Studies of Mixed-Valence Diferrocenyl Selenide and Diferrocenyl Diselenide

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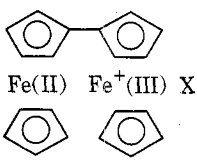
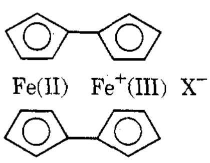
New synthetic routes were devised for the preparation of diferrocenyl selenide (I) and diferrocenyl diselenide (II). The electrochemical and spectroscopic properties of these compounds and their corresponding mono- and dications are reported. The relatively large separation between the first and second oxidation potential of I and II (0.22, 0.14 V) compared with the corresponding methylene and ethylene bridged ferrocenes (0.17, 0.00 V) indicates that the selenium group, because of its polarizability, can effectively transmit the inductive effect of the ferrocenyl substituent. Inasmuch as no intervalence transfer transition (near infrared) was observed for either the monocation of I or of II, these compounds are type I mixed-valence salts. This suggests that electron transfer, both thermal and optical, requires some delocalization via the bridging group. The relatively long C–Se bond and the resulting small resonance integral mitigate against any effective electron transfer in these cations.

Mixed valence compounds, which are composed of two identical or similar moieties in different oxidation states, play an important role in biological, organic, and inorganic reactions. These compounds also exhibit interesting magnetic, electronic, and optical properties which differ from those of similar species not containing paired moieties. Fe_3O_4, a mixed valence compound of FeO and Fe_2O_3, has an electrical conductance 10^6 times greater than that of Fe_2O_3. These phenomena have been explained as the result of delocalization between the sites in the mixed valence species. A mixing parameter α is defined and used to express the extent of this delocalization.[2] The ground state of the mixed valence compound can be expressed in terms of ϕ_i, ϕ_j which are the wave functions of donor and acceptor moieties, and α. When $\alpha = 0$, there is no interaction between components.

$$\psi_G = \sqrt{1 - \alpha^2}\, \phi_i + \alpha\phi_j$$

A totally delocalized mixed valence compound, obtained when $\alpha = 0.707$, should possess a new set of properties. Intermediate cases may possess new properties besides the ones inherited from other progenitors. For example, an "intervalence transfer" band[2a,3] in the near infrared at 1500–1900 nm has been found in monocations of biferrocenes in addition to ferrocene and ferrocenium absorptions in the uv and visible regions. A transition involving an electron transfer between two metallike e_{2g} orbitals has been proposed to account for this transition.





$$[^1A_{1g}(e_{2g})^4(a_{1g})^2]_i \sim [^2E_{2g}(e_{2g})^3(a_{1g})^2]_j \xrightarrow{h\nu} [^2E_{2g}(e_{2g})^3(a_{1g})^2]_i \sim [A_{1g}(e_{2g})^4(a_{1g})^2]_j \quad (1)$$

The mechanism of the intervalence transition still remains uncertain. The study of metallocenes, especially biferrocenes, should enable one to learn more about this phenomenon, because small ligand and functional group changes can be designed and incorporated into such molecules conveniently and the resulting differences may be studied. The intervalence transfer may be accomplished in two different ways, through ligand and through space. The first takes place through a bridge or a "single" bond, between the ligands of two ferrocene units. The second occurs via direct metal–metal interaction. It is often difficult to determine which mechanism is dominant in a particular case. By the proper choice of model systems, one should be able to distinguish qualitatively as to which is the more important mechanism for electron transfer in the ferrocene–ferrocenium system.

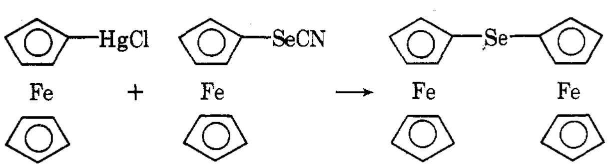
We have observed a near infrared transition for several mixed-valence bridged ferrocene molecules where the bridging group is in (C-π) conjugation with the cyclopentadienyl rings (for example, the monocation of diferrocenylacetylene[7]).

However, to date there has been little work reported regarding the effect of other bridging groups on electron transfer between ferrocene moieties and on the near infrared transition. Selenium could serve as a transmitting bridge in biferrocenes. The relatively long Se–Se (2.29 Å)[4] and C–Se (1.93 Å) bonds might minimize the through space and even through ligand interaction in these selenium bridged biferrocenes.

It is the purpose of this paper to report the synthesis of diferrocenyl selenide (I), diferrocenyl diselenide (II), and their mono- and dications, and to examine the interaction between the two ferrocene moieties of the monocations of I and II.

Results and Discussion

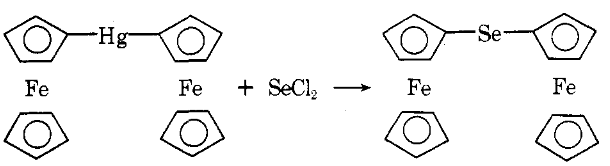
Synthesis. We find that diferrocenyl selenide (I) can be prepared by direct coupling of chloromercuriferrocene and ferrocenyl selenocyanate in quantitative yields (eq 2). Compound I was first synthesized by Nesmeyanov and coworkers[8] via the reaction of diferrocenylmercury and selenium dichloride in 21% yield (eq 3). Diferrocenyl diselenide



(2)

I

100%



(3)

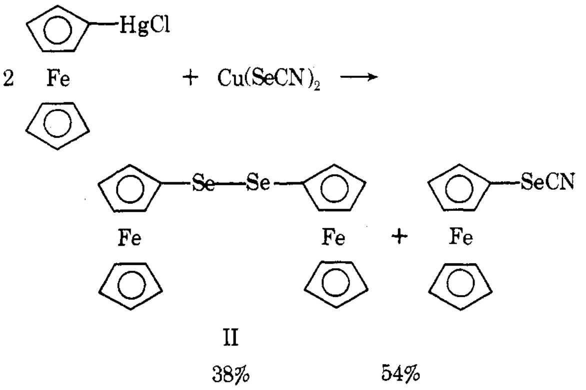
I

21%

Table I. Half Wave Potentials[a] of Bridged Biferrocenes

Compd	Solvent	$E_{1/2}$ (1)	$E_{1/2}$ (2)	$\Delta E_{1/2}$	Ref
Diferrocenyl selenide (I)	CH_3CN	0.46	0.68	0.22	This work
Diferrocenyl diselenide (II)	CH_3CN	0.53	0.67	0.14	This work
Diferrocenemethane (III)	CH_3CN (90% EtOH)	0.39 (0.30)	0.56 (0.40)	0.17 (0.10)	6, 9
Diferrocenylethane (IV)	CH_3CN	0.37	0.37	0	9
[1.1]Ferrocenophane (V)	90% EtOH	0.25	0.44	0.19	6
Diferrocenylacetylene (VI)	CH_2Cl_2[b]	0.61	0.745	0.135	7
Ferrocenyl *n*-butylselenide (VI)	CH_2CN	0.405			This work
Methylferrocene (VIII)	CH_3CN	0.305			c

[a] Volts vs. SCE. [b] n-Bu_4NBF_4 (0.2 M), otherwise Et_4NClO_4 (0.1 M) for those which are unnoted. [c] Unpublished results: D. O. Cowan and C. LeVanda.



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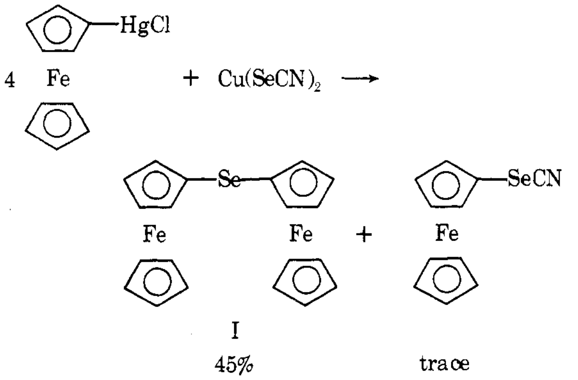

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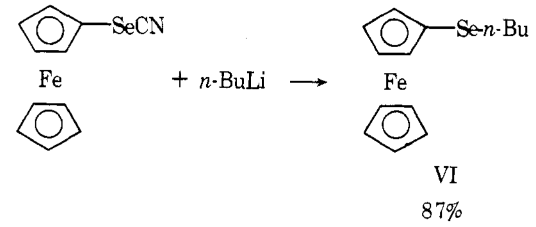

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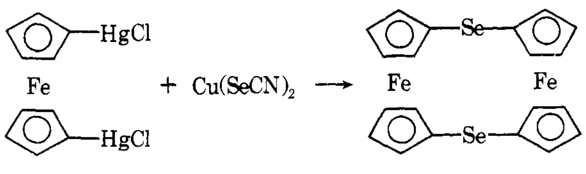


(7)

(II) was obtained as a coproduct with ferrocenyl selenocyanate in the reaction of copper(II) selenocyanate and chloromercuriferrocene in moderate yields (38%) (eq 4). When this reaction was carried out under an inert gas (N_2, Ar) and under anhydrous conditions, a mixture of ferrocenyl selenide (I) and ferrocenyl selenocyanate was obtained (eq 5). Ferrocenyl *n*-butylselenide (VI), a reference compound, was prepared by the reaction of *n*-butyllithium and ferrocenyl selenocyanate (eq 6). Attempts to prepare bis(dicyclopentadienyl selenide)diiron via the reaction shown in eq 7 were not successful.

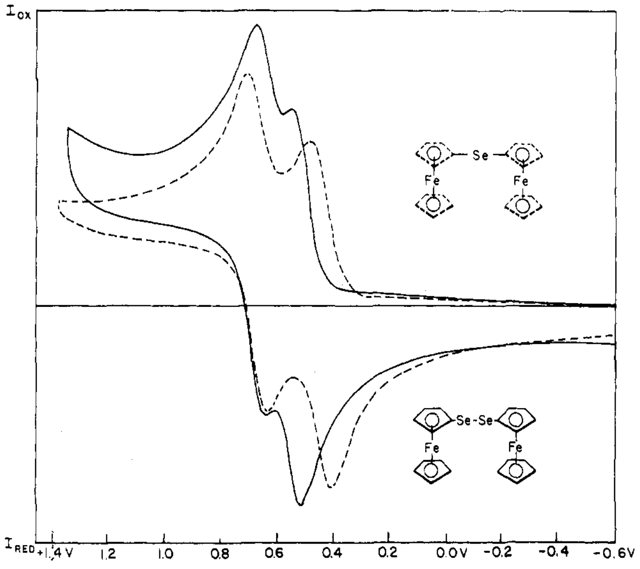


Figure 1.

Electrochemistry. The cyclovoltammograms of I and II are illustrated in Figure 1 and the results are summarized in Table I. As demonstrated by the cyclovoltammogram, both I and II undergo two reversible one-electron oxidations to their mono- and dications, respectively (eq 8).

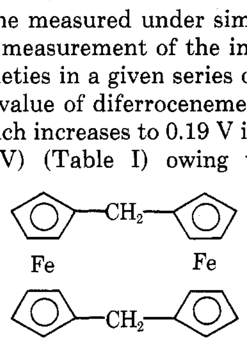
$$I \overset{-e}{\rightleftarrows} I^{+} \overset{-e}{\rightleftarrows} I^{2+}$$

$$II \overset{-e}{\rightleftarrows} II^{+} \overset{-e}{\rightleftarrows} II^{2+} \qquad (8)$$

Peak separations were found to be close to 60 mV at 25 °C and peak ratios were found to be unity.

Acetonitrile solutions of I^+ and II^+ were prepared by coulometric oxidation of I and II with 1.0 F/mol of current. The stability and identity of those monocations were confirmed by cyclic voltammetry and polarography. Exhaustive oxidation in acetonitrile of I and II leads to decomposition. The failure to obtain stable I^{2+} and II^{2+} in acetonitrile solutions is probably due to a trace of moisture which is difficult to remove. However, "stable" solutions of I^{2+} and II^{2+} could be obtained by oxidation of I and II with precisely 2 F/mol in CH_2Cl_2. Identity and stability of those dications were again demonstrated by cyclic voltammetry and polarography. The electrochemically generated solutions of the mono- and dications of I and II are stable enough to permit the recording of their absorption spectra under inert conditions.

It has been proposed by Watts et al.[6] that in bridged biferrocenes, their ΔE values (the differences between the first and second half wave potentials of biferrocenes) is an indication of the amount of electronic interaction between the two portions of the molecule. However, according to the recent report of Cowan and co-workers,[7] diferrocenylacetylene monocation has a near infrared transition even though it has a rather small ΔE value (0.13 V). However, the differences between two oxidation potentials of a bridged diferrocene measured under similar conditions do give a reasonable measurement of the interaction between two ferrocene moieties in a given series of compounds. For example, the ΔE value of diferrocenemethane (III) in 90% EtOH is 0.1 V which increases to 0.19 V in the case of [1.1]-ferrocenophane (V) (Table I) owing to the additional bridge. When the bridge in diferrocenemethane is lengthened by one more CH_2 group, the ΔE for diferrocenylethane is reduced to zero.



[1.1]ferrocenophane (V)

Diferrocenemethane (III) has a ΔE value of 0.17 V in acetonitrile which is less than that of diferrocenyl selenide (I) (ΔE = 0.22 V), suggesting less intramolecular interaction in III. This interaction is further reduced to zero in diferroceneethane (IV) while its selenium analogue still has a ΔE value of 0.14 V. This finding suggests that the $-CH_2-$ group is a more insulating group than is selenium. Two methylene groups can essentially isolate the two ferrocene units in IV, eliminating both through space and through ligand interactions. It is known that the C–Se bond and and Se–Se bond are much longer than the C–C bond. it is reasonable, therefore, to believe that through space interaction is relatively unimportant in diferrocenyl diselenide (II) and diferrocenyl selenide (I). Consequently, the increased interaction between the ferrocene moieties in diferrocenyl selenide and diferrocenyl diselenide vs. diferrocenemethane and diferroceneethane is most likely a through ligand inductive (σ bond) effect which the more polarizable selenium transmits more efficiently.

Electronic Spectroscopy. The visible and near infrared spectra were measured for the monocations of I and II. No near infrared band was observed in either species. However, the ferrocenium absorption[10] of $^2E_{2g} \rightarrow {}^2E_{2u}$ at ~617 nm was shifted to 860 (ϵ 1350) and 840 nm (ϵ 550) for the monocations of I and II, respectively, which is not inconsistent with the conclusion that the selenium moiety transmits the inductive effect more effectively than the $-CH_2-$ group. Such a shift was also observed in the case of the [1.1]ferrocenophane monocation (750 nm, ϵ 3350),[11] and a similar absorption was found in the monocation of *n*-butylferrocenyl selenide at 910 nm, ϵ 375. This is consistent with the proposed origin of the red shifted ligand-to-metal transitions. The assignment of this ferrocenium transition of $^2E_{2g} \rightarrow {}^2E_{2u}$ is further strengthened by the fact that in the dications of I and II, absorptions at 810 (ϵ 1000) and 780 nm (ϵ 1000), for I^{2+} and II^{2+}, respectively, were observed.

Conclusion

From the absence of an intervalence transfer transition (near infrared transition) for the monocations of diferrocenyl selenide (I) and diferrocenyl diselenide (II), we conclude that these two compounds are class I materials where the –Se– group, like the $-CH_2-$ group, does not act as an effective bridge for electron transfer ($\alpha \approx 0$). However, based on the electrochemistry, we conclude that the –Se– bridge does allow a larger inductive communication between the two ferrocene moieties than does the $-CH_2-$ bridge. This conclusion is consistent with the red shift for the ligand-to-metal transition of the ferrocenium portion of the monocations. The lack of near infrared absorption for I^+ and II^+ plus the fact that diferrocenylacetylene has a small ΔE value yet possesses a near infrared transition strongly suggest that there is no correlation between intervalence transition and ΔE values.

Experimental Section

General. Melting points were measured on a Thomas-Hoover Uni-Melt apparatus or a Mel-Temp apparatus and are uncorrected. Microanalyses were performed by the Galbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were recorded with a Perkin-Elmer 457 spectrometer. Ultraviolet, visible, and near infrared spectra were taken with a Cary 14 spectrophotometer. ^1H NMR spectra were recorded on a JEOL MH 100 spectrometer. Mass spectra were taken on a Hitachi Perkin-Elmer RMU-6 mass spectrometer.

Cyclic voltammograms were obtained with a PAR-175 universal programmer and a PAR-173 potentiostat using a standard three-electrode configuration. The working electrode, a platinum button (Beckman), and the reference, a saturated calomel electrode, were connected via a salt bridge containing Et_4NClO_4 in CH_3CN. All electrochemical measurements were performed under argon. The current function $[i_p/V^{1/2}C]$ was constant over a wide range of sweep rate (25–300 mV/s), and a 1:1 relationship for the anodic and cathodic peak currents was observed. These data indicate the electrochemical reversibility of the couples.

In preparative experiments, 0.05 mmol of the ferrocene compound was oxidized (0.1 M in electrolyte) using a platinum basket electrode in a cell holding 50–100 ml of solvent. The cations were generated by constant current oxidation.

Samples for absorption spectra were transferred under argon from the electrolysis cell through 2-mm Teflon tubing to a 1-cm quartz flow cell which has been previously rinsed with the electrolysis solution and then sealed.

Diferrocenyl Selenide (I). Method A. Ferrocenyl selenocyanate (29 mg, 0.1 mmol) and chloromercuriferrocene (43 mg, 0.1 mmol) were refluxed in 15 ml of acetonitrile for 2 h. The reaction mixture showed no trace of starting materials on a TLC sheet (alumina, 1:1 benzene–heptane). This mixture was first filtered through neutral alumina. Upon drying and removal of the solvent, a residue was obtained. Alumina dry column separation with 1:1 CH_2Cl_2–heptane developer yielded I (45 mg, 100%). Recrystallization from heptane yielded crystalline I with mp 161–162 °C.

Method B. Chloromercuriferrocene (1.05 g, 2.5 mmol) was refluxed with freshly prepared $Cu(SeCN)_2$ (0.62 mmol) in 50 ml of dry acetonitrile under Ar for 2 h. The reaction mixture was first filtered through neutral alumina. After drying over anhydrous $MgSO_4$ and removal of the solvent, a yellow residue was obtained. Separation with an alumina dry packed column developed with CH_2Cl_2–heptane (1:1) yielded traces of ferrocenyl selenocyanate and diferrocenyl diselenide (II) along with the desired diferrocenyl selenide (I, 500 mg, 45% yield): mass spectrum (70 eV) *m/e* (rel intensity) 452 (20), 451 (27), 450 (92) (M^+ for $C_{20}H_{18}{}^{56}Fe_2{}^{80}Se$), 449 (15), 448 (57), 447 (20), 446 (24), 320 (25), 307 (20), 306 (100), 305 (18), 305 (18), 304 (80), 302 (10), 249 (20), 225 (10) (M^{2+} for $C_{20}H_{18}{}^{56}Fe^{80}Se$), 192 (18), 186 (28), 129 (18), 128 (15), 121 (24), 71 (20), 57 (34), 56 (21); NMR ($CDCl_3$, Me_4Si) δ 4.05 (4 H, m), 4.1 (10 H, s), 4.22 (4 H, m); ir (KBr) 3100 w, 1413 w, 1390 w, 1150 m, 1108 m, 1000 m, 880 s, 820 s, 490 cm^{-1} s; uv (CH_3CN) 224 nm (ϵ 18 000), 227 (18 500), 262 (10 000), 440 (400).

Ferrocenyl Selenocyanate and Diferrocenyl Diselenide (II). This preparation was in part derived from the procedure of Nefedov[12] in his synthesis of ferrocenyl selenocyanate. Chloromercuriferrocene (7 g, 16 mmol) was heated to reflux temperature with freshly prepared $Cu(SeCN)_2$ (8 mmol) in 250 ml of dried acetonitrile for 2 h. The reaction mixture was first filtered through neutral alumina. A yellow residue was obtained after removal of the solvent. This residue was placed on an alumina dry column and developed with 1:1 CH_2Cl_2 and heptane. Two fractions were obtained: diferrocenyl diselenide (II, 1.61 g, 38% yield), mp 181–183 °C, and ferrocenyl selenocyanate (1.51 g, 54% yield) with a lower R_f value (II): NMR ($CDCl_3$) δ 4.2 (10 H, s), 4.28 (4 H, half of an A_2B_2 pattern, J = 1.8 Hz), 4.33 (4 H, another half of an A_2B_2 pattern, J = 1.8 Hz); ir (KBr) 3080 w, 1400 w, 1380 w, 1145 m, 1100 m, 1040 w, 1010 m, 995 m, 875 m, 815 s, 500 cm^{-1} vs; mass spectrum (70 eV) *m/e* (rel intensity) 530 (15) (M^+ of $C_{20}H_{18}{}^{56}Fe^{80}Se^{80}Se$), 528 (15), 450 (24), 385 (10), 320 (22), 318 (15), 306 (29), 304 (31), 267 (21), 266 (35), 265 (100), 264 (22), 263 (60), 262 (24), 186 (56), 128 (62), 127 (36), 121 (45), 56 (55).

Anal. Calcd for $C_{20}H_{18}Fe_2Se_2$: C, 45.45; H, 3.41. Found: C, 45.55; H, 3.39.

***n*-Butylferrocenyl Selenide (VI).** Ferrocenyl selenocyanate (291 mg, 1 mmol) stirred with 0.5 ml of *n*-butyllithium (2.2 M) in 10 ml of dried *n*-heptane at room temperature in a Schlenck reaction tube under argon for 4 h. A clear yellow solution was obtained. A drop of water was added to decompose unreacted *n*-butyllithium. This solution was then extracted with ether and washed with water. After drying over anhydrous $MgSO_4$ and removal of the solvent, an orange-yellow oil was obtained. After alumina dry column purification (developed with 1:1 CH_2Cl_2 and *n*-heptane), crude VI was obtained (280 mg, 87%). An analytical sample was obtained by further purification with high pressure liquid chromatography (porasil C_{18} column, 15:85 ethylene chloride in *n*-heptane): mass spectrum (70 eV) *m/e* (rel intensity) 324 (14), 323 (13), 322 (75), 321 (8), 320 (41), 319 (15), 318 (17), 267 (21), 266 (19), 265 (100), 264 (11), 263 (57), 262 (20), 261 (24), 186 (11), 129 (39), 128 (17), 121 (23), 56 (20); NMR ($CDCl_3$) δ 0.83 (3 H, t, J = 7 Hz), 1.4 (4 H, m), 2.5 (t, 2 H, J = 7 Hz), 4.1 (5 H, s), 4.1 (2 H, t, J = 2 Hz), 4.2 (2 H, t, J = 2 Hz); ir (CCl_4, 0.1 cm ir tran) 3185 m, 2950 s, 2920 s, 2860 m, 1760 vw, 1725 vw, 1590 vw, 1460 m, 1410 w, 1385 w, 1255 m, 1195 w, 1150 m, 1100 m, 1020 s, and 1000 cm^{-1} m.

Anal. Calcd for $C_{14}H_{17}FeSe$: C, 52.33; H, 5.61. Found: C, 52.28; H, 5.58.

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Registry No.—I, 58463-77-7; II, 58463-78-8; VI, 58463-79-9; ferrocenyl selenocyanate, 58463-80-2; chloromercuriferrocene, 1273-75-2.

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Uvaretin, a New Antitumor Agent from *Uvaria acuminata* (Annonaceae)

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The chloroform extract of *Uvaria acuminata* Oliv. has shown inhibitory activity against the P-388 lymphocytic leukemia test system of the National Cancer Institute. The major constituent of this extract was identified as the new 3′-benzyldihydrochalcone uvaretin, 1-[2,4-dihydroxy-3-(2-hydroxybenzyl)-6-methoxyphenyl]-3-phenyl-1-propanone ($C_{23}H_{22}O_5$). The structure was proven by x-ray crystallography and other methods.

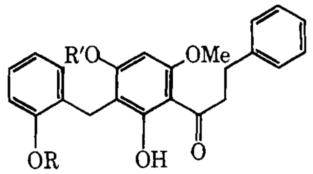
As a result of the continuing search for plants having tumor-inhibiting constituents, the chloroform extract of the roots of *Uvaria acuminata* Oliv. (Annonaceae)[17] was found to have inhibitory activity toward the P-388 (3PS) lymphocytic leukemia test system.

Discussion

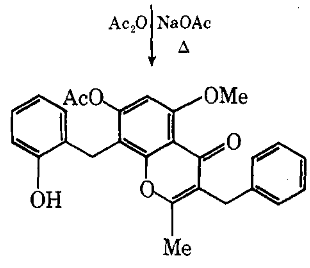
The major constituent of the chloroform extract of *Uvaria acuminata* Oliv. was found to be uvaretin, $C_{23}H_{22}O_5$. Uvaretin, subsequently shown to be I, was found to undergo the Kostanecki reaction[1] to give a 3-benzyl-2-methylchromone (II) characteristic of 2′-hydroxydihydrochalcones (e.g., phloretin).[2] In addition, the ^{1}H NMR spectrum of uvaretin shows the two 2-proton signals of an A_2B_2 pattern, centered at 2.90 and 3.33 ppm, expected for a β-propiophenone moiety. This ^{1}H NMR spectrum also contains a signal (13.9 ppm) for an intramolecularly hydrogen-bonded phenolic hydroxyl group.

Uvaretin (I) forms a monomethyl ether (III) with diazomethane and a dimethyl ether (IV) with dimethyl sulfate, both of which still contain the internally bonded phenolic hydroxyl group.

Uvaretin (I) demonstrated an activity of 133% test/control (T/C) at 10 mg/kg in the 3PS system. The monomethyl ether (III) of uvaretin showed an activity of 132% T/C at 1 mg/kg and the dimethyl ether (IV) demonstrated 144 and 141% T/C at 4 and 2 mg/kg, respectively. Activity in the 3PS system is defined as an increase in the survival of treated animals over that of controls resulting in a T/C ⩾ 125%.[3]



I, R = R′ = H
III, R = H; R′ = Me
IV, R = R′ = Me



II