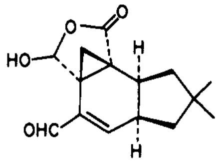
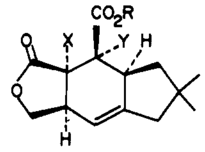
140-144 °C (hexane-methyl acetate), in 40% yield. Treatment of **17** with excess ethereal diazomethane gave methyl isomarasmate (**2**), identical by ir (CCl_4) and ^1H NMR ($CDCl_3$) with that prepared by de Mayo.[9] Although an explanation for the exclusive addition of diazomethane to what appears to be the more hindered side of **7** is not readily available, it is the establishment of the isomarasmic stereochemistry for cyclopropane **10** that places in doubt the assignment of the marasmic acid skeleton to the similar cyclopropane obtained by Wilson and Turner, also via a pyrazoline.[10]

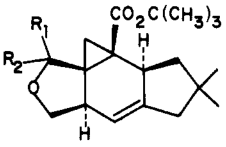


17

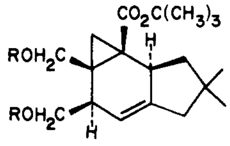


	X	Y	R
20	CH_2Br	H	H
21	H	CH_2Br	H
22	CH_2Br	H	$C(CH_3)_3$
23	H	CH_2Br	$C(CH_3)_3$

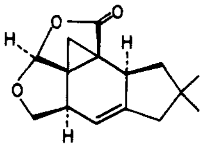
In a second approach to marasmic acid, diene aldehyde **5** was reduced with diisobutylaluminum hydride in benzene, giving the known alcohol **18**[3,6] in 91% yield. Diels-Alder reaction of **18** with bromomethylmaleic anhydride (**19**)[12] in methylene chloride solution (24 h at room temperature) gave a 1:1 mixture of the lactone acids **20**,[6] mp 172-174 °C (hexane-ether), and **21**,[6] mp 177-177.5 °C (hexane-ether). The crude mixture of acids (in methylene chloride solution) was esterified with isobutylene in the presence of *p*-toluenesulfonic acid (4 days at room temperature), affording the *tert*-butyl esters **22** and **23**,[6] mp 139.5-140.5 °C (hexane-ether). Treatment of this mixture of esters with potassium *tert*-butoxide in benzene-*tert*-butyl alcohol (15 min at room temperature) produced the cyclopropane **24**,[6] mp 81.5-83.5 °C (hexane), in 44% overall yield from **18**.



24 $R_1, R_2 = O$
25 $R_1 = OH$, $R_2 = H$



26 R = H
27 R = COCl



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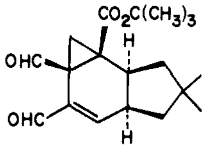

29

Reduction of **24** with diisobutylaluminum hydride in toluene (4 h at −78 °C) afforded the hemiacetal **25**, which could be converted to lactone **28**,[6] mp 87-88 °C (hexane), by exposure to trifluoroacetic acid (65% overall yield from **24**). Reduction of hemiacetal **25** with sodium borohydride in methanol provided the diol **26**[6] (67% overall yield from **24**). Addition of an ether solution of **26** containing 2 equiv of quinoline to an excess of ethereal phosgene at 0 °C provided the dichloroformate **27** in 95% yield. Treatment of **27** with dry dimethyl sulfoxide, followed by 2.1 equiv of triethylamine at room temperature,[13] afforded dialdehyde **29**, mp 111-115 °C (hexane-ethyl acetate), in 25% yield after column chromatography on silica gel. De-esterification of **29** with trifluoroacetic acid in benzene solution completed the synthesis, giving (±)-marasmic acid (**1**)[14] (50% yield) identical with that derived from natural sources[15] by ir ($CHCl_3$), ^1H NMR ($CDCl_3$), uv (95% C_2H_5OH), and mass spectra.[16]

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(2) D. Helmlinger, P. de Mayo, M. Nye, L. Westfelt, and R. B. Yeats, *Tetrahedron Lett.*, 349 (1970).

(3) S. R. Wilson and R. B. Turner, *J. Org. Chem.*, **38**, 2870 (1973).

(4) The stereochemical deductions of Wilson and Turner were in the main based upon steric arguments which paralleled our own during the planning stages of our work, and which we regard as reasonable even now. Consequently, the fact that the pertinent reactions follow the opposite course from that independently predicted by both groups poses a theoretical problem of much interest.

(5) G. Magnusson and S. Thoren, *J. Org. Chem.*, **38**, 2870 (1973).

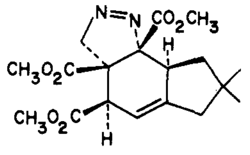
(6) A satisfactory combustion analysis has been obtained for this compound or a suitable derivative thereof.

(7) O. Isler and P. Schudel, *Adv. Org. Chem.*, **4**, 128 (1963).

(8) Y. Watanabe, M. Yamashita, T. Mitsudo, M. Tanaka, and Y. Takegami, *Tetrahedron Lett.*, 3535 (1973).

(9) We are grateful to Dr. P. de Mayo for providing us with copies of his spectra.

(10) Wilson and Turner obtained a single pyrazoline, which they believed should have the structure i;[4] some support for this structure was subsequently



i

put forward on the basis of NMR studies with a lanthanide shift reagent;[11] it now appears that the assumptions underlying these arguments should be re-examined.

(11) S. R. Wilson and R. B. Turner, *J. Chem. Soc., Chem. Commun.*, 557 (1973).

(12) R. A. Laursen, W. Shen, and K. G. Zahka, *J. Med. Chem.*, **14**, 619 (1971).

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(14) Synthetic marasmic acid (racemic) has mp 171-171.5 °C (hexane-ethyl acetate) in an evacuated capillary. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.62; H, 6.99.

(15) We are grateful to Dr. P. de Mayo for a sample of (+)-marasmic acid from natural sources, which we recrystallized twice from hexane-ethyl acetate, mp 172-173 °C [lit.[1b] mp 173-174 °C (ethyl acetate)] in an evacuated capillary.

(16) Although ir spectra in KBr showed minor differences, the solution ir, NMR, uv, and the mass spectra were superimposable.

(17) NSF Predoctoral Fellow (1972-1975).

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An Electrochemical Determination of the pK_a of Isobutane

Sir:

We have described[1,2] the use of electrochemical data in a thermodynamic cycle to determine the pK_a's of triarylmethanes, cycloheptatriene, and various cyclopropenes. The cycle used involved a number of steps:

$$RH \rightarrow ROH \rightarrow R^+ \xrightarrow{e} R\cdot \xrightarrow{e} R^- \ (\rightarrow RH)$$

A related cycle was used to determine the pK_{R^+}'s of some cyclopentadienyl cations.[3]

Most of our work[1] has used electrochemical data from cyclic voltammetry. However, we have recently shown[2] that good reversible potentials can be obtained by the technique of second harmonic ac voltammetry. These data confirm our previous conclusions, but are more reliable. They also allowed us to determine bond dissociation energies ($ROH \rightarrow R\cdot + OH\cdot$) by a simple direct cycle.

So far these methods have required that *one* of the trivalent carbon oxidation states be stable; for the pK_a's, for instance, we started with stable solutions of carbonium ions. We now wish to describe a method without this limitation. With it, we have determined the basicity of *tert*-butyl anion.

The thermodynamic sequence used is direct and simple:

$$RH \xrightarrow{1} R\cdot + H\cdot \underset{+e}{\xrightarrow{2}} R^- + H\cdot \underset{-e}{\xrightarrow{3}} R^- + H^+$$

The first step involves the bond dissociation energy of the hydrocarbon, which is known for many simple systems. The second step involves the *reversible* potential for reduction of the radical to the anion. The third step, oxidation of $H\cdot$ to H^+, is common to all substrates; we can solve for it (or cancel it) by running a compound of known pK_a through the sequence.

Polarography of *tert*-butyl iodide in dimethoxyethane has been reported[4] to show two reduction waves, of which the second at −2.49 V (vs. SCE) is ascribed to reduction of *tert*-butyl radical to *tert*-butyl anion. In Me_2SO a second wave has been reported[5] for *tert*-butyl bromide also, at −2.46 V. We have confirmed the *tert*-butyl iodide results with dc polarography in dimethoxyethane, and have also shown that the two waves can be observed by second harmonic ac polarography. Ac polarography allows determination of the potential for the relevant second reduction wave at Hg (−2.43 V vs. SCE), at Au (−2.56 V) and at Pt (−2.69 V). The close agreement of potentials indicates that formation of organometallic bonds is not appreciably involved in the process. The second harmonic ac polarographs show a good crossing point, invariant with frequency. Thus the potentials obtained are electrochemically *reversible.*[2]

Taking the value at Au as the reversible potential[6] for conversion of free *tert*-butyl radical to free *tert*-butyl anion,[7] we can calculate the pK_a of *t*-BuH. For this we need the bond dissociation energy (91 kcal/mol[8]), and as well the three relevant numbers (bond dissociation energy, pK_a, reduction potential of the radical) for a reference compound. As reference we take triphenylmethane. The bond dissociation energy is reported[9] to be 75 kcal/mol, the pK_a is 31.5,[10] while the radical reduction potential is −0.93 V.[11] Since isobutane bond dissociation requires 16 kcal/mol more energy (free energy, assuming similar entropy changes) and the resulting radical is 1.63 V more difficult to reduce, the pK_a must be 39.2 units ($16/1.38 + 1.63/0.059$) higher. This puts the pK_a of isobutane at 70.7.[12]

Previous estimates[13] of the pK_a's of simple saturated hydrocarbons have ranged from 42 to 85, but none has involved a thermodynamic method. With our technique the only uncertainty is the reliability of bond dissociation energies and reduction potentials, and any solvation effects not mimicked by the reference compound. It is thus relevant to compare our estimated pK_a of 71 for isobutane $\rightleftharpoons$ *tert*-butyl anion with our[2] estimated pK_a of 74 for trimethylcyclopropene $\rightleftharpoons$ trimethylcyclopropenyl anion. The latter is certainly pyramidal at the anionic carbon, so I-strain is not a factor in raising the pK_a. Two other factors should make it *more* acidic than isobutane. In the cyclopropene the C–H bond should have been acidified by increased s character at carbon, and by the inductive effect of two vinyl carbons. The fact that the pK_a is higher than that of isobutane thus indicates that even the pyramidal cyclopropenyl anion has some conjugative destabilization (antiaromaticity).[13] Finally, it should be noted that our new method should make it possible to determine a variety of other pK_a's of interest, and also to obtain important thermodynamic information on simple carbonium ions.

Acknowledgment. Support of this work by the National Science Foundation is gratefully acknowledged.

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(6) For consistency with ref 2, where Au proved to be least involved in adsorption effects.

(7) I.e., unbound to the electrode. No other process seems conceivable for the second wave common to *t*-BuI and *t*-BuBr (isobutylene is not reduced in this region).

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(11) A minor correction from the −0.97 V of ref 2 was applied for the solvent change, by calibration with tropylium cation.

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(13) Cf. ref 1c.

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