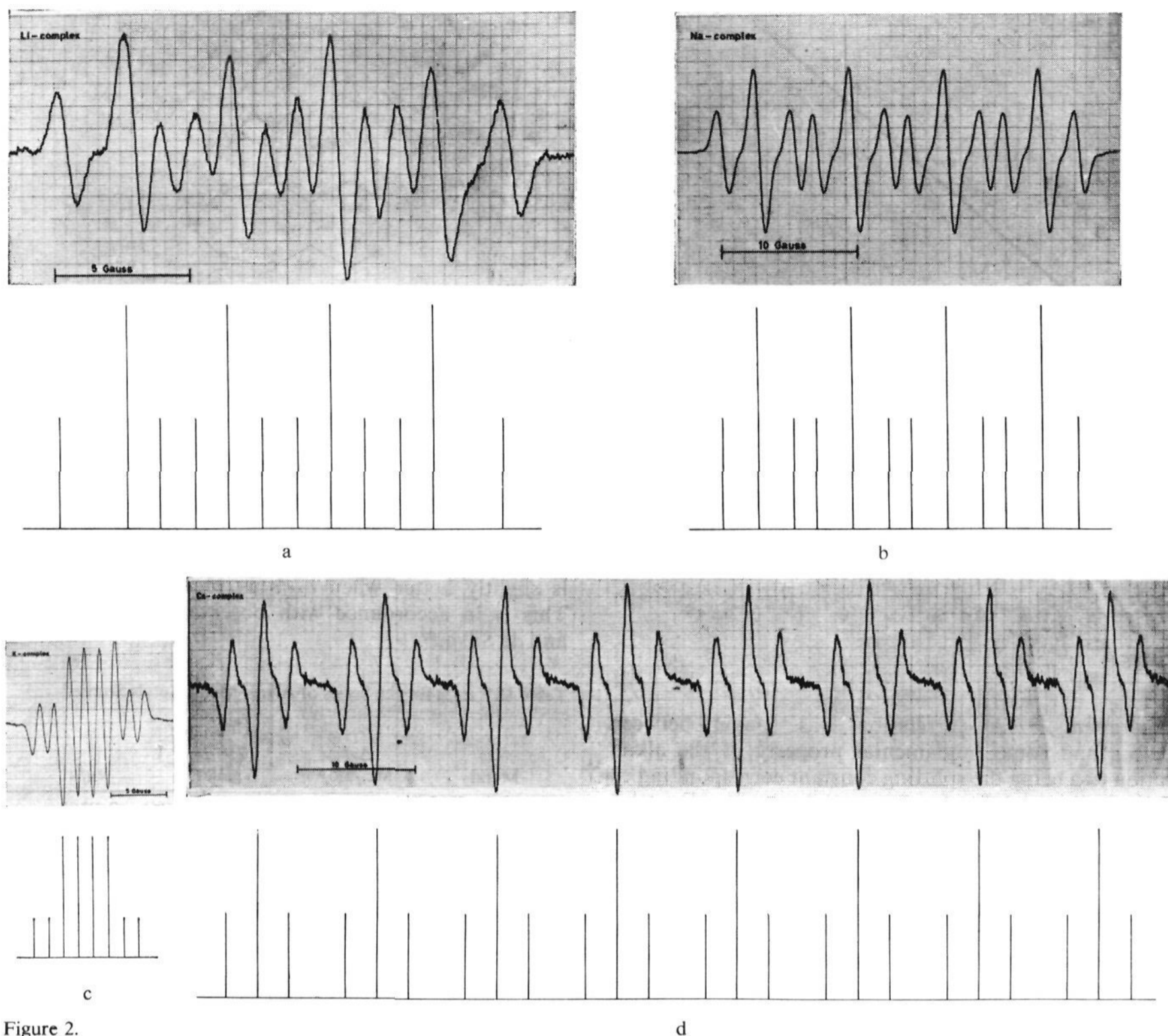


Figure 2.

The measurements were made at room temperature. In low-temperature measurements, no significant change in the value of the splitting constants was detected.²²

Table I. Observed Hyperfine Splitting Constants

	a_H^a , gauss	a_M^b , gauss
Li	2.52	3.75
Na	2.62	6.95
K	2.69	1.33
Cs	2.67	10.2

^a Proton hyperfine constant. ^b Metal hyperfine constant.

Within the experimental error the splitting constants corresponding to the protons and the alkali metal do not depend on the solvent used.

In the case of the sample prepared with potassium using THF as solvent we could resolve an additional splitting by careful dilution. This structure has to be

(22) Measurements were made with the Li compound at various temperatures from -30 to $+50^\circ$, with Na from -90 to $+20^\circ$, and with Cs from -40 to $+60^\circ$.

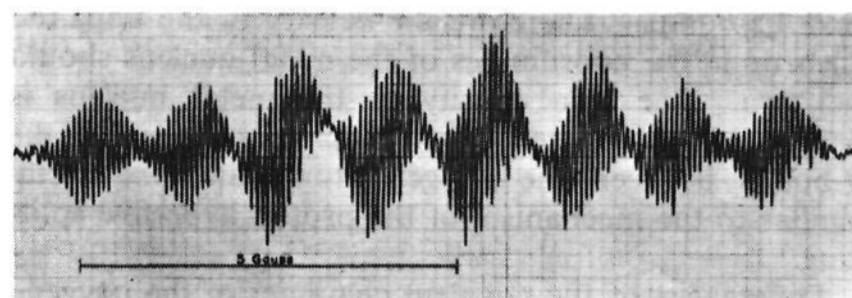


Figure 3.

ascribed to other protons including those of the methyl groups. This spectrum is shown in Figure 3. Its complete interpretation is being investigated.

Discussion

From the published values²³ of the hyperfine splitting separation $\Delta\nu$, measured in atomic spectra, the hyperfine splitting constant a can be calculated. a measures the interaction energy between the unpaired electron and the magnetic nucleus of a free alkali metal atom in its fundamental state in both atomic spectra and e.p.r.

(23) P. Kusch and H. Taub, *Phys. Rev.*, 75, 1477 (1949).

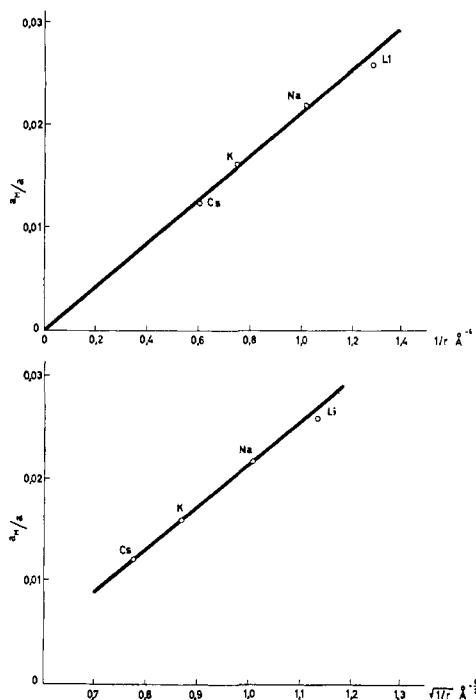


Figure 4.

experiments.²⁴ A correlation was sought between a , a_M , and some fundamental property of the alkali cation (a_M being the splitting constant corresponding to the alkali metal in the spectra observed). For this purpose it was assumed that the molecular orbital of the unpaired electron includes an atomic orbital of the metal, this orbital having some s character. In this case a_M/a should represent the direct contribution from the orbital of the metal to the over-all function of the unpaired electron.

However, our calculations²¹ confirm the qualitative treatment of substituted benzenic radicals,²⁵ according to which the molecular orbital of the unpaired electron has a nodal plane passing through the centers of the 1,2- and 4,5-bonds. Therefore the density of the unpaired electron at the coordinates of the metal nucleus should be zero. The spin density at the metal nucleus is accounted for by a mechanism of spin polarization of the σ -bonds between the oxygen atoms and the metal similar to the mechanism of the proton hyperfine splitting.

Differences in the covalent character of the oxygen-metal bonds result in different values of a_M/a according to the metal. In any case this fraction can be regarded as a relative measure of covalency and decreases regularly from Li to Cs (Table II).

On the other hand, according to the rules of Fajans the anion should be subject to polarization by the neighboring cation.²⁶ The reciprocal of the ionic radius²⁷ can be considered as a measure of this polarization; we found that a linear dependence exists between a_M/a and $1/r$ ²⁸ (Figure 4).

(24) N. F. Ramsey, "Nuclear Moments," John Wiley and Sons, Inc., New York, N. Y., 1953.

(25) A. Carrington, *Quart. Rev.* (London), 17, 67 (1963).

(26) In cases of predominantly ionic bonding with a little covalency, these views are currently considered to be acceptable (ref. 5).

(27) N. V. Sidgwick, "The Chemical Elements and Their Compounds," Vol. I, Clarendon Press, Oxford, 1950.

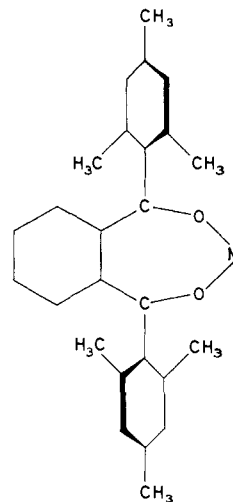


Figure 5.

Although it is usual to correlate the properties of ions with $1/r$, it is shown in Figure 4 that the agreement is slightly better when a_M/a is plotted against $r^{-1/2}$. This is in accordance with observations of Ahrens²⁹ and da Silva.³⁰

Table II. a_M/a for the Series of Alkali Metal Ketyls Studied

Metal	$\Delta\nu$, Mc./sec. ^a	$a = \frac{\Delta\nu}{2.8} \frac{2}{2I + 1}$, gauss	a_M/a
Li ⁷	803.512	143.5	0.0261
Na ²³	1771.61	316	0.0220
K ³⁹	461.723	82.4	0.0161
Cs ¹³³	9192.76	820	0.0124

^a In cases of predominantly ionic bonding with a little covalency these views are currently considered to be acceptable (ref. 5).

It was found that, except for the cesium ketyl, the same interpretation can be extended to explain the changes in the splitting constant a_H corresponding to the two equivalent protons. In terms of LCAO-MO calculations increased polarization of the oxygen atoms by the cation can be expressed by a higher value of the parameter δ in the Coulomb integral $\alpha_O = \alpha_C + \delta\beta_{C-O}$. Appropriately, a decrease of 0.13 in the value of δ from one ketyl to the next in the series Li, Na, and K predicts the right value of the increasing a_H .²¹ A similar discussion for the change of the proton splittings in complexes of *o*-semiquinones with different metal ions was recently published by Eaton.³¹

These facts are consistent with a structure in which the anion forms a chelate ring with the cation. The variable temperature experiments showing a temperature-independent metal splitting also favor the picture of a strongly bound chelate, as well as the fact that a_M does not change with the solvent. The total splitting of only about 1 gauss, attributed to all protons in the mesityl groups, points to their considerable noncoplanarity with the phenylene and chelate rings. The structure proposed for complex is shown in Figure 5.

(28) It can be shown that, as the ionization potential has a linear dependence on $1/r$, the s -orbital contribution is a linear function of this also.

(29) L. H. Ahrens, *J. Inorg. Nucl. Chem.*, 2, 290 (1956).

(30) J. J. R. F. da Silva, Ph.D. Thesis, Oxford, 1962.

(31) D. R. Eaton, *Inorg. Chem.*, 3, 1268 (1964).

Mikhailov⁷ and Garst, *et al.*,³² showed that solvation takes place in several ketyls. However, as the present experiments do not shed light on the degree of solvation of the metal-*o*-dimesitylbenzene ketyl complex the solvating molecules are not shown in Figure 5.

Conclusions

Chelate ring formation with alkali metals has been studied since the earlier work of Sidgwick, *et al.*,³³ with acetylacetonates and benzoylacetonates to the recent results of da Silva³⁰ with complexones. The character of the bond between anion and alkali metal cation has been a subject of much controversy but the evidence offered, usually based on stability constants of the complexes, could not give a definite answer; current views consider these complexes to be electrostatically bonded.⁷ Direct evidence, however, can be obtained when one of the ions is paramagnetic. In this case it is possible to observe unpaired electron

(32) J. Garst, D. Walmsley, C. Hervitt, W. Richards, and E. Zabolotny, *J. Am. Chem. Soc.*, **86**, 421 (1964).

(33) N. V. Sidgwick and F. M. Brewer, *J. Chem. Soc.*, **127**, 2379 (1925).

density at the nucleus or nuclei of the other ion. Copper(II) chelates of diamagnetic ligands have been studied by Wiersema and Windle.³⁴ For alkali metal cations we have to rely upon radical ligands. Chelate formation with a radical anion has been previously postulated by Luckhurst and Orgel¹⁰ to explain the ion association between sodium ion and benzyl ketyl.

Complexes of the type studied here in which the ligand has been reduced by the alkali metal have a certain percentage of covalent bonding.

Acknowledgments. The Varian e.p.r. spectrometer which was used in this study was offered to the Laboratório de Física e Engenharia Nucleares by the International Atomic Energy Agency, and this offer is thankfully acknowledged by the authors. We are grateful to Miss Estela Faustino for her assistance in the preparation of the samples and to Professor G. J. Hoijtink, Dr. J. J. R. F. da Silva, and J. Furtado Coelho for useful discussions. B. J. H. thanks Professor G. Wittig for permission to continue research work started in his laboratory.

(34) A. K. Wiersema and J. J. Windle, *J. Phys. Chem.*, **68**, 2316 (1964).

Diazirines. I. Some Observations on the Scope of the Ammonia-Hydroxylamine-O-sulfonic Acid Diaziridine Synthesis. The Preparation of Certain Steroid Diaziridines and Diazirines

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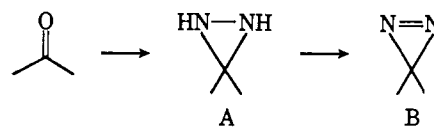
Contribution from the Organic Chemical Research Section, Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York. Received February 13, 1965

Several steroidal diaziridines were prepared from the corresponding ketones by reaction with ammonia and hydroxylamine-O-sulfonic acid. Sharp selectivity was observed; reaction occurred with nonconjugated C-2 and C-3 ketones, but not with C-11, C-17, C-20, or conjugated C-3 ketones. Diazirines were prepared from diaziridines by facile oxidation using silver oxide. Unlike the diaziridines, the diazirines were found to be very stable, relatively nonpolar compounds. The pyrolysis of 3,3-azo-5 α -androst-17 β -ol acetate at 135–145° afforded primarily 5 α -androst-2-en-17 β -ol acetate. 3,3-Azo-17 α -methyl-5 α -androst-17 β -ol showed a high anabolic-androgenic ratio when assayed according to the oral levator ani assay.

Substances containing a diaziridine (A) or diazirine (B) function¹ have been reported in the literature^{2–4}

(1) Since the terms "diaziridine" and "diazirine" refer to the three-membered rings, A and B, respectively, in their entirety, the nomenclature of the steroids having these groups as part of the skeleton becomes impossibly complex. For this reason, these terms will be used only when referring to the general class of three-membered rings containing two nitrogen atoms and the terms "hydrazide" and "azo" will refer only to the pair of singly or doubly bonded nitrogen atoms.

only recently, and the incorporation of either of these groups into a complex molecule has not been noted. Accordingly, we thought it of interest to attempt the synthesis of representative steroidal diaziridines and diazirines in order to shed light on the scope of the reaction and to determine the effect of these groupings on the biological activity of the parent molecule.



The synthetic procedures used in this work are modifications of those already reported⁵ for the preparation of these systems and involve the treatment of a ketone successively with ammonia and hydroxylamine-O-sulfonic acid (or chloramine), affording the

(2) (a) E. Schmitz, *Angew. Chem.*, **71**, 127 (1959); (b) H. J. Abendroth and G. Henrich, *ibid.*, **71**, 283 (1959); German Patent 1,082,889 (1960); (c) S. R. Paulsen, Belgian Patent 588,352 (1959).

(3) S. R. Paulsen, *Angew. Chem.*, **72**, 781 (1960); E. Schmitz and R. Ohme, *ibid.*, **73**, 115 (1961).

(4) E. Schmitz, "Advances in Heterocyclic Chemistry," Vol. 2, A. R. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1963, p. 83.

(5) E. Schmitz and R. Ohme, *Chem. Ber.*, **94**, 2166 (1961).