147. Synthesis of Optically Pure Tricarbonyliron Complexes of 5,6-Dimethylidenebicyclo[2.2.2]oct-2-yl Derivatives

Crystal Structure and Absolute Configuration of (+)-Tricarbonyl[(1*S*,2*S*,4*R*,5*R*,6*S*)-*C*,5,6,*C*-η-(5,6-dimethylidenebicyclo[2.2.2]oct-2-yl *p*-Bromobenzoate)]iron

by **Pierre-Alain Carrupt, Fabienne Berchier,** and **Pierre Vogel***
Institut de Chimie Organique de l'Université, 2, rue de la Barre, CH–1005 Lausanne

and **Alan A. Pinkerton** and **Dieter Schwarzenbach**
Institut de Cristallographie, Bâtiment des Sciences Physiques, CH–1015 Lausanne-Dorigny

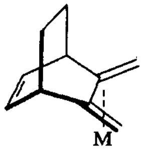
(21.IV.88)

The title complexes have been derived from tricarbonyl[(1*R*,4*S*,5*S*,6*R*)-*C*,5,6,*C*-η-(5,6-dimethylidenebicyclo-[2.2.2]oct-2-ene)]iron (**1**). The crystal structure and absolute configuration of (+)-tricarbonyl[(1*S*,2*S*,4*R*,5*R*,6*S*)-*C*,5,6,*C*-η-(5,6-dimethylidenebicyclo[2.2.2]oct-2-yl *p*-bromobenzoate)]iron ((+)-**6**) determined by X-ray diffraction studies proved earlier attribution of the relative configuration (*endo vs. exo*) of the tricarbonyliron moieties in complexes **1** and **2** of 5,6-dimethylidenebicyclo[2.2.2]oct-2-ene. The structure of (+)-**6** confirms the absolute configuration derived earlier from circular-dichroism spectra of 5,6-dimethylidenebicyclo[2.2.2]oct-2-yl esters and 5,6-dimethylidenebicyclo[2.2.2]octan-2-one.

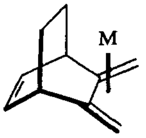
Tricarbonyliron complexes of optically pure 5,6-dimethylidenebicyclo[2.2.1]hept-2-yl derivatives have been shown to be interesting systems for a detailed analysis of the conformation of tricarbonyldieneiron moieties in solution. Their circular dichroism (CD) spectra were solvent- and concentration-independent, but temperature-dependent in accord with the existence of equilibria between rapidly interconverting diastereoisomeric species [1]. Similar properties were also found in the case of *trans*-μ-(2,3,5,6-tetramethylidenebicyclo[2.2.2]octane)bis(tricarbonyliron) complexes [2]. We report here on the synthesis of optically active tricarbonyliron complexes of 5,6-dimethylidenebicyclo-[2.2.2]oct-2-yl derivatives. Their absolute configuration has been established unambiguously by X-ray crystallography of (+)-tricarbonyl[(1*S*,2*S*,4*R*,5*R*,6*S*)-*C*,5,6,*C*-η-(5,6-dimethylidenebicyclo[2.2.2]oct-2-yl *p*-bromobenzoate)]iron.

The treatment of 5,6-dimethylidenebicyclo[2.2.2]oct-2-ene with $Fe_2(CO)_9$ in hexane gave a 4:1 mixture of complexes **1** and **2** in 61% yield [3]. Hydroboration (BF_3/$NaBH_4$/THF) of this mixture followed by oxidative workup (H_2O_2/KOH) yielded a mixture of alcohols **3** and **4** in 57 and 13% isolated yield, respectively. When the oxidative hydroboration was repeated with a pure sample of complex **1**, only alcohol (±)-**3** was obtained [3]. Attempts to carry out an optical resolution of (±)-**3** with *Gerlach*'s technique (fractional crystallization of the corresponding camphanates [4]) all failed.

Asymmetric hydroboration of **1**/**2** with monoisopinocamphenylborane ($IpcBH_2$) [5], followed by oxidative workup, led to (+)-**3** in 62% yield and 16% enantiomeric excess

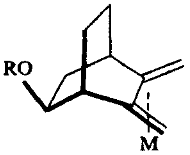


1

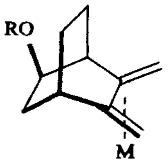


2

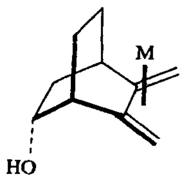
M = Fe(CO)$_3$



(+)-**3** R = H
(+)-**5** R = (1*S*)-camphanoyl
(+)-**6** R = 4-BrC$_6$H$_4$CO

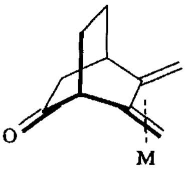


(−)-**3** R = H
(−)-**5** R = (1*S*)-camphanoyl

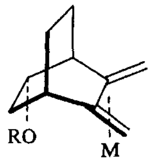


4

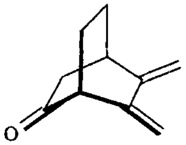
(e.e.). The camphanates derived from that alcohol and (−)-(1*S*)-camphanoyl chloride could be separated by fractional crystallization giving esters (+)-**5** and (−)-**5** in 15 and 14% yield, respectively. Saponification of (+)-**5** and (−)-**5** gave (+)-**3** with 99% e.e. and (−)-**3** with 95% e.e. (by 360-MHz ^{1}H-NMR of the corresponding *Mosher* esters [6]), respectively. Esterification of (+)-**3** with *p*-bromobenzoyl chloride afforded (+)-**6**. *Collins* oxidation (CrO$_3$/pyridine) of (+)-**3** gave (+)-**7** (75%). Similarly, (−)-**3** was transformed into (−)-**7** whose reduction with NaBH$_4$ in THF furnished alcohol (−)-**8** (70%). Acetylation of (−)-**8** gave (−)-**9**. Treatment of (+)-**7** with an excess of Me$_3$NO in acetone [7] removed the tricarbonyliron moiety and gave dienone (+)-**10**. Esterification of (−)-**8** with *p*-bromobenzoyl chloride followed by treatment with Me$_3$NO afforded the known (−)-**11**.



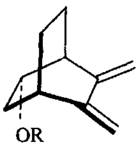
(+)-**7**



(−)-**8** R = H
(−)-**9** R = Ac



(+)-**10**



(−)-**11** R = 4-BrC$_6$H$_4$CO

The absolute configuration (1*R*,4*R*) of (+)-**10** has been derived before from its CD spectrum and by analogy with that of 5,6-dimethylidenebicyclo[2.2.1]heptan-2-one [8]. That of (−)-**11** has also been deduced from its CD spectrum which displayed a typical exciton-split *Cotton* effect due to a coupling between benzoate and exocyclic s-*cis*-butadiene chromophores [9].

Now, the crystal structure and absolute configuration of (+)-**6** (see *Figure*) have been determined by X-ray diffraction studies (see *Exper. Part*). The results confirm our earlier attribution of the relative configuration (*exo vs. endo*) of the tricarbonyliron moieties in complexes **1** and **2** which was based on reactivity criteria [3]. Applying ^{13}C-NMR and mass-spectral criteria, *Hansen* and coworkers had proposed opposite relative configura-

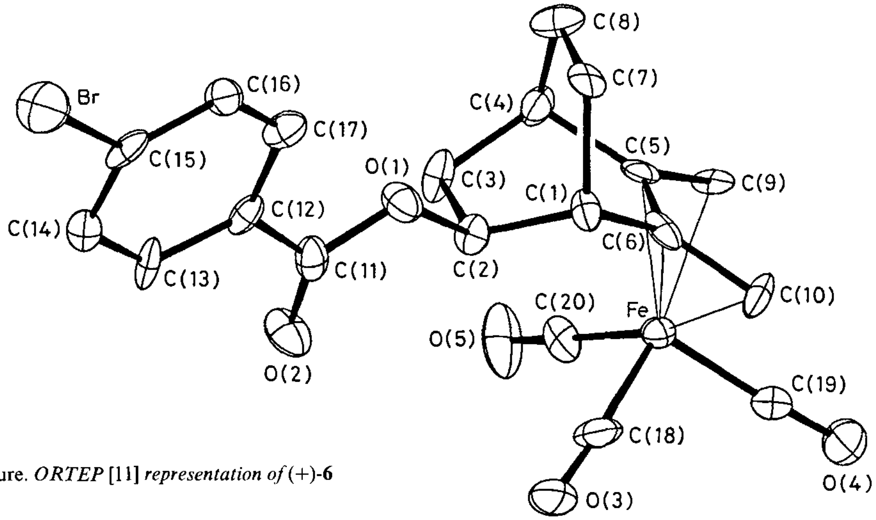


Figure. *ORTEP* [11] *representation of* (+)-**6**

tion for the $Fe(CO)_3$ moieties in **1** and **2** [10]. The structure of (+)-**6** confirms the absolute configuration proposed earlier for dienone (+)-**10**, *p*-bromobenzoate (+)-**11**, and related 5,6-dimethylidenebicyclo[2.2.2]oct-2-yl derivatives. Our results demonstrate the usefulness of the CD analytical method described earlier [8] [9].

We thank *F. Hoffmann-La Roche & Co. AG*, Basel, the *Fonds Herbette*, Lausanne, and the *Swiss National Science Foundation* for generous support.

Experimental Part

General. See [3].

(+)-Tricarbonyl[(1S,2S,4R,5R,6S)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]octan-2-ol)]iron ((+)-**3**, 16% e.e.). A 4:1 mixture **1**/**2** (4 g, 14.7 mmol) [3] was added portionwise to stirred 0.92M $IpcBH_2$ in THF (70 ml, 65 mmol) cooled to 0°. After 5 h at 20°, the mixture was cooled to 0° and MeOH (5 ml) added dropwise, followed by the addition of 3N KOH (18 ml) and 30% H_2O_2 (15 ml). The mixture was heated to 50° for 1 h. After cooling to 0°, H_2O (500 ml) and Et_2O (200 ml) were added. The aq. layer was extracted with Et_2O (200 ml, twice). The org. phases were combined and washed with H_2O (200 ml, twice). After solvent evaporation, pinacol was distilled off at 60° *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/Et_2O). The main fraction was recrystallized from Et_2O/hexane, giving 2.65 g (62%), yellow crystals. M.p. 115–117°. $[\alpha]_D^{25} = 8$ ($c = 3$, $CHCl_3$).

Tricarbonyl[(1S,2S,4R,5R,6S)- and (1R,2R,4S,5S,6R)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]oct-2-yl (1S)-Camphanates)]iron ((+)- and (−)-**5**, resp.). (−)-Camphanoyl chloride (18 g, 83 mmol) was added portionwise to a soln. of (+)-**3** (16% e.e.; 18.9 g, 65 mmol) in anh. pyridine cooled to 0°. After stirring at 20° for 16 h, the mixture was poured onto crushed ice (500 g) and extracted with CH_2Cl_2 (200 ml). The org. extract was washed with 1N HCl (100 ml, 3 times) and H_2O (100 ml, 3 times), dried ($MgSO_4$), and evaporated and the residue dissolved in hot hexane (500 ml). The hot soln. was filtered and allowed to cool slowly to 20°. After 12 h at 20°, the crystals *A* were collected. The mother-liquor was evaporated and the residue was recrystallized from hot hexane giving crystals *B*. *A* and *B* were each recrystallized from hot hexane until constant rotation (4–5 times): 4.8 g (15%) of (+)-**5**, yellow crystals $[\alpha]_D^{25} = +60$ ($c = 2$, $CHCl_3$), and 4.5 g (14%) of (−)-**5**, yellow crystals, $[\alpha]_D^{25} = -74$ ($c = 2$, $CHCl_3$), respectively.

(+)-Tricarbonyl[(1S,2S,4R,5R,6S)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]octan-2-ol)]iron ((+)-**3**, 99% e.e.). To a soln. of (+)-**5** (2.4 g, 4.9 mmol) in CH_2Cl_2 (20 ml), MeOH (150 ml), and THF (20 ml), 1.5N KOH (50 ml) was added. After 2 h at 20°, H_2O (50 ml) was added and the mixture extracted with CH_2Cl_2 (150 ml, twice). The

org. phase was washed with H_2O (100 ml, 3 times), dried ($MgSO_4$), and evaporated. Recrystallization from hexane gave 1.3 g (92%), yellow crystals. M.p. 119–120°. $[\alpha]_{589}^{25} = +48.9$, $[\alpha]_{578}^{25} = +51.4$, $[\alpha]_{546}^{25} = +59.4$ ($c = 3$, $CHCl_3$). Other data: identical to those reported for (±)-**3** [3].

(–)-Tricarbonyl[(1R,2R,4S,5S,6R)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]octan-2-ol)]iron ((–)-**3**, 95% e.e.). Same procedure as for (+)-**3**, using (–)-**5**: 1.35 g (95%), yellow crystals. M.p. 119–120°. $[\alpha]_{589}^{25} = -47.9$, $[\alpha]_{578}^{25} = -50.1$, $[\alpha]_{546}^{25} = -58$.

The enantiomeric excess of (+)-**3** and (–)-**3** was determined by 360-MHz ^{1}H-NMR of the *Mosher* esters derived form (–)-methoxy(phenyl)(trifluoromethyl)acetyl chloride. To a soln. of (±)-**3**, (+)-**3**, or (–)-**3** (50 mg, 0.172 mmol) in anh. pyridine (1 ml), this (–)-acyl chloride (50 µl) was added. After stirring at 20° for 20 min, CH_2Cl_2 (5 ml) was added. The soln. was washed with 2N HCl (5 ml, 3 times) and H_2O (5 ml, 5 times), dried ($MgSO_4$), and evaporated and the residue dissolved in $CDCl_3$ (analysis by 360-MHz ^{1}H-NMR).

(+)-Tricarbonyl[(1S,2S,4R,5R,6S)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]oct-2-yl p-bromobenzoate)]-iron ((+)-**6**). A mixture of (+)-**3** (50 mg, 0.17 mmol) and *p*-bromobenzoyl chloride (73 mg, 0.33 mmol) in pyridine (1 ml) was stirred at 20° for 18 h. After H_2O addition (5 ml), the mixture was extracted with CH_2Cl_2 (10 ml, 3 times). The combined org. phase was washed with 2N HCl (10 ml, 3 times) and H_2O (10 ml, 3 times), dried ($MgSO_4$), and evaporated and the residue purified by column chromatography on silica gel (AcOEt/hexane 1:4). Recrystallization from Et_2O/hexane 1:4 gave 53 mg (66%), yellow crystals. M.p. 107°. $[\alpha]_{589}^{25} = +83.8$, $[\alpha]_{578}^{25} = +88.0$, $[\alpha]_{546}^{25} = 102$, $[\alpha]_{436}^{25} = 194.4$ ($c = 3$, $CHCl_3$). Slow recrystallization from pentane gave crystals which were used for the X-ray structure determination (see below).

(+)-Tricarbonyl[(1S,4R,5R,6S)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]octan-2-one)]iron ((+)-**7**). CrO_3 (1.2 g, 11.9 mmol) was added portionwise to a stirred soln. of anh. pyridine (1.9 g, 23.8 mmol) in anh. CH_2Cl_2 (20 ml) at 0°. After stirring at 20° for 10 min, a soln. of (+)-**3** (521 mg, 1.8 mmol) in anh. CH_2Cl_2 (3 ml) was added dropwise. After stirring at 20° for 10 min, the mixture was filtered through silica gel, washing with CH_2Cl_2 (100 ml). The soln. was washed with 2N HCl (100 ml, 3 times) and H_2O (100 ml, 3 times), dried ($MgSO_4$), and evaporated, and the residue recrystallized from hexane, yielding 390 mg (75%), yellow crystals. M.p. 120–122°. $[\alpha]_{589}^{25} = 21.6$, $[\alpha]_{578}^{25} = +22.8$, $[\alpha]_{546}^{25} = +22.1$ ($c = 3$, $CHCl_3$). Other spectral data: see (±)-**7** [3].

(–)-Tricarbonyl[(1R,4S,5S,6R)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]octan-2-one)]iron ((–)-**7**). Same procedure as above using (–)-**3**: 307 mg (60%), yellow crystals. M.p. 119–120°. $[\alpha]_{589}^{25} = -17.4$, $[\alpha]_{578}^{25} = -17.7$, $[\alpha]_{546}^{25} = -17.8$ ($c = 3$, $CHCl_3$).

(–)-Tricarbonyl[(1R,2S,4S,5S,6R)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]octan-2-ol)]iron ((–)-**8**). A mixture of (–)-**7** (110 mg, 0.38 mmol), THF (1.5 ml), and $NaBH_4$ (29.4 mg, 0.78 mmol) was heated to 70° for 12 h. After cooling to 20°, H_2O (5 ml) was added and the mixture extracted with CH_2Cl_2 (20 ml, twice). The combined extract was washed with H_2O (20 ml, 3 times), dried ($MgSO_4$), and evaporated. The residue was recrystallized from hexane, giving 77 mg (70%), yellow crystals. M.p. 83–84°. $[\alpha]_{589}^{25} = -53.0$, $[\alpha]_{578}^{25} = -56$, $[\alpha]_{546}^{25} = -65.8$ ($c = 10$, $CHCl_3$). Other data: see (±)-**8** [3].

(–)-Tricarbonyl[(1R,2S,4S,5S,6R)-C,5,6,C-η-(5,6-dimethylidenebicyclo[2.2.2]oct-2-yl acetate)]iron ((–)-**9**). A mixture of anh. pyridine (0.08 ml), (–)-**8** (40 mg, 0.14 mmol), and Ac_2O (0.44 ml) was stirred at 20° for 15 h. H_2O (5 ml) was added and the mixture extracted with $CHCl_3$ (5 ml, 3 times). The combined extract was washed with 2N HCl (10 ml, 3 times) and H_2O (10 ml, 3 times), dried ($MgSO_4$), and evaporated: 28 mg (61%), yellow oil. $[\alpha]_{589}^{25} = -46.3$, $[\alpha]_{578}^{25} = -49$, $[\alpha]_{546}^{25} = -58$ ($c = 10$, $CHCl_3$). Other data: see (±)-**9** [3].

*Oxidative Demetallation of the p-Bromobenzoate of (–)-**8** and of (+)-**7**.* Freshly sublimed Me_3NO (340 mg, 4.5 mmol) was added portionwise to a stirred soln. of the *p*-bromobenzoate of (–)-**8** (see [9]) (47.3 mg, 0.1 mmol) in anh. acetone (30 ml). After disappearance of the complex (5 h, control by TLC), H_2O (50 ml) was added and the mixture extracted with CH_2Cl_2 (3 × 50 ml). The org. extract was washed with H_2O (3 × 50 ml) and dried ($MgSO_4$). The solvent was removed by distillation under reflux yielding 17.2 mg of *(1S,2S,4S)-5,6-Dimethylidenebicyclo[2.2.2]octan-2-ol* ((–)-**11**). Spectral data: see [9].

Similar treatment of (+)-**7** yielded *(1R,4R)-5,6-dimethylidenebicyclo[2.2.2]octan-2-one* ((+)-**10**). Spectral data: see [8].

*Crystal-Structure Determination and Absolute Configuration of (+)-**6**.* Compound (+)-**6** crystallized as yellow plates from pentane. The crystal used for structure determination was cleaved from a larger plate in order to have sufficient thickness. X-Ray intensity data collection was carried out at r.t. with an *Enraf-Nonius CAD-4* automatic diffractometer. The crystal data, intensity collection, structure soln. and refinement methods are summarized in the *Table*. The measured intensities were corrected for absorption as before [12], and the variances of the intensities were derived from counting statistics and the fluctuations of three periodically measured check reflections. The computer programs used for data reduction and structure solution were taken from the 'XRAY-72' program system [13]. The scattering factors for the neutral non-H-atoms were taken from *Cromer* and *Mann* [14], Table. *Crystal Data, Intensity Measurements, Structure Solution and Refinement for (+)-***6**

Formula	$C_{20}H_{17}BrFeO_5$	Scan method	2θ–θ
Molecular weight	473.10	$(\sin\theta/\lambda)_{max}$	0.55
Crystal dimensions [mm]	0.43 × 0.30 × 0.14	No. of unique reflections	2355[a])
Crystal system	Orthorhombic	No. of reflections $< 3\sigma$	651
a [Å]	6.6944(8)	No. of observations/ No. of variables	9.6 (8.7[b]))
b [Å]	13.440(2)		
c [Å]	22.107(2)	Structure solution	*Patterson* and *Fourier*
U [$Å^3$]	1988.98		
Z	4	Refinement method	Full matrix least squares
$d_{obsd.}$ [$g \cdot cm^{-3}$]	1.59		
$d_{calcd.}$ [$g \cdot cm^{-3}$]	1.58	Function minimized	$\Sigma w(\|F_o\| - \|F_c\|)^2$
F_{000}	952	w	$1/\sigma^2$
Space group	$P2_12_12_1$	R	0.054
Radiation	MoK_α	R_w	0.038
λ [Å]	0.71069	Goodness of fit	3.00
μ [cm^{-1}]	27.73		

[a]) 730 *Bijvoet* pairs.

[b]) Only those reflections with $I < 3\sigma$ with $|F_c| > |F_o|$ were included in the refinement.

and anomalous scattering coefficients from *Cromer* and *Liberman* [15]. Then, structure was solved by *Patterson* and *Fourier* methods using 1625 reflections with $hkl \geqslant 0$ and refined by full matrix least squares to $R = 0.059$. The data set was then expanded to contain 730 *Bijvoet* pairs and refinement continued to $R = 0.054$. In the last cycles, all atoms were refined anisotropically, but no H-atoms were included in the model. The correctness of the absolute configuration was confirmed by a structure-factor calculation on the other enantiomer ($R = 0.071$). Final atomic coordinates, calculated bond lengths and angles, the observed and calculated structure factors, as well as tables of temperature factors are available as supplementary material. A perspective drawing of the molecule prepared by the program ORTEP [11] is shown in the *Figure*. The benzoate group may be disordered as the Br thermal motion appears rather high. This is also in agreement with the highest peak in the *Patterson* map being an Fe-Fe vector.

REFERENCES

[1] C.A. Barras, R. Roulet, P. Vogel, *Inorg. Chim. Acta* **1984,** *82,* L 1.

[2] R. Gabioud, P. Vogel, *Helv. Chim. Acta* **1986,** *69,* 865.

[3] C.A. Barras, R. Roulet, P.-A. Carrupt, F. Berchier, P. Vogel, *Helv. Chim. Acta* **1984,** *67,* 986.

[4] H. Gerlach, *Helv. Chim. Acta* **1978,** *61,* 2773.

[5] P.K. Jadhav, H.C. Brown, *J. Org. Chem.* **1981,** *46,* 2988.

[6] J.A. Dale, D.L. Dull, H.S. Mosher, *J. Org. Chem.* **1969,** *34,* 2543; see also: N. Kalyanam, D.A. Lightner, *Tetrahedron Lett.* **1979,** 415.

[7] Y. Shvo, E. Hazum, *J. Chem. Soc., Chem. Commun.* **1974,** 336; A.P. Humphries, S.A.R. Knox, *J. Chem. Soc., Dalton Trans.* **1978,** 1514.

[8] P.-A. Carrupt, P. Vogel, *Tetrahedron Lett.* **1981,** *22,* 4721.

[9] Z. Zhichen, P.-A. Carrupt, P. Vogel, *Helv. Chim. Acta* **1984,** *67,* 600.

[10] U. Steiner, H.-J. Hansen, K. Bachman, W. von Philipsborn, *Helv. Chim. Acta* **1977,** *60,* 643.

[11] C.K. Johnson, ORNL-3794, Oak-Ridge National Laboratory, 1971.

[12] A.A. Pinkerton, D. Schwarzenbach, *J. Chem. Soc., Dalton Trans.* **1980,** 1300.

[13] J.M. Stewart, F.A. Kundell, J.C. Baldwin, 'XRAY-72', version of June 1972, Technical Report TR-192 of the Computing Science Center, University of Maryland (as modified by D. Schwarzenbach).

[14] D.T. Cromer, J.B. Mann, *Acta Crystallogr., Sect. A* **1968,** *24,* 321.

[15] D.T. Cromer, D. Liberman, *J. Chem. Phys.* **1970,** *53,* 1891.