[14] Visiting Professor of Chemistry, Department of Chemistry, University of Chicago, Aug-Dec 1974.

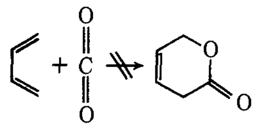
Francis K. Fong[14]
Department of Chemistry, Purdue University
West Lafayette, Indiana 47907

Received December 4, 1974

A Carbon Dioxide Equivalent for the Diels-Alder Reaction

Sir:

Carbon dioxide does not undergo 4 + 2 cycloaddition with dienes[1] (eq 1) nor is there a well-defined procedure which effects this transformation.[2] This communication reports a method which allows for a general synthesis of lactones by use of a carbon dioxide equivalent and describes some useful transformations of these adducts.

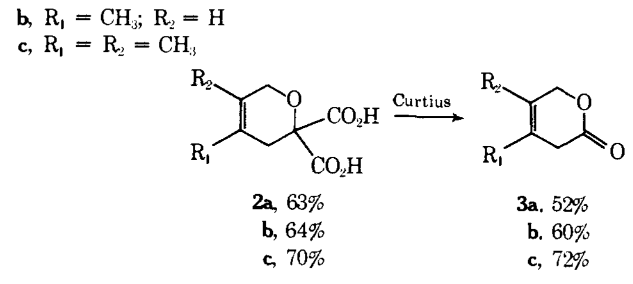

(1)

The simplest members in the triad of carbon and oxygen cumulated systems, allene, ketene, and carbon dioxide ($CH_2{=}C{=}CH_2$, $O{=}C{=}CH_2$, $O{=}C{=}O$) are considered poor partners for the Diels-Alder reaction. Indeed, only allene shows any propensity towards 4 + 2 cycloaddition. Recently, however, new methods have been developed which allow for the facile introduction of the $-CH_2C({=}CH_2)-$[3] and $-CH_2C({=}O)-$[4] grouping in a Diels-Alder sense. Clearly, the addition of a $-OC({=}O)-$ group to a diene requires a substance with a strongly polarized carbon-oxygen double bond. Also attached to this carbonyl, must be a grouping which could readily be transformed into the lactone carbonyl moiety. Furthermore the last step, the release of the lactone carbonyl, would have to be accomplished under mild conditions so as not to effect conjugation of the β,γ-double bond. We considered that diethylketomalonate[2,5] might well serve as a carbon dioxide equivalent, the unmasking step being a bis-Curtius degradation[6] followed by hydrolysis (Scheme I).

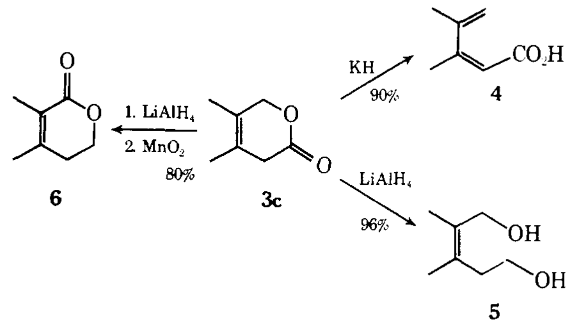
Warming acetonitrile solutions of dienes **1a–c** and diethylketomalonate with a trace of hydroquinone to 130° for 4 hr, afforded the known adducts in good yield.[1,7,8] Hydrolysis of these adducts proceeded smoothly with KOH in aqueous THF at room temperature to afford the diacids **2a–c** in overall yields of 63–70%.[8]

The conversion of these stable diacids to their corresponding lactones could be accomplished in less than 5 hr, without isolation of intermediates. Treatment of the diacids with oxalyl chloride in benzene with a trace of pyridine at reflux for 2–2.5 hours afforded almost pure diacid chloride. Removal of the solvent at reduced pressure and redissolution in acetonitrile followed by the addition of excess activated sodium azide[9] afforded, after 1 hr at room temperature, the bisacylazide. Filtration of the acetonitrile solution to remove excess sodium azide and replacement of the acetonitrile with cyclohexane followed by heating the solution for 1 hr at reflux effected the rearrangement. It should be noted that benzene and other moderately polar solvents were inefficacious and led to little or none of the desired bisisocyanate. The final step, hydrolysis of the bisisocyanate, was accomplished with 5% aqueous oxalic acid in THF at room temperature for 30 min. The overall yield of lactone, after distillation, from diacid was quite acceptable (see Scheme I).[10,11]

Scheme I



Scheme II



These adducts show promise as being versatile intermediates in synthesis. A few examples of their utility are described below (Scheme II). Treatment of lactone **3c** with 1 equiv of potassium hydride in THF at 0° afforded the dienoic acid **4**[10] (mp 54.5–56°). The tetrasubstituted olefin **5** (λ_{max} 3.0 μm), could be readily prepared by reduction of **3c** with lithium aluminum hydride in THF at 0°. This diol could then be transformed to a new lactone **6** (λ_{max} 5.83 μm), simply by stirring a CH_2Cl_2 solution of **5** with activated MnO_2.[12]

We are continuing to explore the chemistry of these adducts.[13]

References and Notes

(1) J. Hamer and J. A. Turner, "1,4-Cycloadditions", J. Hamer, Ed., Academic Press, New York, N.Y., 1967, pp 205–215.
(2) (a) O. Achmatowicz and A. Zamojski, *Chem. Abstr.*, **52**, 6333 (1958); *ibid.*, **57**, 13713*h* (1962); A. Zamojski and K. Jankowski, *ibid.*, **62**, 1560*d* (1965). These workers report the additions of diethylketomalonate to a variety of dienes and their attempted conversion of these adducts to the lactones. They were unable to do so when the double bond was present. (b) For a general review see S. B. Needleman and M. C. Chang Kuo, *Chem. Rev.*, **62**, 405 (1962).
(3) R. A. Ruden and R. Bonjouklian, *Tetrahedron Lett.*, 2095 (1974), and references therein.
(4) E. J. Corey, T. Ravindranathan, and S. Terashima, *J. Am. Chem. Soc.*, **93**, 4326 (1971).
(5) Available from Aldrich Chemical Co.
(6) P. A. S. Smith, *Org. React.*, **3**, 337 (1946).
(7) Diene **1b** gave an 11:1 mixture of **2b** and its isomer **2d**, R_1 = H, R_2 = CH_3 by NMR analysis.
(8) Yield is based on diethylketomalonate. **2c** was crystalline (mp 138–140°). **2a** and **2b** were both oils.
(9) J. Nelles, *Ber.*, **65**, 1345 (1932).
(10) Infrared, NMR, and mass spectral data were all in agreement with the assigned structures.
(11) The sodium azide Curtius degradation was found to be superior to the following alternate procedures: (a) Oxidative decarboxylation using lead tetraacetate directly afforded 60% of **3c**, 40% of **3b**, and no lactone **3a**. (See J. J. Tufariello and W. Kissel, *Tetrahedron Lett.*, 6145 (1966), and references within.) (b) One-pot bisisocyanate formation using trimethylsilylazide on the bisacid chloride in refluxing cyclohexane followed by hydrolysis yielded 55% of **3c**, 30% of **3b**. (See S. S. Washburne and W. R. Peterson, Jr., *Synth. Commun.*, **2**, 227 (1972).) (c) Standard Curtius degradation as well as modified Curtius degradation (see J. Wienstock, *J. Org. Chem.*, **26**, 3511 (1961)) afforded less than 20% of the desired lactones.

(12) J. A. Marshall and N. Cohen, *J. Am. Chem. Soc.*, **87**, 2773 (1965).

(13) The generous support of the Research Corporation is gratefully acknowledged.

Ronald A. Ruden,* Rosanne Bonjouklian
Department of Chemistry, Rutgers, The State University
New Brunswick, New Jersey 08903

Received May 19, 1975

Sequential Deuterium Exchange Reactions of Protonated Benzenes with D_2O in the Gas Phase by Ion Cyclotron Resonance Spectroscopy

Sir:

Deuterium exchange has been used in mass spectrometric studies to determine the number of acidic hydrogens in a molecule. Together with knowledge of the heteroatom content from high resolution mass spectrometry, the results afforded by this method aid considerably in functional group identification and hence the elucidation of complex molecular structures.[1,2] Hunt and co-workers have developed a simplified procedure utilizing chemical ionization mass spectrometry (CIMS) with D_2O as the reagent gas.[3] Their findings indicate that hydrogen bonded to heteroatoms in aliphatic alcohols, phenols, carboxylic acids, amines, amides, and mercaptans undergo essentially complete exchange in the ion source prior to protonation by the reagent ions. In addition they report that unsaturated compounds such as benzene, stilbene, and 3,3-dimethyl-1-butene fail to exchange, and that the extent of substitution with ketones, aldehydes, and esters is negligible.

We wish to report preliminary results on a novel deuterium exchange reaction, observed using ion cyclotron resonance (ICR) spectroscopy,[4] which have a bearing on the above findings and interesting implications for further study. In apparent contrast to the results of Hunt et al., sequential reactions of protonated aromatic compounds with D_2O in the gas phase occur which lead to various degrees of ring deuteration. For example, in a mixture of benzene and D_2O (Figure 1), reactions 1 and 2 lead to the formation of $C_6H_6D^+$ which in further reaction with D_2O undergoes rapid stepwise exchange of H for D (reaction 3).[5] From these data it is possible to determine the number of deuteriums exchanged in addition to kinetic parameters describing the exchange process.[6]

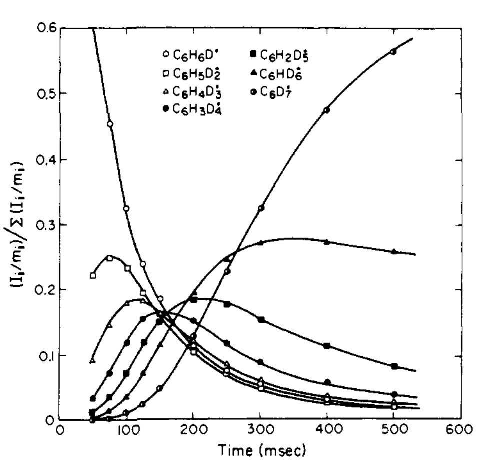


Figure 1. Temporal variation of the abundances of the variously deuterated benzene ions observed in a mixture of benzene (2×10^{-7} Torr) and D_2O (3.5×10^{-6} Torr) at an electron energy of 70 eV. Other species present, not included in the normalization, are D_2O^+ and D_3O^+, which are precursors to $C_6H_6D^+$, as well as $C_6H_6^+$ and fragment ions derived from benzene.

$$D_2O^+ + C_6H_6 \rightarrow C_6H_6D^+ + OD \tag{1}$$

$$D_3O^+ + C_6H_6 \rightarrow C_6H_6D^+ + D_2O \tag{2}$$

$$C_6H_{7-n}D_n^+ + D_2O \rightarrow C_6H_{6-n}D_{n+1}^+ + HDO \quad (n = 1\text{–}6) \tag{3}$$

From the data summarized in Table I for the halo and alkyl substituted benzenes it is apparent that deuterium exchange varies significantly for different structural isomers. Thus while *o*- and *p*-difluorobenzene exchange all hydrogens rapidly, the meta isomer slowly exchanges only a single hydrogen. A similar comparison can be made for the xylenes and trisubstituted benzenes. *These results are especially important since the mass spectra of these isomeric compounds are in general indistinguishable.*[7,8]

Species such as the benzoyl cation, radical cations, and $C_7H_7^+$ derived from toluene and cycloheptatriene do not undergo exchange. It appears that ring protonation is a necessary condition for exchange to occur. Two experiments which ascertain the site of protonation of substituted aromatics (Table I) include the observation of thermoneutral

Table I. Summary of Deuterium Exchange Results

	No. of exchanges starting with deuterated parent ion[a]						Relative rate of first exchange[b]	Site of protonation[c]
Compound	1	2	3	4	5	6		
Benzene	+	+	+	+	+	+	f	R
Fluorobenzene	+	+	+	+	+	NA	f	R
o-Difluorobenzene	+	+	+	+	NA	NA	f	R
m-Difluorobenzene	+	–	–	–	NA	NA	m	R
p-Difluorobenzene	+	+	+	+	NA	NA	f	R
1,3,5-Trifluorobenzene	–	–	–	NA	NA	NA	–	R
1,2,4-Trifluorobenzene	+	+	+	NA	NA	NA	f	R
Toluene	+	+	+	+	+	NA	m	R
o-Xylene	+	+	+	+	NA	NA	m	R
m-Xylene	+	–	–	–	NA	NA	s	R
p-Xylene	+	+	+	+	NA	NA	m	R
Mesitylene	–	–	–	NA	NA	NA	–	R
Anisole	–	–	–	–	–	NA	–	R
Benzonitrile	–	–	–	–	–	NA	–	S
Benzaldehyde	–	–	–	–	–	NA	–	S
Acetophenone	–	–	–	–	–	NA	–	S

[a] NA indicates not applicable, + exchange observed, and – exchange not observed. [b] The symbols f, m, and s indicate, respectively, fast ($1–5 \times 10^{-10}$ cm³ mol⁻¹ sec⁻¹), medium ($10^{-11}–10^{-10}$ cm³ mol⁻¹ sec⁻¹), and slow ($\leq 10^{-11}$ cm³ mol⁻¹ sec⁻¹) reaction rates. [c] R and S indicate that evidence was obtained for the *favored* site of protonation being on the ring and substituent, respectively. With sufficiently acidic donors both sites may be protonated.