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Conformations of the Radical Anions from Dialkyl Maleates and Fumarates

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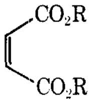
Both dialkyl maleates and fumarates give the same mixture of monoanion radicals, as several workers have noted. It is proposed that all the conformations observed are trans at the original carbon–carbon double bond, and that syn and anti alkyl conformations are observed with primary alkyl groups. This proposal requires that surprisingly slow carbonyl carbon–alkoxyl oxygen rotation occurs in the radical anions.

Electrolytic reduction of dialkyl maleate (**1**) and fumarate (**2**) esters in DMSO produces the same mixture of radical anion ESR spectra, indicating that cis-trans isomerization occurs rapidly in the radical anions.[1] Our attribution of the two isomers of $(\mathbf{1,2})\cdot^-$ which we observed to the trans and cis radical anions was incorrect, as the simple fact that we saw substantial amounts of both isomers should have told us; the cis isomer is far more sterically hindered than the trans one, and both of the reported isomers must be trans.[2] The ESR spectra[3] and electrochemistry[4] of these and similar compounds were studied in DMF by Il'yasov and coworkers, and Bard and coworkers have greatly extended such studies.[5] Kemp and coworkers[6] have studied the ESR spectra of these radical anions in liquid ammonia using solvated electrons for generation, and were able to discern no less than four dimethyl maleate–fumarate radical anions. They point out that the two major components A and B (see Table I), which correspond to the species we reported in DMSO, are accompanied by minor components C and D, which have significantly larger *g* factors. Diethyl fumarate–maleate behaved in a similar manner except that only one minor component was discerned. They attributed the major components A and B to conformations of the fumarate radical anion **3** and **4**, and the minor components C and D to the maleate anions **5** and **6**, stating that **7** was not observed because it would have inequivalent vinyl splittings, whereas A–D were observed to have equivalent ones. They also said additional components cannot be ruled out of these complex spectra, which show many overlapping lines. The remaining symmetrical trans form **8** is also a possibility for A or B.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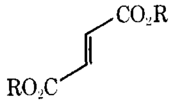
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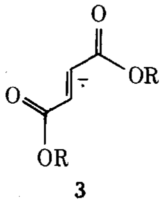
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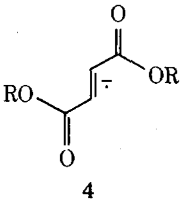
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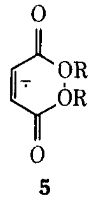
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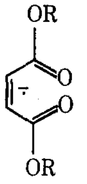
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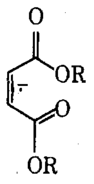
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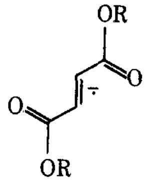
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In the earlier work, we also reported that a second type of species was generated at higher potential and longer electrolysis times, and attributed it to the anion radical of monoalkyl maleate-fumarate anion.[1] Il'yasov and coworkers[3] stated disbelief in this assignment, and wish to attribute the species to oligomers of some sort, for which they give a couple of structures.

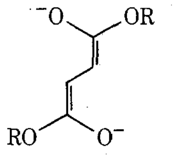
In hopes of discovering more about the isomers of the maleate–fumarate radical anion conformations, we have done additional ESR work on these systems.

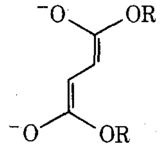
Results and Discussion

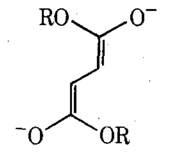
The radical anions from dimethyl and diethyl fumarate–maleate give complex spectra which are not very long lived in DMSO, and we had significantly less resolution then Kemp and coworkers.[6] The minor conformations they report in ammonia are quite probably also present in DMSO. Since alkyl can be on either of the two types of oxygen present, which we will refer to as "inner" and "outer", there are three dialkyl fumarate conformations (the oi and io conformers being identical when the alkyl groups are the same). If all were of equal energy, one would observe a 1:2:1 mixture of oo, oi, and ii conformations, and the oi confor-

Table I
ESR Data for Some Dialkyl Maleate–Fumarate Anion Radicals

Starting compd	Species	Relative	a(H$_v$)	a(alkyl)	g shift
1 or **2** ($R = R' = Me$)[6]	A	Major	6.83 (2 H)	1.39 (4 H)	
	B	Major	6.62 (2 H)	1.39 (4 H)	+0.0001
	C	Minor	6.73 (2 H)	1.35 (4 H)	+0.0003
	D	Minor	6.73 (2 H)	1.35 (4 H)	+0.0006
9	I	~0.5	6.53 (2 H)		
	II	~0.3	6.30, 6.54		+0.00008
	III	~0.2	6.42		+0.00005
10	I	~0.6	7.01, 6.44	1.17	
	II	~0.2	6.76, 6.51	1.18	+0.00009
	III	~0.2	6.98, 6.25	0.82	+0.00038


oo (**4**)

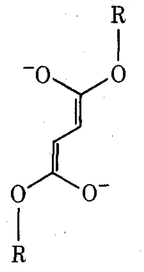

oi (**3**)


ii (**8**)

mation would have nonequivalent hydrogen splittings. To simplify the spectra and increase the anion radical lifetime,[5b] we have investigated two additional cases, di-*tert*-butyl maleate **9** (**1**, R = R′ = *t*-Bu) and *tert*-butylmethyl maleate **10** (**1**, R = *t*-Bu; R′ = Me); the *tert*-butyl groups, as expected, showed no splitting. The ESR data for these compounds appears in Table I. From both **9** and **10**, we were definitely able to distinguish three isomers, but small unattributed lines were present, and it is certainly possible that even isomers present in substantial amount would be so completely masked by lines from the attributed species that we might have missed them. The "amount" column is only estimated by peak height, and is not at all reliable.

The three observed isomers from **9** correspond well with the expectation for oo, oi, and ii. There is a slight preference for either oo or ii, but all three are actually present in substantial amount, and there is very little preference between "inner" and "outer" alkyl group in fumarate anion radical. All three have very similar g factors, making it likely that all three are actually present in dimethyl and diethyl fumarate as well, but not discernible because of the complexity of the spectra. No large g factor forms were observed, and the simplicity of the spectra require that we would have seen such species had they been there in substantial amount. For the radical anions from **10**, we were only able to discern two of the four possible (and presumably present) "low g factor" conformations. Presumably the other two are lurking somewhere under the major peaks, but it is not obvious where. We also saw one other conformation (**10**, III) which has the larger g factor that Kemp and coworkers observed for minor conformations from dimethyl and diethyl maleate–fumarate, and attributed to maleate forms.

If conformation III from **10** is attributed to a maleate form, however, one is hard pressed to explain why a similar conformation was not observed from **9**, since the *tert*-butyl groups of maleate conformations **6** and **7** could be tucked away from other parts of the molecule as efficiently as they could in the fumarate forms. Furthermore, attribution of C and D of Table I, and hence **10**, III, to the maleate form is inconsistent with the experimental results of Bard and coworkers,[5c] who found that reduction and reoxidation of the maleate gave complete isomerization to the fumarate. We suggest that even the high g factor radical anions are fumarate forms, and that the reason that more than three isomers are observable is that in addition to isomerism between "inner" and "outer" oxygens, syn–anti isomerism at the *O*-alkyl groups is being observed. There would then be in principle ten different isomers (six of the 16 possible isomers generated by each end having i or o alkyl group in s or a position are identical with six others), as is shown for the oo and ii isomers below (there are also now four oi isomers, not shown). These isomers would not have equivalent steric interactions. There is little or no steric difference between oa, oa, oa, ia, and ia, ia conformations, but all syn conformations are sterically destabilized, and it is clear that is conformations are considerably destabilized compared to os conformations. It is also worth noting that all fumarate conformations are less destabilized sterically than any maleate conformations (of which there are also ten, considering s,a isomerization, although all is maleate conformations are absurdly hindered).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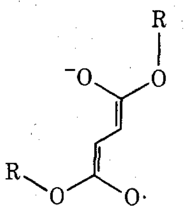
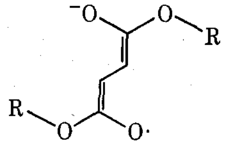

oa, os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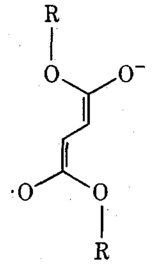
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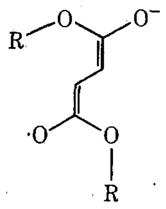
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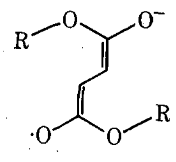

is, is

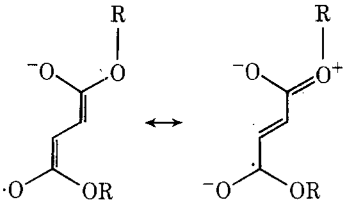
If the high g factor conformation(s) observed are attributed to conformations having "outer" syn alkoxyl groups (such as oa, os), this would take care of both of the objections raised above to the maleate assignment, since the bulky *tert*-butyl group would be unlikely to present syn in detectable amount, and of course all fumarate radical anions will oxidize to neutral fumarate.

The problem with this assignment is, of course, whether one would really expect carbonyl carbon–oxygen rotation to be slow on the ESR time scale at room temperature, so that syn conformations would give distinct spectra. Although we find such slow rotation as we are forced to pos-

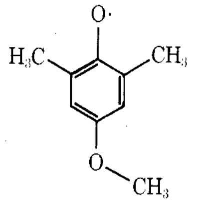
Table II
ESR Data for Monoalkyl Fumarate Dianion Radicals (15, 16)

Alkyl group	Species	a(Hv)	a(alkyl)	g factor shift	Registry no.
tert-Butyl	I	9.80, 2.77			
	II	9.78, 2.60		0.00011	55569-43-2
Isopropyl	I	9.84, 3.11	0.47 (1 H)		
	II	9.80, 2.93	0.33 (1 H)	0.00009	55569-44-3
Ethyl[1]	I	10.24, 2.78	0.91 (2 H)		
	II	10.13, 2.69	0.69 (2 H)	0.00012	55569-45-4
Methyl[1]	I	10.11, 2.81	1.02 (3 H)		
	II	10.03, 2.75	0.77 (3 H)	0.00012	55569-46-5

tulate surprising, stabilization of the oxadienyl fragment by a conjugated alkoxyl oxygen, as shown in resonance structures 11 ↔ 12, could lead to such behavior. The best model we have thought of for such an interaction is the 4-alkoxyphenoxy radical 13, for which an activation energy for aryl-O rotation of 7.8 ± 1 kcal/mol was measured by ESR.[7] This is a far higher barrier than is observed for diamagnetic alkoxybenzenes;[8] *p*-dimethoxybenzene has a methoxy rotational barrier of only 0.88 kcal/mol.[8a] A conjugative interaction of the sort shown in 11 ↔ 12 was invoked to rationalize the increase in barrier height.[7] Such delocalization might be predicted to be more favorable in the case of 11 ↔ 12 than for 13 because of the anionic oxygen substituent, which should electrostatically favor charge separation in the sense of 12.



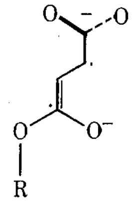
11 **12**



13

At higher applied potentials and longer electrolysis times, all of the dialkyl maleates and fumarates studied gave a second mixture of spectra, for which the ESR data are summarized in Table II. The species designated II was present in smaller amount in all cases, and the ratio of I/II varied from about 2.4:1 for methyl and ethyl to about 1.3:1 for *tert*-butyl. Since the monoalkyl maleates give the same species (I and II) as the second one from the dialkyl maleates and fumarates, and the spectra show only splittings for the quite inequivalent vinyl hydrogens and one alkyl group, we assign these spectra to monoalkyl fumarate dianion radicals. We have previously observed exactly analogous formation of benzaldehyde-*o*-carboxylate radical dianions directly from the acid, or as second species from the esters or pseudo-esters.[2] The dimeric species proposed by Il'yasov and coworkers[3] would certainly show additional splittings.

We have been unable to observe these monoalkyl fumarate dianion radicals in DMF or butyronitrile, and believe their lifetimes to be far shorter in these solvents. Since the g factors are quite similar for the two isomers observed in each case, and only two isomers were distinguished even for the methyl and ethyl cases, we assign I and II as "inner" and "outer" oxygen isomers 15 and 16. As was the case in the *o*-carboxylate benzaldehyde dianion radicals, the carboxylate has a relatively minor effect on the spin distribution, and is probably substantially twisted out of conjugation with the rest of the molecule. Ethylacrylate anion radical has vinyl splittings of 12.18 (2 H_β) and 1.57 (H_α) G,[6] compared to around 10 and 2.8 G for our radicals, which bear a β-carboxylate substituent. We see no evidence for the added complexity of still more conformations, as was observed with methyl and ethyl dialkyl fumarate anions. The presence of the carboxylate would be expected to increase the C–OR rotation rate, so we do not find this surprising. We do not have a plausible rationale for the significantly smaller alkyl splitting for the II conformations.



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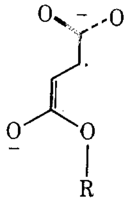

16

Ester exchange is easily noted if excess alcohol is mixed with the DMSO used as the reducing medium, as it was with the aromatic systems.[2] When 2-propanol–DMSO was used for reduction of dimethyl maleate, the first mixture species observed was an ill-resolved mixture of diisopropyl fumarate radical anions, and at longer reduction times, **15–16** (R = *i*-Pr) was observed. The exchange may well proceed by attack of electrolytically generated alkoxide upon starting ester. Another mechanism is suggested by the results of Il'yasov and coworkers,[3,4] who found that diphenyl maleates and fumarates did not give stable enough radical anions for observation, even at low temperature, and proposed "phenoxide stripping", loss of PhO from the radical anion, to account for this unstability. The ketene thus formed could capture either alcohol or adventitious water, and this is an alternative mechanism for **15–16** formation. The mixed ester **10** gave only the *tert*-butyl substituted **15–16**, as would be expected by either pathway.

Experimental Section

Di-*tert*-butyl maleate (**9**) was prepared by reaction of maleic acid and methyl maleate with isobutylene in methylene chloride in the presence of sulfuric acid.[9] Crystallization from ether gave **9**, mp 68° (lit.[10] mp 68°).

tert-Butyl methyl maleate (**10**) was prepared by stirring 10 g of maleic anhydride in 150 ml of methylene chloride with 3.6 g of anhydrous methanol and a trace of sodium methoxide overnight, and then *tert*-butylating as above. The residue was distilled at 5 mm (bp 50–85°), yielding 7 g of a mixture of **10** and dimethyl maleate (ca. 3:1), from which **10** was isolated by redistillation [bp 80–82° (5 mm)]. Dimethyl maleate or other impurities were not detected by NMR. The empirical formula was established by high-resolution mass spectroscopy.

ESR measurements were carried out on a Varian E-15 spectrometer using intra muros reduction with a mercury pool cathode in a flat quartz cell to generate the radical anions.[2]

Acknowledgment. We thank the National Science Foundation and the donors of the Petroleum Research

Fund, administered by the American Chemical Society, for partial financial support of this work. We thank Professor Bard for communication of his results prior to their publication.

Registry No.—**1**, 624-48-6; **2**, 624-49-7; *cis*-**9**, 18305-60-7; *trans*-**9**, 7633-38-7; *cis*-**10**, 55556-65-5; *trans*-**10**, 55556-66-6; butenedioic acid, dimethyl ester radical ion, 55569-40-9; butenedioic acid, di-*tert*-butyl ester radical ion, 55569-41-0; butenedioic acid, methyl, *tert*-butyl ester radical ion, 55569-42-1.

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Selective Lithiation of Bromoarylalkanoic Acids and Amides at Low Temperature. Preparation of Substituted Arylalkanoic Acids and Indanones[1]

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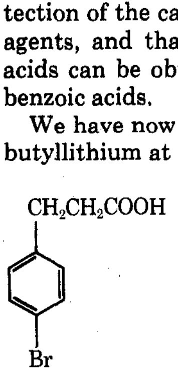
Received December 5, 1974

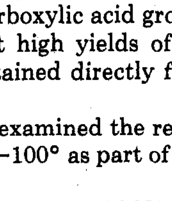
Studies of *p*-bromophenylpropanoic acid suggest that *p*-, and presumably *m*-, bromoarylalkanoic acids can be conveniently elaborated by selective halogen–metal exchange with *n*-butyllithium at −100° followed by reaction with E^+. Metal–halogen exchange is also selective for ortho-substituted acids; however, *o*-bromoarylpropanoic acids lead directly to indanones in high yield. Amide anions have been shown to be less reactive toward organolithium derivatives than carboxylate; consequently, by masking the carboxylic acid group by conversion to the amide anion, indanone formation can be obviated and elaboration of *o*-bromophenylpropanoic acid can be achieved. *o*-Bromophenylacetic acid (**3**) reacts with *n*-butyllithium at −100 or at −78° to give the dilithio derivative **21** and the trilithio derivative **23**. The trilithio derivative undergoes anion decay, with time, by reaction with solvent, to give **21**; consequently, by control of conditions, products can be obtained selectively from either **21** or **23**. Similar results were obtained with *p*-bromophenylacetic acid (**4**); however, in contrast to the results obtained with **3**, alkylation of intermediate anions with *n*-butyl bromide, formed during metal interchange, occurs which detracts from synthetic applications in the latter case.

Although Grignard (or lithium) reagents of aryl halides are useful intermediates for formation of aryl–carbon bonds, utilization of such derivatives has been of limited value for aromatic nuclei containing sensitive electron-withdrawing groups. Meyers and Temple[2] have obviated problems associated with aromatic carboxylic acids by disguising the carboxylic function as the corresponding oxazoline derivative. Recently we have shown[3a,b] that the lithium salt of aryl carboxylic acid function provides adequate protection of the carboxylic acid group at −100° to lithium reagents, and that high yields of elaborated arylcarboxylic acids can be obtained directly from *o*-, *m*-, and *p*-bromobenzoic acids.

We have now examined the reaction of acids **1**–**4** with *n*-butyllithium at −100° as part of a program designed to test the generality of the above method for the elaboration of alkanoic acids. Acid **1** was selected as a model for the behavior expected for a broad series of para- and meta-substituted bromoarylalkanoic acids. Limitations for utilization of bromoarylalkanoic acids were anticipated where favorable entropy relationships might result in intramolecular reaction of derived aryllithium reagents with carboxylate functions (as in **2**), and in phenylacetic acids (**3** and **4**) where the methylene group α to the carboxylate function is more acidic. In all cases, progress of metal–halogen exchange was followed by quenching aliquots[4] with dilute acid and determining the ratio (by NMR) of recovered bromo acid to acid derived by replacing bromine with hydrogen.



1



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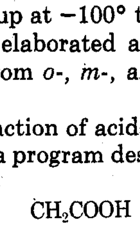

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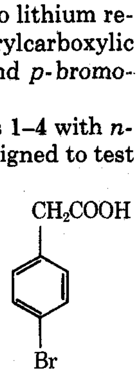

4

A. β-(*p*-Bromophenyl)propanoic Acid (1). Two equivalents of *n*-butyllithium was added rapidly to a solution of **1** in THF–hexane at −100° at such a rate that the temperature did not exceed −90°. Examination of an aliquot showed that halogen–lithium exchange was $\sim$80% after 30 min and the ratio did not change appreciably after an additional 90 min at −100°. Additional *n*-butyllithium (up to 0.4 to 1 equiv) increased the degree of exchange only slightly (ratio of **1**:**6** was $\sim$85%); however, with excess *n*-butyllithium and time, small quantities of butylated products were detected (NMR) in the neutral component of the aliquots. In subsequent experiments 2.2 equiv of *n*-butyllithium was employed and the mixture was stirred at −100° for 45 min prior to quenching. In one experiment (see Scheme I) the mixture was quenched with water; the yield