Synthesis of Metal Furoylacetonates and Their SE Reactions. I. Studies on Heteroaromaticity. X[1]

TADASHI SASAKI, KEN KANEMATSU, AND GORO KINOSHITA

Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya, Japan

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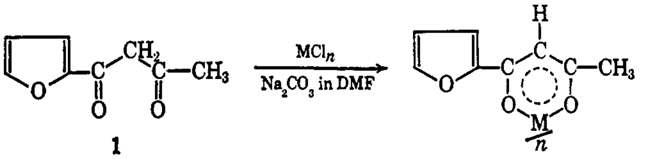
Nitration and bromination were carried out on the trisfuroylacetonates of chromium(III) and cobalt(III) for the purpose of comparing the aromatic character of the furan ring with that of the chelate ring from the standpoint of their SE reactions. The products were the trinitro and tribromo derivatives substituted at the central carbon of the chelate rings, not at the furan rings. The structures of these products were elucidated by their infrared, ultraviolet, nuclear magnetic resonance, and mass spectra. Furthermore, preparation of the bisfuroylacetonates of cobalt(II), nickel(II), and copper(II) and of the trisfuroylacetonates of iron(III) were described.

Many studies on the aromatic character of metal acetylacetonate complexes have been published by using X-ray diffraction,[2] infrared spectra,[3-5] ultraviolet spectra,[6] nmr spectra,[6] and electrophilic substitution reactions.[7-14]

However, no reports have been recorded on the comparison of the aromatic character of a chelate ring with that of an aromatic ring. This paper will describe the results of nitration and bromination on some metal furoylacetonates in order to determine whether the furan or the chelate ring is exclusively substituted by these electrophilic reagents.

Following Collman's procedure,[8] furoylacetone[15] (**1**) was treated with cobalt, chromium, and ferric chloride to give the corresponding bisfuroylacetonate of cobalt(II) (**2b**) and trisfuroylacetonates of chromium(III) (**2d**) and of iron(III) (**2e**), respectively. The expected bisfuroylacetonates of copper(II) (**2a**) and nickel(II) (**2c**) were not obtained; β-ketoamino-type chelates were produced instead, presumably because in these reactions the ammonia which was evolved from urea reacted with furoylacetone to form β-ketoamine. This anomalous reaction, however, was avoidable by using sodium carbonate instead of urea (Chart I).

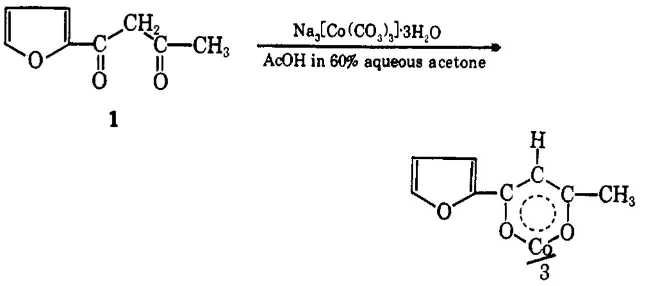
CHART I



2a, M = Cu(II)
b, M = Co(II)
c, M = Ni(II)
d, M = Cr(III)
e, M = Fe(III)

Our initial attempt to obtain the trisfuroylacetonate of cobalt(III) (**2f**) by the known method of Bauer and Drinkard[16] failed, resulting only in the formation of an intractable oily mixture possibly due to degradation of the acid-sensitive furoylacetone. When acetic acid was used instead of nitric acid in this reaction, the desired trisfuroylacetonates could be obtained in good yields after purification on a silica gel column (Chart II).

CHART II



2f

The infrared spectrum of **1** shows a sharp absorption at 1720 cm^{-1} caused by a free carbonyl of the keto form of the 1,3-diketone and does not manifest any intense band near 1500 cm^{-1}. In contrast, **2** shows no absorption near 1700 cm^{-1}, but has a strong absorption at 1520 cm^{-1} due to a chelated carbonyl group.[3-5] The infrared spectrum of **2c** resembles that of the corresponding **2b**; the spectra of **2d**, **2e**, and **2f** resemble each other. This similarity indicates that **2c** and **2b** have the same type of structure as do the other three chelates.

The ultraviolet spectra of the above-mentioned chelates are summarized in Table I along with those of the corresponding metal acetylacetonates.

Comparison of the spectrum of each metal furoylacetonate with that of the corresponding metal acetylacetonate affords good evidence of the existence of an extended conjugation in **2a–f** and of coplanarity of the furan ring with the chelate ring.

The chromium(III) chelate of benzoylacetone and dibenzoylmethane have been reported to decompose in the presence of copper nitrate–acetic anhydride

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[9] J. P. Collman and E. T. Kittleman, *ibid.*, **83**, 3529 (1961).

[10] J. P. Collman, R. L. Marshall, W. L. Young, and S. D. Goldby, *Inorg. Chem.*, **1**, 704 (1962).

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[14] R. H. Barker, J. P. Collman, and R. L. Marshall, *ibid.*, **29**, 3216 (1964).

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[16] H. F. Bauer and W. C. Drinkard, *ibid.*, **82**, 5031 (1960).

TABLE I

ULTRAVIOLET DATA FOR CHELATES IN TETRAHYDROFURAN

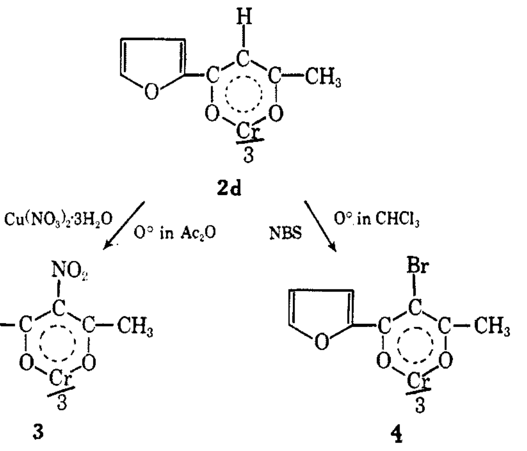
Chelate	λ_{max}, mμ	ϵ_{max}	λ_{max}, mμ	ϵ_{max}
$(Acac)_2Cu^a$	239	11,000	292	21,600
$(Acac)_2Co$	231	7,700	272	16,100
$(Acac)_2Ni$			291	22,400
$(Acac)_3Fe$	269	26,600	352	2,500
$(Acac)_3Co$	255	37,400	330	8,300
$(Acac)_3Cr$	270	10,000	332	15,600
$(Frac)_2Cu^b$	282	23,600	330	37,100
$(Frac)_2Co$	265	16,000	318	29,000
$(Frac)_2Ni$	266	16,900	332	28,200
$(Frac)_3Fe$	305	59,500	368	13,900
$(Frac)_3Co$	294	52,200	361	20,400
$(Frac)_3Cr$	306	36,000	367	39,900

[a] (Acac) represents acetylacetone. [b] (Frac) represents furoylacetone.

mixture.[10] Treatment of **2d** with the same mixed reagent afforded a mixture of two products as revealed by thin layer chromatography. The brown crude mixture was purified by silica gel column chromatography, which afford a trinitrofuroylacetonate of chromium(III) (**3**) of green crystals as the main product and a small amount of the dinitrofuroylacetonate of chromium(III).

2d was easily brominated with N-bromosuccinimide at 0° to give a tribromo derivative (**4**) accompanied by a small amount of monobromo derivative as shown in Chart III. The ultraviolet spectra of chromium(III) chelates, **2d**, **3**, and **4**, are shown in Figure 1.

CHART III



The spectral patterns of these compounds are grossly similar, each having two absorption peaks. The two peaks of tribromo chelate **4** exhibit some bathochromic and hypochromic shifts as compared with those of the parent chelate **2d**. In the spectrum of trinitro chelate **3**, both peaks exhibit some hyperchromic shifts and, furthermore, only the lower wavelength absorption shows bathochromic shift.

Because of the paramagnetic character of chromium(III), it is impossible to determine the position of a nitro or bromo group by using nmr spectroscopy in **3** and **4**. For the purpose of nmr investigation, a trinitro (**5**) and a tribromo derivative (**6**) of the diamagnetic cobalt(III) were synthesized in a similar manner (Chart IV).

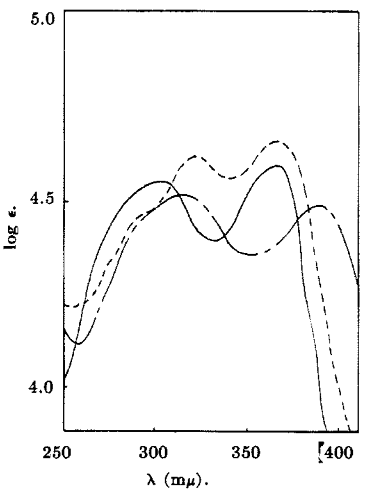


Figure 1.—Ultraviolet spectra of chromium(III) chelates in tetrahydrofuran: ———, **2d**; – – – –, **3**; — — —, **4**.

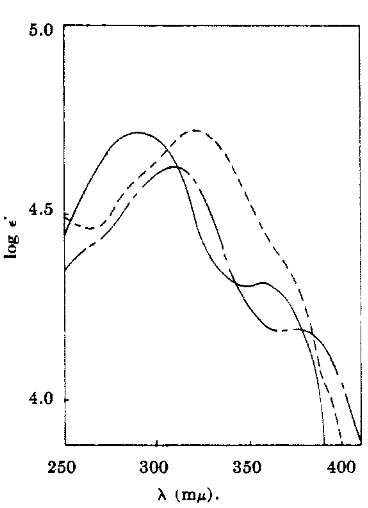
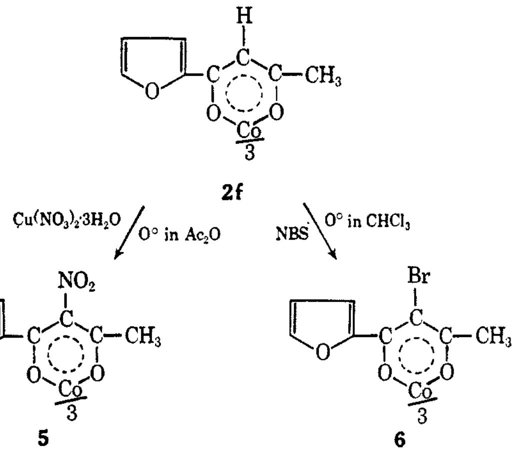


Figure 2.—Ultraviolet spectra of cobalt(III) chelates in tetrahydrofuran: ———, **2f**; – – – –, **5**; — — —, **6**.

CHART IV



The infrared spectra of cobalt(III) chelates **2f**, **5**, and **6** are quite similar to those of the corresponding chromium(III) chelates **2d**, **3**, and **4**. This infrared spectroscopic consistency gives evidence for the skeletal and positional identity of these derivatives. The ultraviolet spectra of these cobalt(III) chelates, **2f**, **5**, and **6**, as shown in Figure 2 also confirm this assignment.

By comparison of Figures 1 and 2, it is found that the three spectra of cobalt(III) chelates **2f**, **5**, and **6** show similar behavior with those of the chromium(III) chelates **2d**, **3**, and **4**.

TABLE II

MASS FRAGMENTATIONS OF CHROMIUM(III) CHELATES

$Cr(Frac)_3$[a] 2d		$Cr(Frac\text{-}NO_2)_3$ 3		$Cr(Frac\text{-}Br)_3$ 4	
Cation	m/e (rel intensity)	Cation	m/e (rel intensity)	Cation	m/e (rel intensity)
Cr^+ (Frac)	203 (11)			Cr^+ (Frac-Br)	283 (3)
					281
$Frac^+$	151 (2)			$Frac^+$-Br	231 (5)
					229
$C_4H_3OCr^+$	119 (19)			$C_4H_3OCr^+$	119 (8)
$C_4H_3OC{\equiv}O^+$	95 (53)	$C_4H_3OC{\equiv}O^+$	95 (100)	$C_4H_3OC{\equiv}O^+$	95 (72)
$CH_3COCHC{\equiv}O^+$	83 (5)				
Cr^+-CH_3	67 (12)			Cr^+-CH_3	67 (15)
Cr^+	52 (50)			Cr^+	52 (10)
$CH_3C{\equiv}O^+$	43 (100)	$CH_3C{\equiv}O^+$	43 (82)	$CH_3C{\equiv}O^+$	43 (100)
$C_3H_3^+$	39 (22)	$C_3H_3^+$	39 (30)	$C_3H_3^+$	39 (10)

[a] (Frac) represents furoylacetone.

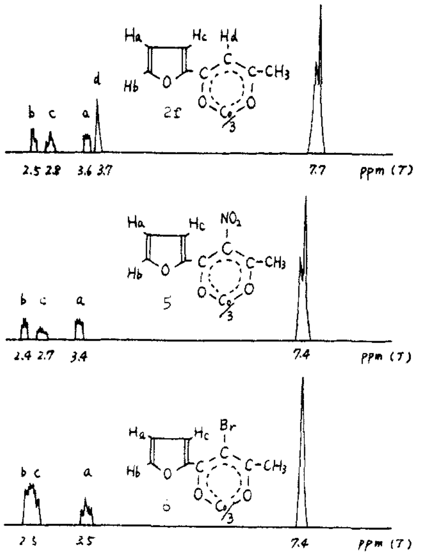


Figure 3.—Nmr spectra of cobalt(III) chelates in $CDCl_3$.

The nmr spectra of these three cobalt(III) chelates, **2f**, **5**, and **6**, are shown in Figure 3.

A deuteriochloroform solution of **2f** exhibits signals at τ 2.5, 2.8, 3.6, 3.7, and 7.7 with the relative intensities of 1:1:1:1:3. Comparison with the spectrum of the parent compound **1** confirms that the τ 2.5, 2.8, and 3.6 peaks are attributable to H_b, H_c, and H_a protons of the furan ring, respectively, and a sharp singlet at 3.72 is due to an H_d proton of the chelate ring. A doublet at τ 7.7 is attributable to methyl protons.

The spectrum of **5** in $CDCl_3$ exhibited peaks at τ 2.4, 2.7, 3.4, and 7.4 with the relative intensities of 1:1:1:3. This comparison with **2f** showed that peaks at τ 2.4, 2.7, and 3.4 are caused by the H_b, H_c, and H_a protons of the furan ring, respectively, and a doublet at 7.4 is due to methyl protons. The *cis* isomer of a metal benzoylacetonate is known to show a single methyl resonance in the nmr spectrum, though the *trans* isomer exhibits a doublet or triplet methyl signal.[17] By tlc **2f**, **5**, and **6** each showed one spot and it could thus be concluded that the doublets in **2f** and **5** are due to methyl protons of the *trans* isomer and the singlet in **6** to those of the *cis* isomer.

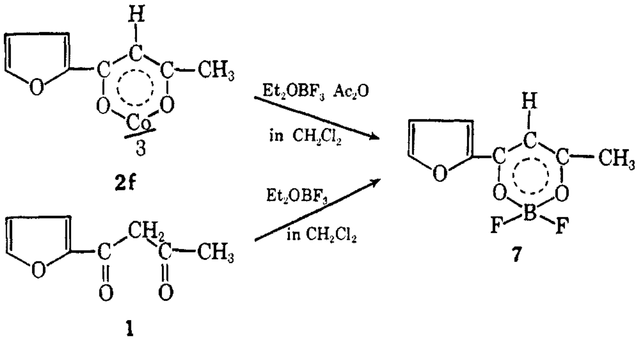
The disappearance of the chelate ring proton signal after nitration provided conclusive proof that nitration had occurred on the chelate ring and, analogously, bromination was also on the chelate ring.

From the infrared and ultraviolet similarity of the substituted cobalt(III) chelates with the corresponding chromium(III) chelates, it may be concluded that nitration and bromination of the chromium(III) chelates have also occurred on the chelate ring.

The mass fragmentations of chromium(III) chelates in the low mass region are listed in Table II.[18] In this table, the masses due to furyl cations are clearly observed but those due to the nitrofuryl or bromofuryl cation are not. The absence of such a nitrofuryl or bromofuryl cation confirms the conclusion that the chelate ring was substituted even in the case of the chromium(III) chelate.

An attempt to acetylate **2f** with a mixture of acetic anhydride and boron trifluoride etherate failed and unexpectedly afforded the difluoroborane complex **7**, which was prepared directly from furoylacetone and boron trifluoride (Chart V).[19]

CHART V



When a catalytic amount of boron trifluoride etherate was used in the above reaction, the parent chelate (**2f**) was perfectly recovered. This exchange reaction between chelated metal and difluoroborane seems to afford new application in chelate chemistry; for example, the nmr investigation of paramagnetic chelates might become possible by using this exchange reaction.

Nitration and bromination of **7** with a copper nitrate–acetic anhydride mixture and with N-bromosuccinimide, respectively, only resulted in recovery of the starting material. Presumably, the decrease of the elec-

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[17] R. C. Fay and T. S. Piper, *J. Am. Chem. Soc.*, **84**, 2303 (1962).

[18] A full paper concerning the mass spectra of these compounds will be published elsewhere.

[19] Other attempts to acetylate **2f** under various conditions are in progress.

tron density over the chelate ring by the electron-attractive effect of a fluorine atom might prevent such substitution reactions.

Experimental Section[20]

Tris[1-(2-furyl)-1,3-butanediono]chromium(III) (2d).—Chromium(III) chloride hexahydrate (0.7 g, 0.0027 mole), (furoylacetone[15]) (1.2 g, 0.008 mole), and sodium carbonate (1.2 g, 0.004 mole) were dissolved in 26 ml of aqueous 96% dimethylformamide. The solution was maintained at 110–120° for 15 hr and after cooling it was poured onto an equal volume of ice water. The brown precipitates were collected, washed several times with water, and then dried to afford 1.3 g (quantitative yield) of a crude product. An analytical sample was obtained by three recrystallizations from tetrahydrofuran as brown crystals, mp 287–288°; infrared (KBr) bands were at 1600, 1550, 1520, 1470, 1400, and 1370 cm^{-1}.

Anal. Calcd for $C_{24}H_{21}O_9Cr$: C, 57.02; H, 4.20. Found: C, 56.89; H, 4.19.

Bis[1-(2-furyl)-1,3-butanediono]copper(II) (2a).—Cuprous chloride, furoylacetone, and sodium carbonate in aqueous 96% dimethylformamide were maintained at 110–120° for 15 hr and worked up as above to afford a crude product in 80% yield. An analytical sample was obtained by recrystallization from ethanol as dark green crystals, mp 231–232°; infrared (KBr) bands were at 1600, 1550, 1520, 1470, 1450, and 1420 cm^{-1}.

Anal. Calcd for $C_{16}H_{14}O_6Cu$: C, 52.53; H, 3.86. Found: C, 53.09; H, 4.06.

Bis[1-(2-furyl)-1,3-butanediono]nickel(II) (2c).—Nickel chloride, furoylacetone, and sodium carbonate in aqueous 96% dimethylformamide were maintained at 110–120° for 15 hr and worked up as above to afford a crude product in 94% yield. An analytical sample was obtained by recrystallization from ethanol as green crystals, mp 177–178°; infrared (KBr) bands were at 1590, 1560, 1520, 1480, and 1410 cm^{-1}.

Anal. Calcd for $C_{16}H_{14}O_6Ni \cdot 2H_2O$: C, 48.40; H, 4.57. Found: C, 48.23; H, 4.56.

Tris[1-(2-furyl)-1,3-butanediono]iron(III) (2e).—Ferric chloride, furoylacetone, and sodium carbonate in aqueous 96% dimethylformamide were treated as above to afford a crude product in 28% yield. An analytical sample was obtained by recrystallization from tetrahydrofuran as brown-red crystals, mp >300°; infrared (KBr) bands were at 1600, 1550, 1520, 1470, 1400, and 1370 cm^{-1}.

Anal. Calcd for $C_{24}H_{21}O_9Fe$: C, 56.59; H, 4.16. Found: C, 56.44; H, 3.99.

Bis[1-(2-furyl)-1,3-butanediono]cobalt(II) (2b).—Cobalt chloride, furoylacetone, and sodium carbonate in aqueous 96% dimethylformamide were treated as above to afford a crude product in 93% yield. An analytical sample was obtained by recrystallization from ethanol as orange crystals, mp 130–131°; infrared (KBr) bands were at 1580, 1560, 1520, 1470, and 1410 cm^{-1}.

Anal. Calcd for $C_{16}H_{14}O_6Co \cdot 2H_2O$: C, 48.38; H, 4.57. Found: C, 48.06; H, 4.60.

Tris[1-(2-furyl)-1,3-butanediono]cobalt(III) (2f).—To a mixture of furoylacetone (2.3 g, 0.015 mole) and sodium triscarbonatocobaltate(III) trihydrate (1.8 g, 0.005 mole) in a 60% acetone–water mixture was added 1 ml of acetic acid. The reaction mixture was refluxed for 15 min; then the cold reaction mixture was extracted with chloroform. The chloroform extracts were washed with saturated aqueous sodium bicarbonate and then with water. After the organic layer was dried over sodium sulfate, the solvent was removed under vacuum. The residue was purified by silica gel column chromatography and afforded 1.0 g (39%) of green powder. An analytical sample was obtained by recrystallization from ether, mp 204–205°; infrared (KBr) bands were at 1600, 1550, 1520, 1470, and 1400 cm^{-1}.

Anal. Calcd for $C_{24}H_{21}O_9Co$: C, 56.26; H, 4.14. Found: C, 55.89; H, 4.18.

Tris[2-nitro-1-(2-furyl)-1,3-butanediono]chromium(III) (3).—A slurry of copper(II) nitrate trihydrate (1.45 g, 0.006 mole) in 30 ml of acetic anhydride was stirred for 45 min at 0°. To this slurry was added **2d** (0.84 g, 0.0017 mole) at 0° and stirring was continued at the same temperature for 2 hr; then a spot of **2d** disappeared and instead two new green spots were observed by thin layer chromatography. The slurry was decomposed by stirring for 1 hr with a mixture of 150 ml of water, 250 g of ice, and 20 g of sodium acetate. The resulting deep green precipitates were collected and washed with water. Chromatography on a silica gel column with benzene as an eluent afforded two products; the main product was obtained as green crystals from the first fraction, mp 164–166°, and the yield was 0.71 g (66%); infrared (KBr) bands were at 1540, 1470, 1360, and 1010 cm^{-1}.

Anal. Calcd for $C_{24}H_{18}N_3O_{15}Cr$: C, 45.01; H, 2.84; N, 6.56. Found: C, 44.77; H, 2.86; N, 6.27.

From the second fraction, there was obtained 0.33 g of green crystals, mp 111–115°, which showed a very similar spectral pattern with **3**; considering its elemental analysis and that it afforded one spot by thin layer chromatography, this compound is concluded to be the corresponding dinitro complex; infrared (KBr) bands were at 1540, 1470, 1360, and 1010 cm^{-1}.

Anal. Calcd for $C_{24}H_{19}N_2O_{13}Cr$: N, 4.68. Found: N, 4.18.

Tris[2-nitro-1-(2-furyl)-1,3-butanediono]cobalt(III) (5).—Compound **2f** was nitrated with a copper(II) nitrate–acetic anhydride mixture as above and afforded green crystals in 55.1% yield after purification by silica gel column chromatography. An analytical sample was obtained by recrystallization from ether, mp 160–161°; infrared (KBr) bands were at 1540, 1470, 1360, and 1010 cm^{-1}.

Anal. Calcd for $C_{24}H_{18}N_3O_{15}Co$: C, 44.53; H, 2.80; N, 6.49. Found: C, 44.70; H, 2.94; N, 6.41.

Tris[2-bromo-1-(2-furyl)-1,3-butanediono]chromium(III) (4).—A mixture of N-bromosuccinimide (1.3 g, 0.007 mole) and **2d** (1 g, 0.002 mole) in 100 ml of chloroform was stirred at 0° for 15 min until a spot of **2d** disappeared completely and new two spots were observed by thin layer chromatography. The chloroform solution was thoroughly washed with water and dried over sodium sulfate. After the solvent was removed under vacuum, the residue was purified by silica gel column chromatography with benzene as an eluent, to give two products. From the first fraction, 0.6 g of **4** was obtained as green crystals, mp 224–225°. The yield was 41%; infrared (KBr) bands were at 1530, 1470, 1420, 1330, and 1010 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}O_9Br_3Cr$: C, 38.84; H, 2.45. Found: C, 39.27; H, 2.44.

From the second fraction, there was obtained 0.203 g of green crystals, mp 155–159°, which showed a very similar spectral pattern with **4** and from its elemental analysis was found to be the corresponding monobromo complex; infrared (KBr) bands were at 1530, 1470, 1420, 1330, and 1010 cm^{-1}.

Anal. Calcd for $C_{24}H_{20}O_9BrCr$: C, 49.33; H, 3.45. Found: C, 49.97; H, 4.01.

Tris[2-bromo-1-(2-furyl)-1,3-butanediono]cobalt(III) (6).—A chloroform solution of N-bromosuccinimide and **2f** were stirred for 10 min at 0° and worked up as above to afford dark green crystals in 60% yield. An analytical sample was obtained by recrystallization from ether as green crystals, mp 140–141°; infrared (KBr) bands were at 1530, 1470, 1420, 1330, and 1010 cm^{-1}.

Anal. Calcd for $C_{24}H_{18}O_9Br_3Co$: C, 38.48; H, 2.42. Found: C, 38.74; H, 2.43.

Difluoro[1-(2-furyl)-1,3-butanediono]borane (7).—To a solution of furoylacetone (1.52 g, 0.01 mole) in 50 ml of methylene chloride was added boron trifluoride etherate (1.3 ml, 0.01 mole with stirring at room temperature. This solution was stirred overnight at this temperature and washed with 2% aqueous potassium acetate and then with water. After this solution was dried over sodium sulfate, the solvent was removed under vacuum to give 1.5 g (75%) of white powder. An analytical sample was obtained by three recrystallizations from ethanol, mp 120°; infrared (KBr) bands were at 1610, 1550, 1470, 1400, and 1370 cm^{-1}.

Anal. Calcd for $C_8H_7O_3BF_2$: C, 48.06; H, 3.53. Found: C, 47.92; H, 3.43.

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(20) Microanalyses were performed on a Yanagimoto C.H.N. Corder, Model MT-1. The melting points were measured with a Yanagimoto micromelting point apparatus and are not corrected. The infrared absorption spectra were taken with a JASCO Model IR-S infrared spectrophotometer. The ultraviolet absorption spectra were determined with a JASCO Model ORD/UV-5 optical rotatory dispersion recorder. The nmr spectra were taken with a Hitachi Model H-6013 nmr spectrometer and with a Varian Model A-60 nmr spectrometer with tetramethylsilane as an internal standard, and the chemical shift values are expressed in τ values. The mass spectra were obtained on a Hitachi RMU-D double-focusing mass spectrometer operating at ionization potential of 70 eV. The solid samples were ionized by electron bombardment after sublimation directly into the electron beam at 200°.

The same substance was also obtained from acetylation of **2f** with a mixture of acetic anhydride and boron trifluoride in methylene chloride at room temperature in 67% yield and by treatment of **2f** with boron trifluoride in quantitative yield (Chart V).

Registry No.—**2a**, 15273-07-1; **2b**, 15273-22-0; **2c**, 15273-08-2; **2d**, 15273-09-3; **2e**, 15273-10-6; **2f**, 15273-11-7; **3**, 15233-12-8; **4**, 15350-49-9; **5**, 15273-14-0; **6**, 15273-13-9; **7**, 15273-15-1; $(Acac)_2Cu$, 13395-16-9; $(Acac)_2Co$, 14024-48-7; $(Acac)_2Ni$, 14024-60-3; $(Acac)_3Fe$, 14024-18-1; $(Acac)_3Co$, 13681-88-4; $(Acac)_3Cr$, 13681-82-8.

Acknowledgments.—The authors wish to express their gratitude to the Chemical Research Laboratories, The Takeda Pharmaceutical Co., Ltd., for measuring the mass spectra.

Synthesis of the Eight Stereoisomers of a Tetrahydrocannabinol Congener

HERBERT S. AARON AND C. PARKER FERGUSON

Organic Chemistry Department, Chemical Research Laboratory, Research Laboratories, Edgewood Arsenal, Maryland 21010

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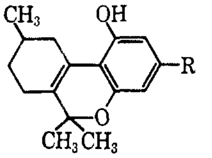
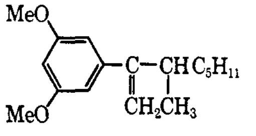
The eight stereoisomers of a tetrahydrocannabinol congener (**2**) have been synthesized from the eight pyrones (**9**) obtained by the condensation of (+)- and of (−)-2-carbethoxy-5-methylcyclohexanone (**8**) with each of the four optical stereoisomers of (demethylated) 2-(3,5-dimethoxyphenyl)-3-methyloctane (**6**). The four *threo* isomers of **6** were obtained optically pure; the four *erythro* isomers of **6** were obtained only as partially resolved materials. The relative configurations of the *erythro* and *threo* isomers of **6** have been assigned by two independent methods. The final products (**2**) were isolated as their acetate esters. Glpc analysis of the latter revealed the presence of two minor unidentified impurities.

The structures and stereochemistry of the physiologically active tetrahydrocannabinol principles of marijuana (hashish) have been recently elucidated.[1] Earlier, in an extensive series of investigations, Adams,[2] Todd,[3] and co-workers independently synthesized a material (**1**) that differed from the natural products by the position of the alicyclic double bond. A series of homologous congeners also were prepared, and structure–activity studies revealed the most active compound to be the 1,2-dimethylheptyl analog (**2**).[4a]



1, R = C_5H_{11}
2, R = $CH(CH_3)CH(CH_3)C_5H_{11}$

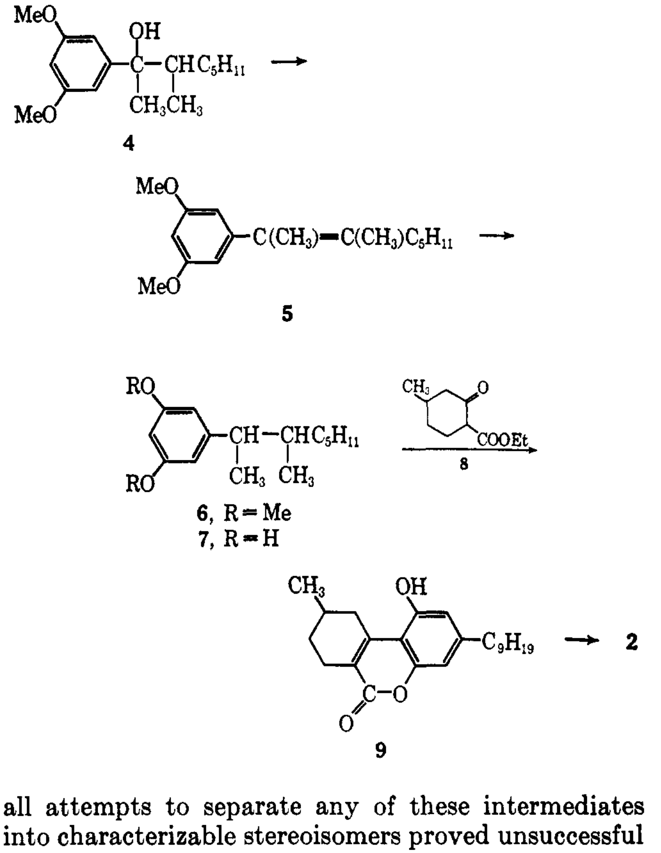


3

Because it possesses three asymmetric carbon atoms, **2** can exist as four diastereoisomeric racemates, each consisting, in turn, of a (+) and (−) enantiomorph. Since the stereochemical composition of the Adams product (**2**) was not known, we decided to synthesize the isomers of this interesting material.

The synthesis of **2** by the Adams procedure[4] is summarized, in part, in Scheme I. By this route, the carbinol **4**, obtained in two steps from 3,5-dimethoxybenzamide, was dehydrated to the olefin **5**, and then reduced to the alkane **6**. Reinvestigation of this reaction sequence revealed that the dehydration tends to give, initially, the vinyl olefin **3** ($\nu_{H_2C=}^{neat}$ 3080; $\delta_{H_2C=}$ 898 cm^{-1}) which then rearranges into a *cis–trans* mixture of **5** under the acidic conditions. However, all attempts to separate any of these intermediates into characterizable stereoisomers proved unsuccessful in our hands.[5] A new synthetic procedure had to be devised, therefore, which would give, unambiguously, the stereoisomers of the final product. Since **6** represents the key intermediate in the process, its synthesis was investigated from this point of view. Eventually, two independent routes were achieved.

SCHEME I



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(1) Y. Gaoni and R. Mechoulam, *J. Am. Chem. Soc.*, **86**, 1646 (1964); E. C. Taylor, K. Lenard, and Y. Shvo, *ibid.*, **88**, 367 (1966); R. L. Hively, W. A. Mosher, and F. W. Hoffmann, *ibid.*, **88**, 1832 (1966).

(2) R. Adams and B. R. Baker, *ibid.*, **62**, 2405 (1940).

(3) R. Ghosh, A. R. Todd, and S. Wilkinson, *J. Chem. Soc.*, 1121 (1940).

(4) (a) R. Adams, S. MacKenzie, and S. Loewe, *J. Am. Chem. Soc.*, **70**, 664 (1948); (b) R. Adams, K. H. Chen, and S. Loewe, *ibid.*, **67**, 1534 (1945).

(5) It was subsequently found, after this approach had been abandoned, that the isomers of **5** and **6** (and to some extent, **4**) could be separated by gas–liquid partition chromatography, a technique not available to us at that time.