plexes in solution by absorption spectroscopy and have correlated the spectral characteristics with those expected of charge transfer complexes. Russell[17] has demonstrated solvent effects upon the chemistry of chlorine atoms and has attributed these effects to atom–molecule complexes. It appears that such radical–molecule complexes may play an important role in many areas of free radical chemistry.

Conclusion.—In summary, it seems worthwhile to re-emphasize that our results are entirely and quantitatively in agreement with the Boozer and Hammond postulate for the initial reaction sequence between alkylperoxy radicals and diphenylamine. The production of the radical, diphenylnitric oxide, as a product of that sequence is important since this material contributes significantly to the stoichiometry of the over-all process and to the rate of oxidation during the inhibition period. The effect of inhibitor structure upon the activity of the material as an antioxidant must, however, control this property largely through its influence upon the properties of the alkylperoxy–inhibitor complex rather than through its influence upon the properties of the product nitric oxide radical.

[17] G. A. Russell, *J. Am. Chem. Soc.*, **80**, 4987 (1958).

[CONTRIBUTION NO. 2866 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA, CALIF.]

Nuclear Magnetic Resonance Spectroscopy. Long-Range H–F Spin–Spin Coupling in 1,1-Difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane[1]

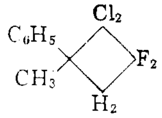
BY MASAAKI TAKAHASHI, DONALD R. DAVIS AND JOHN D. ROBERTS

RECEIVED MARCH 7, 1962

A 2 c.p.s. long-range H–F spin–spin coupling has been observed over five saturated bonds in 1,1-difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane, involving one of the fluorines at the 1-position and the protons of the 3-methyl group. Comparison of the spectrum with that of stereospecifically labeled 4-deuterio derivatives suggests that the fluorine involved in the long-range coupling is the one *cis* to the methyl group.

Several long-range H–F spin–spin couplings have been reported,[2,3] but couplings over five consecutive saturated single bonds appear to be previously unknown.

The fluorine n.m.r. spectrum of 1,1-difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane (I, from addition of 1,1-difluoro-2,2-dichloroethylene to α-methylstyrene)[4] shows the resonances of two non-equivalent fluorines (F_1 and F_2) with a chemical shift difference of 435 c.p.s., each split by the F_1–F_2 coupling (J_{12} = 187 c.p.s.) and couplings with the two non-equivalent methylene protons attached to the 4-carbon (J_{HF_1} = 1.9 and 9.5 c.p.s.; J_{HF_2} = 13.2 and 20.3 c.p.s.) (Fig. 1A). In addition, the fluorine whose resonance comes at the higher field shows further splitting into 1:3:3:1 quartets with J = 2.0 c.p.s. (Fig. 1C). This strongly implies a coupling with three equivalent protons, presumably those of the methyl group at the 3-position and, indeed, the proton n.m.r. spectrum of I shows a doublet methyl resonance with J_{F_2,CH_3} = 2.1 c.p.s. (Fig. 2A).



I

The five-bond, H–F coupling is indicated to be a *cis* interaction by the following, rather involved, argument. We have designated the fluorines F_1 and F_2 and the protons H_3 and H_4, where F_2 and H_4 have been arbitrarily assigned as being at higher field than, respectively, F_1 and H_3.

From the spectrum of the methylene region (Fig. 2B) we can deduce the two coupling constants for H_3 (9.4 and 20.5 c.p.s.) and for H_4 (1.8 and 13.7 c.p.s.) and the mutual coupling constant J_{34} = 13.1 c.p.s. The eight peaks of the low-field H_3 are seen to be somewhat broadened, probably by long-range coupling with either the methyl or phenyl group, or both. This coupling was too small to be analyzed. The chemical shifts of H_3 and H_4 were determined by trial and error fitting of calculated[5] and observed spectra. The final calculated spectrum (Fig. 2C) is based on the above coupling constants, ν_3 = 194.3 c.p.s. and ν_4 = 160.4 c.p.s. Finally, comparison with the fluorine spectrum requires that we assign the coupling constants as follows: J_{13} = 9.4 c.p.s., J_{14} = 1.8 c.p.s., J_{23} = 20.5 c.p.s., J_{24} = 13.7 c.p.s. (and J_{34} = 13.1 c.p.s.).

The stereochemical relationships of H_3 and H_4 with respect to the phenyl group have been established by substitution of deuterium at the 4-position. Mixtures of I and *trans*-4-deuterio-1,1-difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane

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[1] Supported in part by the Kureha Chemical Ind. Co. (Japan) and the Office of Naval Research.

[2] D. R. Davis, R. P. Lutz and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 246 (1961).

[3] J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chap. 3.

[4] Structure I for the adduct rather than 1,1-difluoro-2,2-dichloro-4-methyl-4-phenylcyclobutane is in good agreement with the magnitudes of the coupling constants between the methylene protons and the *gem*-fluorines. It is also supported by extensive analogy; J. D. Roberts and C. M. Sharts, in A. C. Cope, Ed., "Organic Reactions," Vol. XII (1962).

[5] The calculations were set up for the two protons and two fluorines as an ABXY system using the program described by K. B. Wiberg and B. J. Nist, "Theoretical NMR Spectra," W. A. Benjamin, Inc., New York, N. Y., in press, on an IBM 7090 computer at the Computing Center of the Jet Propulsion Laboratory. We are indebted to Mr. L. Sloan for his assistance with these calculations.

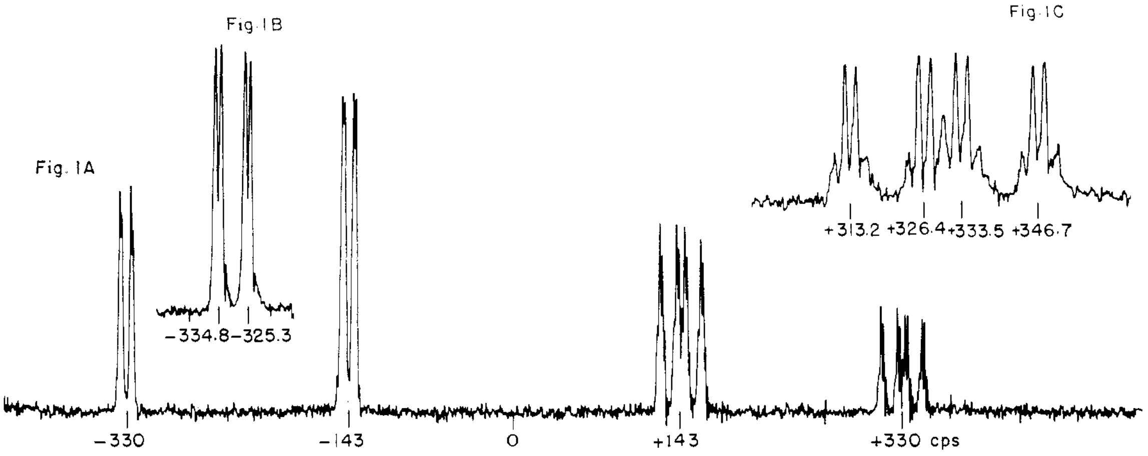
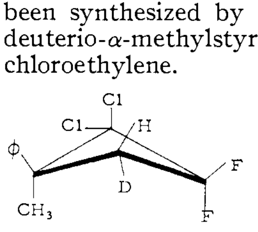
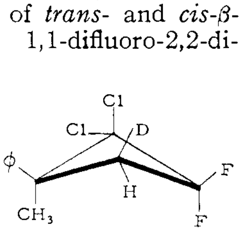


Fig. 1.—Fluorine resonance spectra at 56.4 Mc.; 1A, 1,1-difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane (I) in CCl_4; 1B, the low-field fluorine resonance, expanded scale; 1C, the high-field fluorine resonance, expanded scale.

(*trans*-II) and *cis*-4-deuterio-1,1-difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane (*cis*-II) have been synthesized by addition of *trans*- and *cis*-β-deuterio-α-methylstyrene[6] to 1,1-difluoro-2,2-dichloroethylene.



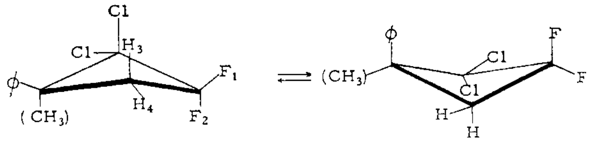
trans-II



cis-II

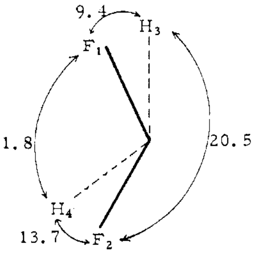
The total area of the low-field methylene peaks was larger than that of the high-field methylene peaks for the mixture in which *trans*-II predominated, and the reverse was true for the mixture in which *cis*-II predominated. The high-field methylene proton H_4 is therefore *trans*, and the low-field methylene proton H_3 *cis* to the phenyl group. We consider now the stereochemical relationship of the long-range coupled F_2 with respect to H_3 and H_4.

It is possible to draw two conformers of I (Ia and Ib), if it is assumed that the cyclobutane ring is non-planar. These would then have substituents which are at least partially "axial" and partially "equatorial" in character like those of cyclohexane. Of the two, Ia with the phenyl group "equatorial" and the methyl group "axial" is almost sure to be favored. The degree of puckering of the ring may well be considerable because the chemical shift difference between the fluorines (435 c.p.s.) is about half of the 874 c.p.s. difference between the fluorines of 1,1-difluorocyclohexane when this substance undergoes slow ring inversion at −80°.[7]

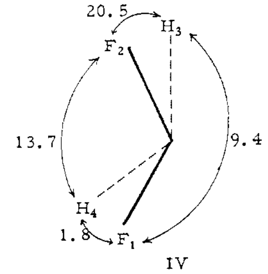


Ia Ib

Of course the validity of this conclusion regarding the degree of puckering depends on there being comparable influences determining chemical shift differences for *gem*-fluorines on cyclobutane and cyclohexane rings, as well as only small long-range effects on the chemical shifts due to differences in diamagnetic shieldings produced by the methyl and phenyl groups. The theory of fluorine chemical shifts[8] indicates that the latter effects would surely be small. Perhaps the best way to clarify our argument that F_2 has the *cis* relationship to the methyl group is to consider the two possible alternatives in the light of the previously determined coupling constants. The geometries of each arrangement (III and IV) are shown below in projection along the 1,4-bond.



III



IV

It is well known that *trans* (axial–axial) couplings between protons on neighboring carbon atoms in saturated ring systems are larger than *gauche* (axial–equatorial or equatorial–equatorial) couplings.[9] Similar arguments appear to apply to H–F coupling.[2] Assuming that the *trans* coupling is the larger, and that the ring is puckered as shown, the arrangement (III) with F_2 *cis* to H_4 (and to the methyl group) is more consistent than IV with the coupling constants, particularly those involving the most nearly *trans* and *cis* groups. The argument hinges on the assumption that *trans* H–F couplings are larger than the corresponding *gauche* couplings. The conclusion here would have to be reversed if further analysis should show that

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(6) D. R. Davis and J. D. Roberts, *J. Am. Chem. Soc.*, **84**, 2252 (1962).

(7) Unpublished experiments by K. Nagarajan and J. D. Roberts, *J. Vsesouznoe Chem. Soc.*, in press.

(8) A. Saika and C. P. Slichter, *J. Chem. Phys.*, **22**, 26 (1954).

(9) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chap. 8.

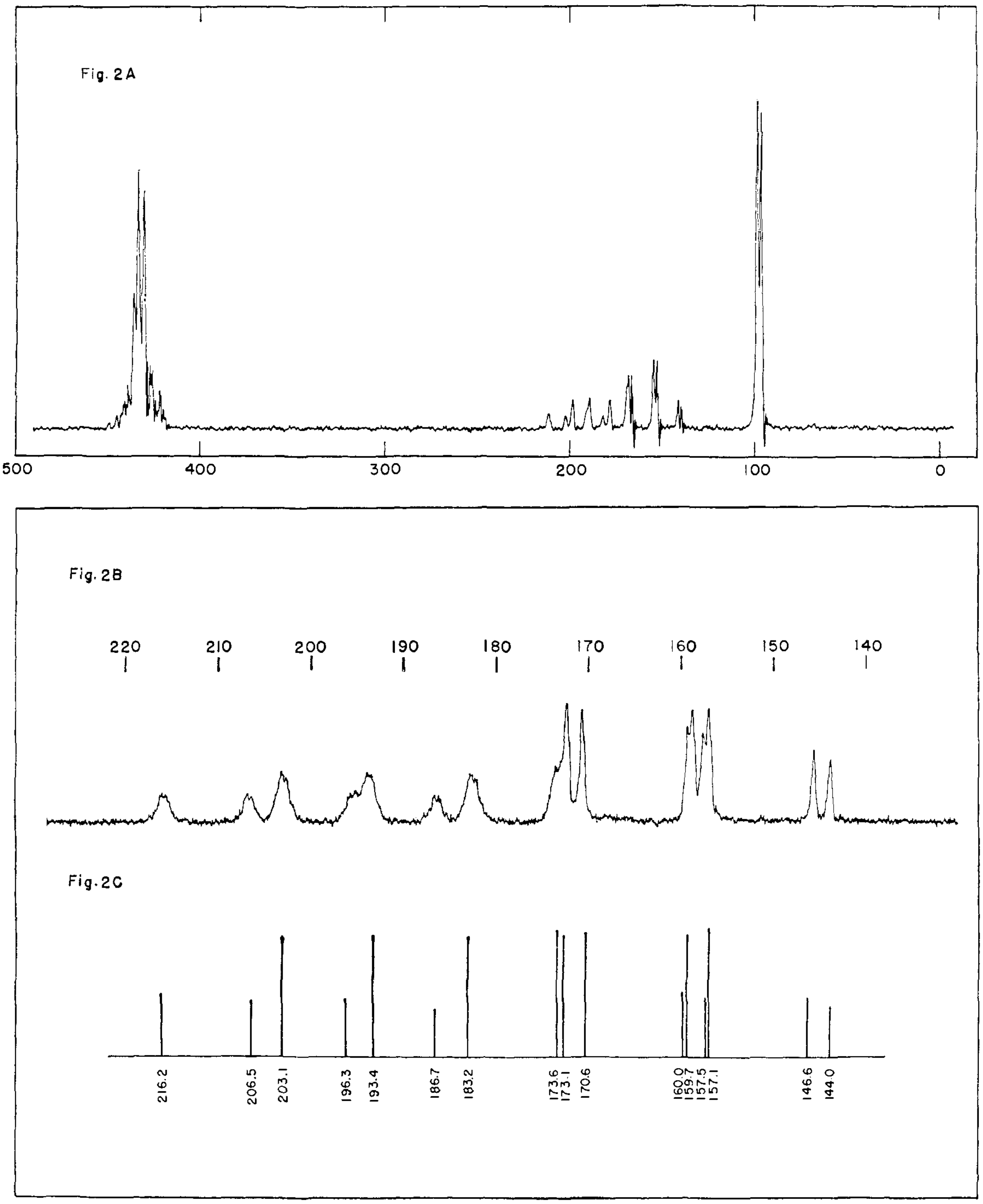

Fig. 2.—Proton resonance spectra at 60 Mc. taken with Varian A-60 spectrometer at ambient temperature. The calibration is in c.p.s. downfield from tetramethylsilane (external reference): 2A, 1,1-difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane (I), 1:1 in CCl_4; 2B, the methylene resonances of I on expanded scale; 2C, calculated methylene resonances with chemical shifts and coupling constants as given in the text.

$J_{\text{gauche}} > J_{\text{trans}}$ for H–F interactions. On the basis of our present evidence, we favor the assignment of stereochemistry as in Ia with the long-range coupled fluorine (F_2) *cis* to the methyl group.[10] This five-bond H–F coupling may well be exerted through space[2,11] instead of through the bonds, particularly because, if the ring is strongly puckered, the groups involved are expected to be rather close together in space.

Experimental Part

1,1-Difluoro-2,2-dichloro-3-phenyl-3-methylcyclobutane (I).—A mixture of 59 g. (0.50 mole) of α-methylstyrene and

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[10] Similar conclusions as to the preferred stereochemistry for long-range H–F couplings have been arrived at independently by A. D. Cross and P. W. Landis, *J. Am. Chem. Soc.*, **84**, 1736 (1962), through studies of fluorine-substituted steroids.

[11] L. Petrakis and C. H. Sederholm, *J. Chem. Phys.*, **35**, 1243 (1961).

74 g. (0.55 mole) of 1,1-difluoro-2,2-dichloroethylene (Genetron 1112, General Chemical Division) was heated in a sealed glass tube at 130° for 24 hr. The tube was cooled with Dry Ice, opened, and the light-yellow oil distilled through a 10-cm. Vigreux column. The yield of crude adduct was 66 g. (61%), b.p. 91–98° (2.5–3.0 mm). Redistillation through a 20-cm. Vigreux column gave 56 g. (52%) of product, b.p. 84–86° (1.5 mm.).

Anal. Calcd. for $C_{11}H_{10}F_2Cl_2$: C, 52.50; H, 3.98; Cl, 28.30. Found: C, 52.58; H, 4.01; Cl, 28.20.

[CONTRIBUTED FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

L(+)-2,3-Butanedithiol: Synthesis and Application to the Resolution of Racemic Carbonyl Compounds[1]

BY E. J. COREY AND RAJAT B. MITRA

RECEIVED APRIL 2, 1962

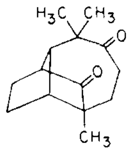
A four-step synthesis of L(+)-2,3-butanedithiol from D(−)-2,3-butanediol is reported. The applicability of the dithiol as an agent for resolution is illustrated by the preparation of dextro- and levo-forms of flavan-4-one and flavan.

The method previously described for the total synthesis of *d,l*-longifolene[2] in principle can be modified in a number of ways to allow the preparation of pure enantiomers. Of the numerous possibilities which were considered, one appeared to be by far the most attractive even though it had not previously been utilized and would require extensive preliminary study before application to the longifolene problem. This paper reports some details of this preliminary investigation which demonstrate the new technique.

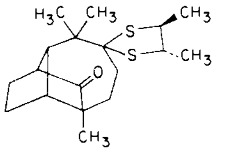
The tricyclic diketone I represented a particularly attractive intermediate for resolution in the longifolene synthesis, and, since the carbonyl group of the four carbon bridge must be reduced to a methylene group in the last stages of the process *via* a thioketal, it appeared advantageous to combine resolution and reduction, using a thioketal from an optically active 1,2-dithiol. 2,3-Butanedithiol seemed attractive as the dual-purpose reagent because of its probable accessibility.

The possibility of separating the diastereomeric thioketals II by vapor phase chromatography as well as by more conventional crystallization techniques provided further incentive.[3]

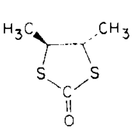
The synthesis of optically active L(+)-2,3-butanedithiol from the readily available (by fermentation[4]) D(−)-2,3-butanediol was carried out by the sequence:



I



II



III

D(−)-diol → D(+)-ditoluenesulfonate (*p*-toluenesulfonyl chloride–pyridine, 94% yield) → L(+)-dithiocyanate (potassium thiocyanate–dimethyl sulfoxide, 74% yield) → L(−)-2,3-*cyclo*-dithiocarbonate (hydriodic acid–phosphorus, 41% yield) → L(+)-dithiol (lithium aluminum hydride, 92% yield). Thiocyanate ion was chosen for the introduction of sulfur over the other possible sulfur nucleophiles because of the expectation that the introduction of the second sulfur substituent would be a critical step stereochemically. The possibility of internal nucleophilic displacement (participation of sulfur) at the stage of the 2-S-monosubstituted-3-toluenesulfonate, which would lead to racemic product, imposes the requirement that the sulfur substituent in this intermediate be a relatively poor nucleophile. On the basis of this consideration, thiocyanate ion seemed the most satisfactory nucleophile for the stereospecific introduction of sulfur with inversion of configuration at C_2 and C_3 in the butane chain. In fact, the reaction of thiocyanate ion with the bis-toluenesulfonate affords bis-thiocyanate of about 80% optical purity which indicates that even in the case of thiocyanate racemization occurs to an appreciable degree and hence that the choice of sulfur nucleophile is indeed critical. The limited amount of racemization encountered in the replacement process is only a minor disadvantage since the next intermediate in the synthetic sequence, L(−)-2,3-cyclo-dithiocarbonate (III), is a solid which can easily be recrystallized to a state of optical purity. Because III is crystalline, stable and easily converted to the optically active dithiol, we have found it convenient to accumulate this intermediate for subsequent conversion to 2,3-butanedithiol as needed.[5]

The applicability of L(+)-2,3-butanedithiol to the resolution of racemic ketones can be illustrated by the experiments in the flavan-4-one series which are shown in Fig. 1. Racemic flavan-4-one (IV) is readily and completely converted to a mixture of diastereomeric ketals which is easily separated by recrystallization; isomer VA is far less soluble than VB in benzene and the solubilities are reversed in methanol. Hydrolysis of the individual isomers VA and VB using mercuric chloride–mercuric oxide promoter in aqueous methanol afforded optically

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[1] This study was supported by the National Science Foundation, G-9999.

[2] E. J. Corey, M. Ohno, P. A. Vatakencherry and R. B. Mitra, *J. Am. Chem. Soc.*, **83**, 1251 (1961).

[3] For the resolution of *d,l*-camphor by vapor phase chromatography of the ketals derived from D(−)-2,3-butanediol, see J. Casanova, Jr., and E. J. Corey, *Chemistry & Industry*, 1664 (1961).

[4] A. C. Neish, *Can. J. Res.*, **23B**, 10 (1945); **25B**, 70 (1948).

[5] Two other routes to optically active 2,3-butanedithiol from the di-*p*-toluenesulfonate were investigated with unsatisfactory results: (1) *via* the diisothiuronium salt (see *Org. Syntheses*, **30**, 35 (1950)) and (2) *via* the cyclotrithiocarbonate (see A. Husemann, *Ann.*, **123**, 83 (1862)).