Enthalpy of the Metal Catalyzed Isomerizations of Quadricyclane and of Tricyclo[4.1.0.0^{2,7}]heptane[1]

Sir:

The reactivity of small ring hydrocarbons has been of considerable interest. However, the lack of experimental thermochemical data has made it difficult to consider the reactivities in more quantitative terms, and in many cases the conventional methods of determining heats of formation (i.e., from heats of combustion) are not readily applicable either because the compounds may only be obtained in small amount or because they can only be obtained as solutions. A study of the heats of metal catalyzed rearrangements provides a way in which to circumvent both of these difficulties. We wish to report the results of the first of our studies of these reactions, the isomerizations of quadricyclane to norbornadiene, and of tricyclo[4.1.0.0^{2,7}]heptane to 3-methylenecyclohexene.

The reactivity and strain energy of quadricyclane have been of interest and have led to three studies of the enthalpy of the isomerization to norbornadiene. Turner et al.[2] obtained $\Delta H_r = -24 \pm 0.9$ kcal/mol (acetic acid solution, 25 °C) from the heats of hydrogenation of quadricyclane and norbornadiene. Hall et al.[3] obtained $\Delta H_r = -10.0 \pm 0.5$ kcal/mol (gas phase, 25 °C) from the heats of combustion of the two compounds, and Kabakoff et al.[4] obtained $\Delta H_r = -21.2 \pm 0.2$ kcal/mol for the heat of thermal isomerization in toluene solution at 190 °C and which was corrected to give $\Delta H_r = -22 \pm 1$ kcal/mol for the isomerization in the gas phase at 25 °C.

The range of values which have been reported has led us to reinvestigate the isomerization. A direct measurement of the enthalpy of reaction is desirable. The procedure of Kabakoff et al.[4] has the disadvantage that the experimental data refer to an elevated temperature and must be corrected to room temperature using uncertain values of the heat capacities. This difficulty is circumvented in the metal catalyzed reaction since it may be carried out at room temperature.

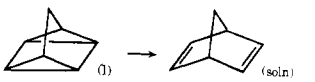
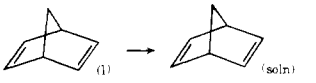
The isomerization was effected using di-μ-chloro-bis(bicyclo[2.2.1]hepta-2,5-diene)dirhodium(I) as the catalyst which leads to a rapid reaction at room temperature.[5] When the reaction was carried out in chloroform solution, a rapid temperature change occurred which was followed by a very slow, small increase in temperature over that expected from heat transfer from the external bath. This presumably involved equilibration of the catalyst with the norbornadiene formed in the reaction.[5] It could be completely suppressed by the addition of a tenfold excess of norbornadiene to the reaction solvent.

The observed enthalpies of reaction are given in Table I.[6] The quadricyclane contained 2.2 ± 0.2% of norbornadiene[7] and the data have been corrected for this. The NMR spectrum of the reaction solution indicated quantitative conversion to norbornadiene. The enthalpy of solution of norbornadiene also was measured so that the enthalpy of reaction in the liquid phase could be obtained. The observed enthalpy change (−26.2 kcal/mol) is in quite good agreement with the results of Turner et al.[2] The enthalpy change in the gas phase may be obtained using the known heats of vaporization[3] and is −27.1 kcal/mol.

The heat of isomerization of bicyclo[1.1.0]butane to butadiene may be calculated from the heats of formation which are known,[8] and is −25.8 kcal/mol. Little is known about the effects of structural modifications on the heat of this reaction. The rearrangement of tricyclo[4.1.0.0^{2,7}]heptane[9] to 3-methylenecyclohexene appeared to be an interesting example, especially since the course of the reaction depends on the catalyst used.[10]

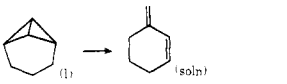
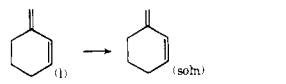
The enthalpy of the rhodium dicarbonyl chloride dimer catalyzed isomerization, which is rapid at room temperature,

Table I. Enthalpy of Isomerization of Quadricyclane to Norbornadiene at 25 °C

	−ΔH (kcal/mol)
	27.03 26.32 26.55 26.80 26.60
	av 26.66 ± 0.24[a]
	0.498 0.495 0.499
	av 0.497 ± 0.002[a]
$\Delta H_r = -26.16 \pm 0.24$ kcal/mol[a] (liquid phase) $= -27.13 \pm 0.24$ kcal/mol (gas phase)	

[a] Uncertainty is given as 2$\bar{s}$.

Table II. Enthalpy of Isomerization of Tricyclo[4.1.0.0^{2,7}]heptane to Methylenecyclohexene at 25 °C

	−ΔH (kcal/mol)
	30.44 30.29 30.50 30.43 30.32 30.27
	av 30.38 ± 0.08[a]
	0.383 0.406 0.384
	av 0.391 ± 0.015[a]
$\Delta H_r = -29.99 \pm 0.08$[a] (liquid phase)	

[a] Uncertainty is given as 2$\bar{s}$.

was studied giving the data in Table II.[6] The enthalpy of solution of methylenecyclohexene also was measured so that the enthalpy of reaction in the liquid phase could be obtained. The value for the gas phase should not differ significantly since one would expect the reactant and product to have similar enthalpies of vaporization.

The isomerization of the tricycloheptane is somewhat more exothermic than that of bicyclobutane. This would be expected since the product diene has alkyl substituents which should stabilize it as compared with butadiene. If the heat of formation were known, the heat of formation of the tricycloheptane and its strain energy could be obtained. Values have been reported,[11] but lead to unreasonable values for the heat of hydrogenation to methylcyclohexane. The small difference between the heats of reaction of the tricycloheptane and bicyclobutane shows the strain energies of the two to be comparable.

The metal catalyzed isomerizations provide a useful process for studying the thermochemistry of many strained hydrocarbons and for interrelating compounds for which heats of formation have been derived via combustion calorimetry. Additional examples are being studied and will be reported subsequently.

Supplementary Material Available: Experimental results (2 pages). Ordering information is available on any current masthead page.

References and Notes

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(2) R. B. Turner, P. Goebel, B. J. Mallon, W. v. E. Doering, J. F. Coburn, and M. Pomerantz, *J. Am. Chem. Soc.*, **90**, 4315 (1968).
(3) H. K. Hall, Jr., C. D. Smith, and J. H. Baldt, *J. Am. Chem. Soc.*, **95**, 3197 (1973).
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(5) H. Hogeveen and H. C. Volger, *J. Am. Chem. Soc.*, **89**, 2486 (1967); H. C. Volger and H. Hogeveen, *Recl. Trav. Chim. Pays-Bas*, **86**, 1066 (1967). Our reaction conditions gave a half-life of about 25 s.
(6) The experimental results are available as supplementary material. The calorimetric data were obtained using an LKB Model 8700 isothermal environment submarine calorimeter.
(7) Quadricyclane was prepared by the procedure of F. I. Sonntag and R. Srinivasan, *Org. Photochem. Synth.*, **1**, 97 (1971), and was distilled through a 24 in. spinning band column collecting the fraction having bp 74.0–74.7 °C at 200 mm. The amount of norbornadiene present was determined by gas chromatography using a $\frac{1}{8}$ in. × 10 ft Carbowax 400 column and an HP 3370A integrator. Repeated injections gave a deviation of ±0.2%. The response ratio was determined by adding a small known amount of norbornadiene and reanalyzing the mixture.
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(9) W. R. Moore, H. R. Ward, and R. F. Merritt, *J. Am. Chem. Soc.*, **83**, 2019 (1961).
(10) P. G. Gassman and T. J. Atkins, *J. Am. Chem. Soc.*, **93** 1042 (1971); L. A. Paquette, G. R. Allen, Jr., and R. P. Henzel, *ibid.*, **92**, 7002 (1970). Our reaction conditions gave a half-life of about 35 s.
(11) O. S. Pascual and E. Almeda, *Philipp. A. E. C.* [*Rep.*], PAEC(D)CH-634 (1963) (*Chem. Abstr.*, **60**, 10521*g* (1964), reported $\Delta H_c = -996.9$ kcal/mol ($\Delta H_f = -3.0$) whereas Y. Imanishi, S. Karragawa, and T. Higashimura, *Makromol. Chem.*, **175**, 1761 (1974), reported $\Delta H_c = -1026$ kcal/mol ($\Delta H_f = +26.0$), both presumably for the liquid state. From other data one may estimate that ΔH_f should be between +4 to +9 kcal/mol.

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Received May 17, 1976

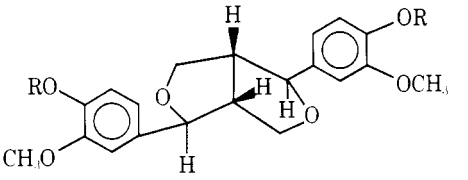
Isolation and Synthesis of Pinoresinol Diglucoside, a Major Antihypertensive Principle of Tu-Chung (*Eucommia ulmoides, Oliver*)

Sir:

Tu-Chung (*Eucommia ulmoides, Oliv.*) is one of the oldest herbs known and its medicinal value has been noted for several thousand years in China.[1] Tung Chung extract has long been known as a tonic for old people who can apparently drink it daily as tea without ill effects. Oral administration of Tu-Chung bark tea or wine to hypertensive patients showed that improvement occurred after 2–4 months in 93.6% of 62 cases of hypertension. Several investigators have confirmed the hypotensive action of aqueous and ethanol extracts of Tu-Chung bark in anesthetized dogs, cats, rabbits, rats, and guinea pigs.[2-5] The systemic arterial hypotension caused by the Tu-Chung extract is apparently the result of peripheral vasodilation by its direct action on the vascular smooth muscle.[5] Although much had been done on the study of the chemical composition of leaves and bark of *E. ulmoides*,[6] there has not been a systematic study of the pharmacologically active principles of this drug. We herein report the identification and synthesis of pinoresinol di-β-D-glucoside as the major antihypertensive principle of Tu-Chung bark.

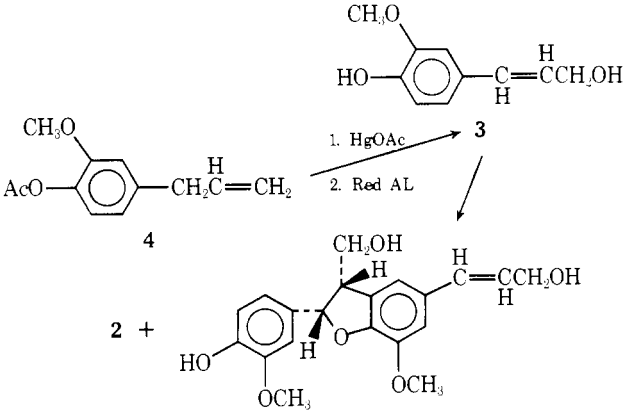
The antihypertensive activity was measured by the fall in the arterial blood pressure in anesthetized hypertensive rats.[7] Four successive chromatographies of the 95% ethanol extract of Tu-Chung bark (4.75 kg) over silica gel (MN-Kieselgel Brinkmann) columns using chloroform:methanol:water as eluent afforded 2.2 g of a glycoside, **1**: mp 221–230 °C; $[\alpha]^{25}D$ −27.3° (*c* 0.54, H_2O); uv (H_2O) 276 nm (ε 6750), 226 (ε 21 500). Anal. Calcd for $C_{32}H_4O_{16}\cdot 4H_2O$: C, 50.92; H, 6.68. Found: C, 51.23; H, 6.70.

Hydrolysis of **1** with β-glucosidase[8] (Sigma) afforded 2 mol of glucose, characterized by paper chromatography (ethanol:H_2O:1-butanol, 1:5:4) and oxidation with glucose oxidase, and an aglycone, **2**: mp 158–159 °C; molecular ion at *m/e* 358.141 63 (theory 358.141 10); its NMR and infrared spectra were found to be identical with those of an authentic specimen of (+)-pinoresinol.[9] As **2** is devoid of optical activity, it is apparent that the glycoside (**1**) consists of (±)-pinoresinol (**2**) linked to two D-glucose residues via β-glucosidic bonds.



1, R = D-glucose
2, R = H

Although two chemical syntheses[10,11] of (±)-**2** were reported, neither of these is applicable to the preparation of **2** in quantities sufficient for in-depth pharmacological evaluation. Syringaresinol may be efficiently prepared either by the incubation of syringin with crude emulsin[12] or by the exposure of 4-hydroxy-3,5-dimethoxycinnamyl alcohol to the action of mushroom laccase.[13] Unfortunately, when coniferin and coniferyl alcohol[14] (**3**) were, respectively, used as substrates in these enzyme systems, the major product formed was dehydrodiconiferyl alcohol,[15] and only traces of **2** were detected. On the other hand, the chloroperoxidase[16]-containing microorganism, *Caldariomyces fumago*, catalyzed the dimerization of coniferyl alcohol, prepared by oxidation of eugenol acetate (**4**) with mercuric acetate,[17] to (±)-pinoresinol. In a typical experiment, when 1 g of coniferyl alcohol (**3**) was exposed to *C. fumago*[18] for 16 h, 115 mg of (±)-pinoresinol, mp 158–159 °C, accompanied by 123 mg of (±)-*cis*-dehydrodiconiferyl alcohol[19] (**5**), mp 160–161 °C, was formed.



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Reaction of (±)-**2** with α-bromoacetoglucose,[20] in the presence of Ag_2O, followed by alkaline hydrolysis, afforded **1** (50%) as a mixture of α,β-anomers, mp 232–235 °C; $[\alpha]^{25}D$ −33.5° (*c* 0.57, H_2O); its infrared, NMR spectra and antihypertensive activity[21] were found to be indistinguishable from those of **1**, obtained from *E. ulmoides*.

Isolation and characterization of other minor biologically active components are currently in progress and will be reported later.

Acknowledgments. The authors express their appreciation to Dr. Paul K. T. Sih for bringing this problem to our attention, and to Drs. John Rowe and John Harkin for supplies of (+)-pinoresinol. This research was supported by grants from the Wisconsin Alumni Research Foundation, the National Institutes of Health under Grant AM-4874, and the Miles Laboratories.

References and Notes

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