ORGANIC MASS SPECTROMETRY, VOL. 27, 891-895 (1992)

Participation of Halogen Atoms in Hydrogen Transfer Between Remote Positions in Gas-phase Ionized Isomeric Haloresorcinols

Adrian Weisz*
Division of Colors and Cosmetics, US Food and Drug Administration, Washington, DC 20204, USA

Denis Andrzejewski
Division of Contaminants Chemistry, US Food and Drug Administration, Washington, DC 20204, USA

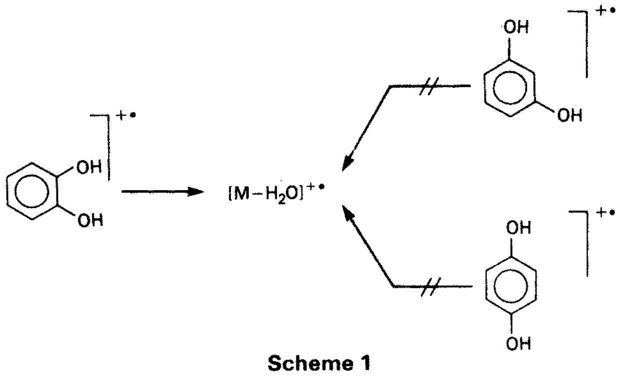
Asher Mandelbaum
Department of Chemistry, Technion—Israel Institute of Technology, Haifa, Israel

Mono, di- and trihaloresorcinols substituted by a halogen atom at position 2 exhibit a highly specific elimination of H_2O on electron impact ionization and under conditions of collisionally induced dissociation (CID). The high isomer specificity suggests the intermediacy of a hydrogen transfer from one of the hydroxy groups to the adjacent halogen atom. A subsequent hydrogen migration to the other hydroxy group readily explains the facile elimination of H_2O from the $M^{+\cdot}$ ions of these particular isomers. An analogous three-step hydrogen transfer has not been observed in 2,3-dihalo-1,4-hydroquinones. 4-Bromo- and 4-iodoresorcinol undergo elimination of the halogen atom followed by a very fast loss of CO under CID conditions, affording $[M - Hal]^+$ ions of low abundance and highly abundant $[M - Hal - CO]^+$ ions. The elimination of CO is suppressed in the isomeric 5-haloresorcinols, resulting in very highly abundant $[M - Hal]^+$ ions. This behavior suggests that a 'hidden hydrogen transfer' accompanies the elimination of the halogen atom from the molecular ions of 4-haloresorcinols.

INTRODUCTION

Catechol exhibits elimination of H_2O during analysis by electron impact (EI) ionization mass spectrometry, in contrast to the other two isomeric dihydroxybenzenes.[1] This specific behavior suggests the occurrence of hydrogen migration from the 1- to the 2-hydroxy group in the molecular cation of catechol (Scheme 1). A similar specific elimination of H_2O, indicating hydrogen transfer between vicinal hydroxy groups, has been also observed in isomeric dihydroxynaphthalenes,[2] and it may be a general feature of dihydroxyaromatic positional isomers.

We have been interested in 'hidden hydrogen transfers' whereby an initial hydrogen atom migration produces an intermediate which is capable of fragmentation that may or may not involve another hydrogen transfer.[3] In this context, it was of interest whether the introduction of an electronegative substituent between two remote hydroxy groups would induce a hydrogen transfer between them that otherwise would be impossible. The US *Code of Federal Regulations* limits the total brominated resorcinol intermediates in D&C Red No. 27 (2′,4′,5′,7′-tetrabromo-4,5,6,7-tetrachlorofluorescein) and its disodium salt, D&C Red No. 28, to not more than 0.4%.[4] Several isomeric haloresorcinols, which were synthesized as part of an ongoing effort to prepare and characterize reference materials for use in investigating the composition of regulated color additives, seemed to be good candidates for a study of 'hidden hydrogen transfer' during EI mass spectrometry. The results of the investigation of hydrogen transfer processes in isomeric haloresorcinols are presented in this paper.



Scheme 1

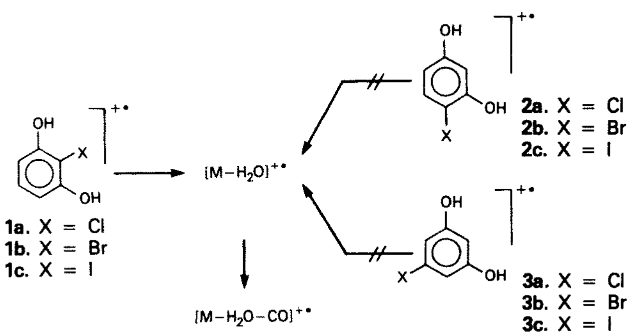
RESULTS AND DISCUSSION

Elimination of H_2O

The 70 eV EI mass spectrum of 2-chlororesorcinol (**1a**) is strikingly different from those of the other two positional isomers (**2a** and **3a**). The $[M - H_2O]^{+\cdot}$ ion (*m/z* 126 and 128) is relatively abundant in the mass spectrum of **1a** but is almost absent in those of **2a** and **3a** (Scheme 2 and Fig. 1). A subsequent loss of CO, affording $[M - H_2O - CO]^{+\cdot}$ ion (*m/z* 98 and 100), is also highly specific to isomer **1a**. The analogous isomeric

0030-493X/92/080891-05 $07.50

Received 27 February 1992
Revised manuscript received 28 May 1992
Accepted 28 May 1992



Scheme 2

bromo- and iodoresorcinols exhibit a similar specificity under EI conditions (Fig. 1). Elimination of H_2O occurs only in the 2-haloresorcinols (**1b** and **1c**) but not in the other isomers (**2b**, **2c**, **3b** and **3c**).

A similar behavior was observed under conditions of collisionally induced dissociation (CID) (Fig. 2). The major fragmentation process occurring in the molecular ions of the 2-haloresorcinols (**1**) leads to the formation of $[M - H_2O]^{+\bullet}$, which subsequently undergoes decarbonylation. These two ions are absent in the CID spectra of the 4- and 5-halo-isomers, **2** and **3**.

Deuterium labeling indicates quantitative involvement of the two hydroxylic hydrogen atoms in the elimination of H_2O from **1**. The deuterium-labeled 2-bromoresorcinol (**1b**-d_2) exhibits exclusive elimination of D_2O (Scheme 3).

Isomeric dihaloresorcinols exhibit a similar specificity in their fragmentation behavior upon EI. Isomers **4a** and **4b**, which contain a halogen substituent at position 2, undergo water elimination, in contrast to 4,6-dihalo-

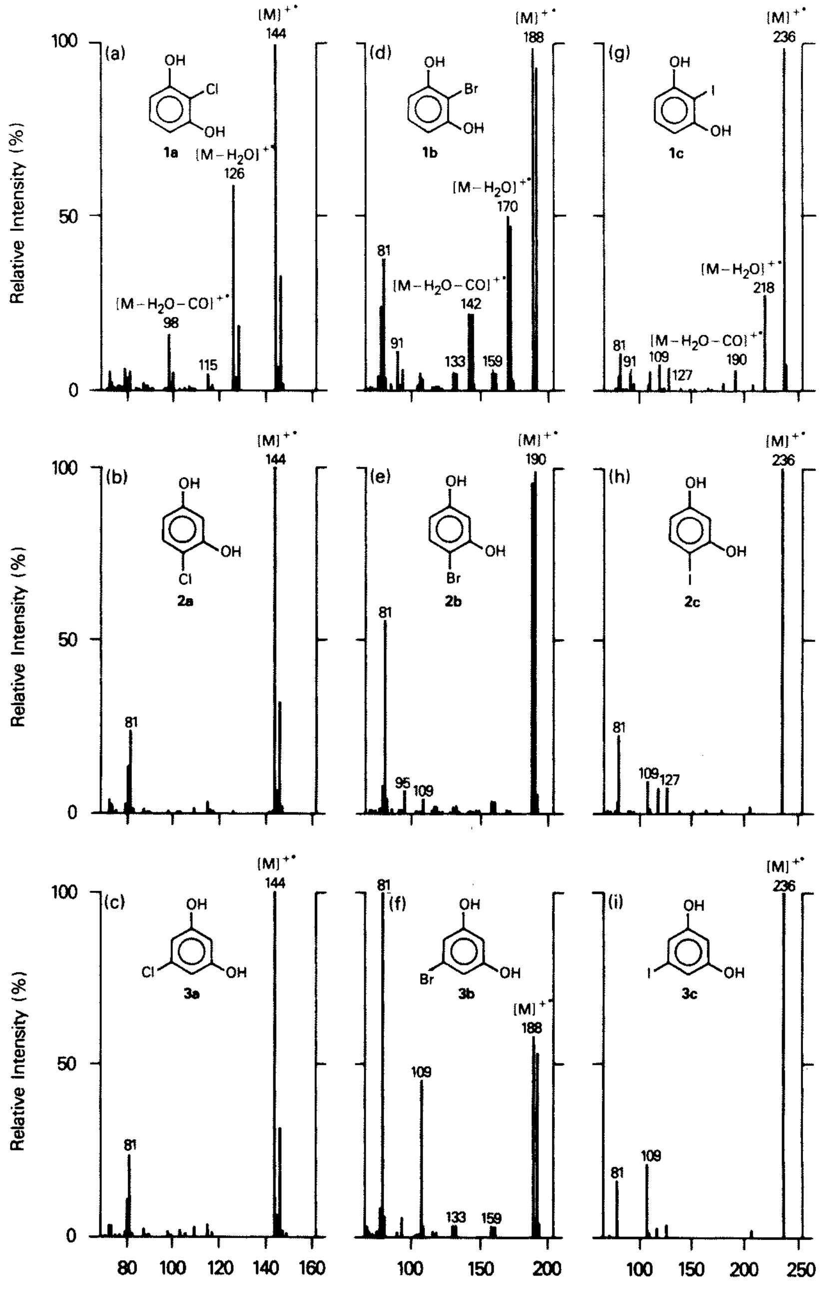


Figure 1. 70 eV EI mass spectra of isomeric chloro-, bromo- and iodoresorcinols.

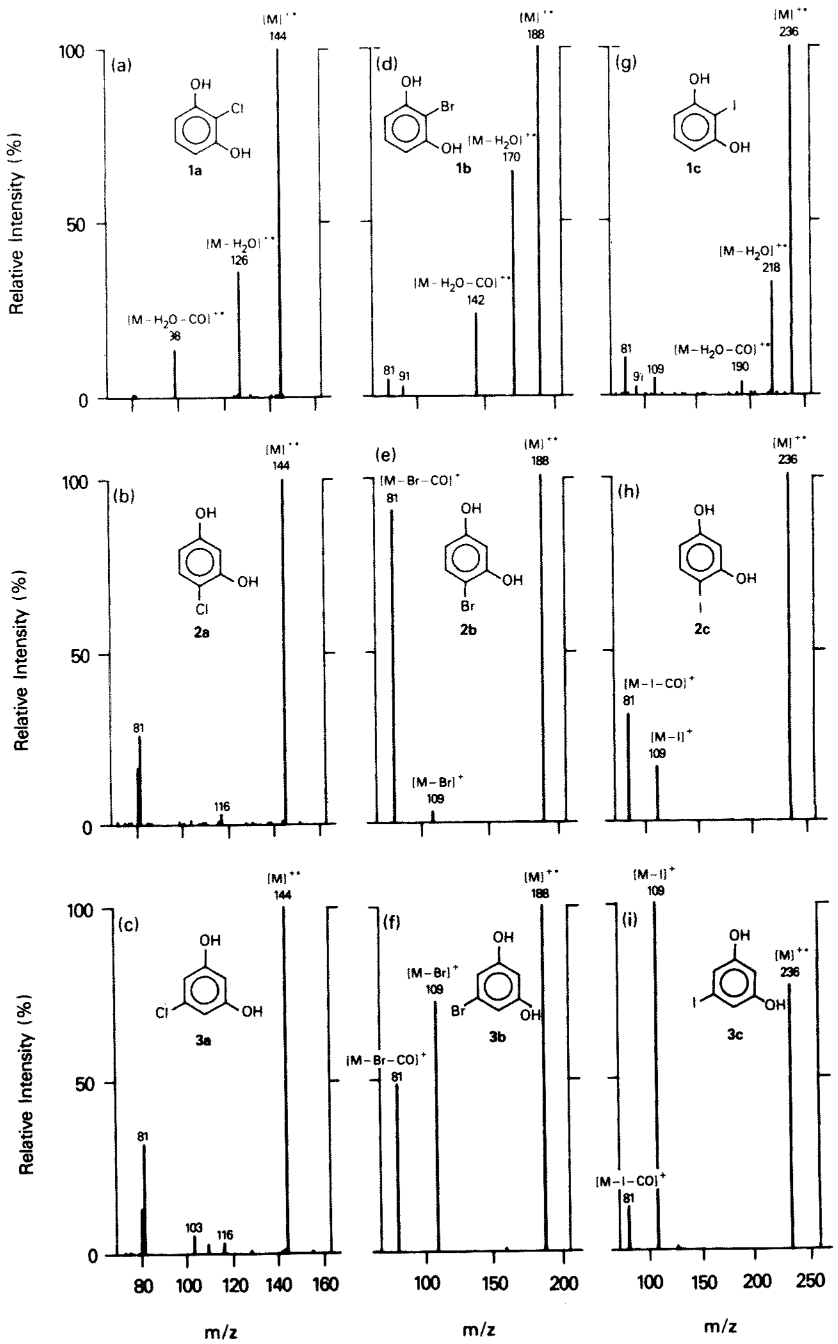
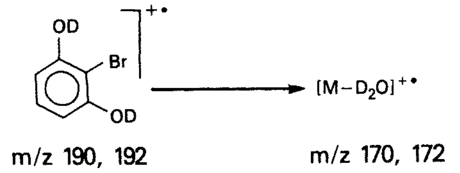


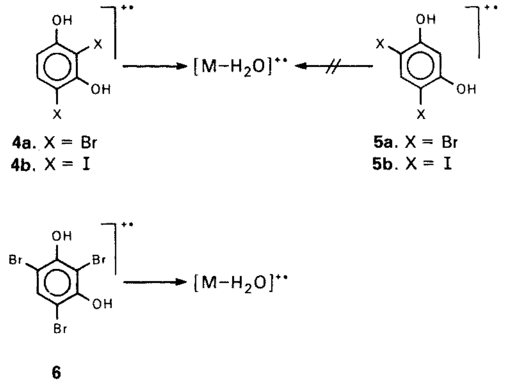
Figure 2. Low-energy CID spectra of $M^{+\bullet}$ ions of chloro(^{35}Cl)-, bromo(^{79}Br)- and iodoresorcinols.

resorcinols (**5a** and **5b**, Scheme 4). 2,4,6-Tribromoresorcinol (**6**) affords $[M - H_2O]^{+\bullet}$ ion upon EI, as expected from the presence of a halogen substituent at position 2.

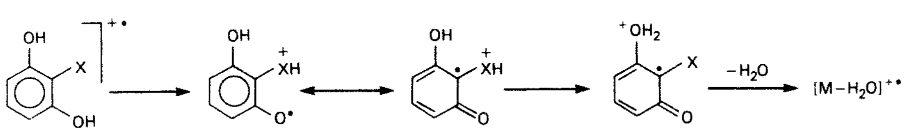
The above results lead to the conclusion that the molecular ions of the isomeric haloresorcinols do not isomerize to common structures before fragmentation,



Scheme 3



Scheme 4

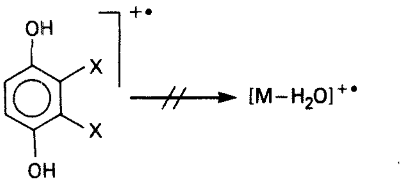


Scheme 5

and that no exchange of the hydroxylic and aromatic ring hydrogen atoms takes place before the elimination of H_2O. The highly specific dehydration process observed in the molecular ions of the resorcinols that are substituted by a halogen at position 2 indicates the occurrence of a two-step hydrogen transfer from the 1-OH to the 3-OH group (Scheme 5). The initial 1,4-migration from a hydroxy group to the halogen atom gives rise to intermediate A, which undergoes a subsequent 1,4-hydrogen transfer affording intermediate B, which is capable of eliminating a molecule of H_2O.

The involvement of Cl and Br in migrations of hydrogen and certain groups has been reported.[5] The participation of iodine atoms in such transfers is apparently rare. We are aware of only one previous report of a hydrogen migration involving an I atom.[6] It should be noted that the extent of the hydrogen transfer (demonstrated by the abundance of the $[M - H_2O]^{+\cdot}$ ions) is relatively low for 2-iodoresorcinols. The relative rates are Cl > Br > I, which parallel their relative electronegativities and the relative bond strengths of HCl, HBr and HI.

The elimination of H_2O from 2-haloresorcinols is an additional example of a fragmentation process occurring by a sequential series of hydrogen transfers that are made possible by the presence of the halogen substituent between the two relevant hydroxy groups. It was of interest to examine whether an analogous hydrogen transfer would occur by multiple 1,4-hydrogen migrations between two remote hydroxy groups separated by more than one halogen atom. 2,3-Dichloro- and 2,3-dibromo-1,4-hydroquinone (**7a** and **7b**) do not eliminate H_2O under EI conditions, indicating the non-occurrence of such a three-step hydrogen transfer (Scheme 6).

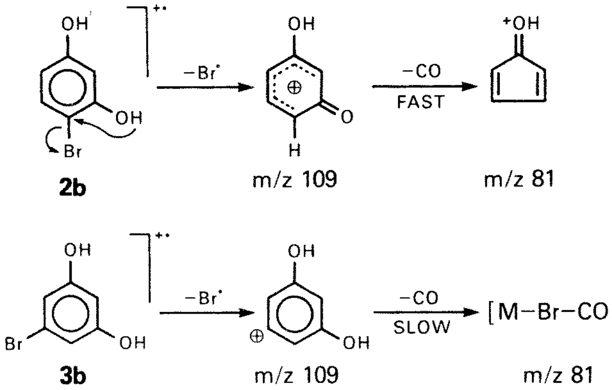


7a. X = Cl
7b. X = Br

Scheme 6

Elimination of Br and CO

Significantly different abundances of $[M - Br]^+$ and $[M - Br - CO]^+$ ions are exhibited by 4- and 5-bromoresorcinols (**2b** and **3b**) under CID conditions and to a lesser extent under EI conditions. The *m/z* 109 $[M - Br]^+$ ion is highly abundant in the case of **3b** but negligible for **2b**. The *m/z* 81 $[M - Br - CO]^+$ ion is very highly abundant for **2b** but less abundant in the case of **3b** (Fig. 2). The abundance ratios of the above two ions are 0.03 for **2b** and 1.5 for **3b** under CID conditions. The extremely low abundance of the $[M - Br]^+$ ion for **2b** results from a fast subsequent decarbonylation process in this particular isomer. Here again the stepwise mechanism shown in Scheme 7, involving a 'hidden hydrogen transfer' that is possible only in **2b**, provides a plausible explanation for the highly specific behavior of the two isomers.



Scheme 7

A similar behavior was observed for the isomeric 4- and 5-iodoresorcinols (**2c** and **3c**), although the difference between the two isomers is less pronounced than that between the corresponding bromoresorcinols. The analogous chlororesorcinols (**2a** and **3a**) do not show the above specificity. The abundance of the *m/z* 109 $[M - Cl]^+$ ion is low for both isomers.

CONCLUSION

A hydrogen atom is transferred from a hydroxy group to an adjacent halogen (Cl, Br or I) atom in the molecular cations of various 2-haloresorcinols obtained by electron ionization. This hydrogen migration followed by a subsequent transfer of the hydrogen atom from the halogen to the other hydroxy group gives rise to the highly specific elimination of H_2O from resorcinols substituted by a halogen at C(2). In addition to the interesting mechanistic aspects of this sequential hydrogen migration involving one halogen and two oxygen atoms, these results may be of diagnostic importance in the differentiation of isomeric substituted resorcinols.

EXPERIMENTAL

Materials

The isomeric bromo- and iodoresorcinols in this study are used as standards in the analysis of samples submitted for color certification.

Compound **2a** was purchased from Pfaltz and Bauer and **2b** and **6** from Aldrich. The following were synthesized by literature procedures: **1a**,[7] **1b**,[8,9] **3a** (by BBr_3 cleavage[10] of 3-chloro-5-methoxyphenol), **3b** (by Sandmeyer reaction of 3,5-dimethoxyaniline with CuBr[11] and subsequent BBr_3 cleavage of the methoxy groups[10]), **4a**,[9] **5a** (by bromination of 1,3-dimethoxybenzene[12] and subsequent BBr_3 cleavage of the methoxy groups[10]), **7a**[13] and **7b**.[14] Compounds **1c**, **2c**, **4b** and **5b** were obtained from the Colors Certification Section of the Division of Colors and Cosmetics of the Food and Drug Administration (FDA), Washington, DC. Compound **3c** was prepared by diazotization of 3,5-dimethoxyaniline, followed by treatment with KI[15] and subsequent BBr_3 cleavage of the methoxy groups.[10] The deuterium-labeled 2-bromoresorcinol was prepared by exchange with D_2O,[16] and its mass spectrum was measured in the presence of D_2O in the ion source.

Mass spectral measurements

The EI mass spectra were obtained at the FDA on a Finnigan MAT TSQ-46 instrument interfaced to an INCOS 2300 data system with TSQ software (Revision D). The instrument parameters were source temperature 130 °C, emission current 0.35 mA, ionizing energy 70 eV, conversion dynode −5 kV and scan from m/z 35 to 535 in 1.0 s. Separations were performed on an HP-Ultra 1 methylsilicone column (10 m × 0.25 mm i.d., 0.25 μm film thickness). The column temperature was programmed from 50 to 280 °C at 15 °C $\min^{-1}$; the injector temperature was 210 °C, the transfer line temperature 220 °C and the helium flow 40 cm s^{-1}. CID measurements were carried out in the daughter ion mode, using 10 eV collision energy and a 1.4 mTorr (1 Torr = 133.3 Pa) argon target gas pressure (indicated).

Acknowledgements

We thank Dr Sandra J. Bell, Division of Colors and Cosmetics, FDA, for samples of **1c**, **2c**, **4b** and **5b**. This work was supported by the FDA and by the Fund for Promotion of Research at the Technion.

REFERENCES

1. T. Aczel and H. E. Lumpkin, *Anal Chem.* **32**, 1819 (1960).
2. L. Prajer-Janczewska, J. Wroblewski and K. Chmielenska, *Pol. J. Chem.* **52**, 1675 (1978).
3. (a) A. Weisz and A. Mandelbaum, *J. Chem. Soc., Chem. Commun.* 521 (1978); (b) R. Bar-Shai, A. Bortinger, J. Sharvit and A. Mandelbaum, *Isr. J. Chem.* **20**, 137 (1980); (c) H. Schwarz. *Top. Curr. Chem.* **97**, 1 (1981); (d) D. Bornstein, A. Weisz and A. Mandelbaum, *Org. Mass Spectrom.* **21**, 225 (1986); (e) I. Vidavsky, A. Mandelbaum, T. Tamiri and S. Zitrin, *Org. Mass Spectrom.* **26**, 287 (1991); (f) D. Bornstein, B. Domon, A. Mandelbaum, D. Mueller, W. J. Richter and I. Vidavsky, *Org. Mass Spectrom.* **26**, 793 (1991).
4. *Code of Federal Regulations*, Title 21, Part 74. US Government Printing Office, Washington, DC (1991).
5. S. Hammerum, *Mass Spectrom. Rev.* **7**, 145 (1988) (references 54–56, 63, 83, 84, 162–168).
6. J. L. Holmes, F. P. Lossing, J. K. Terlouw and P. C. Burgers, *Can. J. Chem.* **61**, 2305 (1983).
7. R. F. Milligan and F. J. Hope, *J. Am. Chem. Soc.* **67**, 1507 (1945).
8. R. A. Eade, F. J. McDonald and H. P. Pham, *Aust. J. Chem.* **31**, 2699 (1978).
9. T. L. Davis and V. F. Harrington, *J. Am. Chem. Soc.* **56**, 129 (1934).
10. F. L. Benton and T. E. Dillon, *J. Am. Chem. Soc.* **64**, 1128 (1942); J. F. W. McOmie, M. L. Watts and D. E. West, *Tetrahedron* **24**, 2289 (1968).
11. N. B. Dean and W. B. Whalley, *J. Chem. Soc.* 4638 (1954).
12. K. Adachi, *Mem. Osaka Inst. Technol. Ser. A, Sci. Technol.* (*Osaka Kogyo Daigaku Kyo Riko-Hen*), **28**, 33 (1983); *Chem. Abstr.* **100**, 138683q (1984).
13. A. P. Ter Borg, *Recl. Trav. Chim. Pays-Bas* **73**, 5 (1954).
14. A. E. Gal and J. P. Voorstad, *J. Labelled Compd. Radiopharm.* **24**, 397 (1987); R. K. Norris and S. Sternhell, *Aust. J. Chem.* **26**, 333 (1973).
15. H. Heaney and I. T. Millar, *Org. Synth., Coll. Vol.* **5**, 1120 (1973); A. C. Schram and C. P. Christenson, *Tex. J. Sci.* **28**, 253 (1977).
16. F. K. Muenzberg, *Z. Phys. Chem., Abt. B* **33**, 23 (1936).