Determining Centrosymmetric Dimers by Infrared and Raman Spectroscopy

H. ZIFFER AND I. W. LEVIN

National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland 20014

Received May 9, 1969

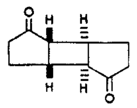
Infrared and Raman spectra of cyclobutane photodimers of 2-cyclopentenone, 2-cyclohexenone, 3-methyl-2-cyclohexenone, and isophorone were recorded. A comparison of the vibrational data for the head-to-head and head-to-tail *anti* species of each of the four sets of dimers has been used, in conjunction with the Mutual Exclusion Rule, to identify the centrosymmetric dimer.

Although the photodimerization of conjugated carbonyl derivatives to form cyclobutane dimers is a well-known reaction,[1] the problems associated with determining the stereochemistry about the cyclobutane ring remain formidable. Since one of the more frequent reaction products has the head-to-tail (h-t) *anti* configuration, a simple method for distinguishing this dimer from the other possible products would prove useful in structural determinations. The cyclobutane ring of dimers with an h-t or h-h configuration exists in two conformations, planar or puckered, depending upon the nature of the substituents on the ring. Thus, since only the (h-t) *anti* dimer with a planar cyclobutane ring possesses an inversion center, techniques that specifically identify centrosymmetric species are particularly worth examining in these systems.

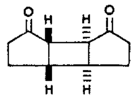
In addition to X-ray methods, which are sometimes unwieldy, vibrational spectroscopy offers a means of characterizing molecules with a center of symmetry. The difference in vibrational selection rules for infrared and Raman transitions of molecules with this symmetry element provides a theoretical basis for determining its presence or absence through the Rule of Mutual Exclusion;[2] that is, for centrosymmetric molecules, a vibrationally active infrared transition cannot be active in the Raman; and conversely, a vibrationally active Raman transition cannot be active in the infrared. In molecules lacking the inversion center, vibrations of the same frequency, which are termed coincidences, appear in both the infrared and Raman spectrum. To detect this symmetry element, Raman and infrared spectral comparisons are commonly employed in structural determinations of small molecules.[3] Since even the simplest photodimers, however, have a relatively large number of atoms and, consequently, rich and complex vibrational spectra, it is necessary to assess the usefulness of the vibrational method for significantly large molecular species. Thus, for this study we examined the infrared and Raman spectra of several pairs of structurally known photodimers with progressive structural complexities. For comparison purposes one member of each pair possessed an (h-t) *anti* configuration and contained a possible center of symmetry (point group C_i). The other member of the set possessed no element of symmetry other than the identity element (point group C_1).

Results

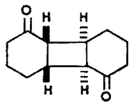
The vibrational spectra of the photodimers of cyclopentenone (**1** and **2**),[4] cyclohexenone (**3** and **4**),[5] 3-methylcyclohexenone (**5** and **6**),[6] isophorone (**7**, **8**, and **9**),[7] and benzindenone (**10** and **11**) were recorded with the samples in the form of KBr disks for the infrared and as pure solids for the Raman spectra. Although the accuracy of the Raman displacements and the infrared frequencies are each about ±2 cm^{-1}, transitions within 5 cm^{-1} for the infrared and Raman comparisons were considered coincidences. Crystal effects may arise in the Raman spectra of the pure solids; however, the 5-cm^{-1} interval accepted for coincidences between infrared absorptions and Raman emission lines should allow for crystal perturbations. Tables I–III summarize the infrared and Raman data for the first three pairs of compounds (only obvious shoulders are differentiated in the tables). Since the detector of the Raman spectrometer falls in sensitivity in the 3000-cm^{-1} displacement region on the Stokes side of the exciting line, the carbon–hydrogen motions appear as weak structureless bands. Consequently, the Raman and infrared comparisons were started at 2000 cm^{-1}. No transitions occurred between 2000 cm^{-1} and the carbon–hydrogen stretching region at approximately 3000 cm^{-1}. Although we obtained Raman data within 75–100 cm^{-1} of the exciting line,



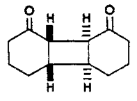
1



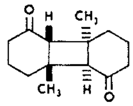
2



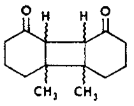
3



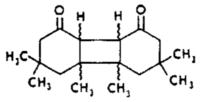
4



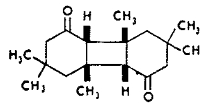
5



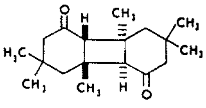
6



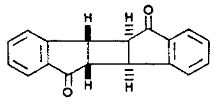
7



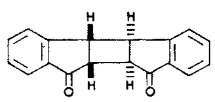
8



9



10



11

---

[1] N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N. Y., 1965, p 194.

[2] R. P. Bauman, "Absorption Spectroscopy," John Wiley & Sons, Inc., New York, N. Y., 1962, p 462.

[3] D. F. Koster and F. A. Miller, *Spectrochim. Acta*, **24A**, 1487 (1968).

[4] P. E. Eaton, *J. Amer. Chem. Soc.*, **84**, 2344 (1962).

[5] D. Valentine, N. J. Turro, Jr., and G. S. Hammond, *ibid.*, **86**, 5202 (1964).

[6] H. Ziffer, unpublished results.

[7] O. L. Chapman, P. J. Nelson, R. W. King, D. J. Trecker, and A. A. Griswold, *Rec. Chem. Progr.*, **28**, 167 (1967).

TABLE I

COMPARISON OF THE RAMAN DISPLACEMENTS AND INFRARED FREQUENCIES FOR THE CYCLOPENTENONE PHOTODIMERS

1, head-to-tail		**2**, head-to-head	
Raman, cm^{-1}	Infrared, cm^{-1}	Raman, cm^{-1}	Infrared, cm^{-1}
325		299	
413		429	432
	476	445	444
513		490	490
	522	542	544
552		554 (sh)[a]	556
	632	619	617
639			643
	673	667	
	763 (sh)[a]	765	767
	767 (sh)[a]	791	790
770	771	801	
795			814
	831		867 (sh)[a]
	876		870
886		886	887
905		899	
	913	935 (sh)[a]	938
	952	947	948 (sh)[a]
966		967	968
	990	1019	1019
1023		1053	1055
1037	1033	1062	
1066			1082
1100		1122	1124
	1139	1150	1152
1151		1165	1164 (sh)[a]
	1162		1180
1172	1175		1197
	1217	1213	1217
1261 (sh)[a]		1227	1227
1272			1240
	1282	1262	1264 (sh)[a]
1295		1274	1271
	1309		1282
	1321	1310	1312 (sh)[a]
1330			1316
1413	1415	1402	1404
1454	1454	1455	1456
1717		1723	1722
1726 (sh)[a]	1724	1737 (sh)[a]	1736
	1735		

[a] sh denotes shoulder.

TABLE II

COMPARISON OF THE RAMAN DISPLACEMENTS AND INFRARED FREQUENCIES FOR THE CYCLOHEXENONE PHOTODIMERS

3, head-to-tail		**4**, head-to-head	
Raman, cm^{-1}	Infrared, cm^{-1}	Raman, cm^{-1}	Infrared, cm^{-1}
328		300	
400		382	384
	424	401	403
438	439	446	445
	462	455	
473		487	490
	480	534	582
	489 (sh)[a]	590	
	497		600
539	542	666	669
615		707	709
	649	739	
724			762
743	740	850 (sh)[a]	852
	761	860	864
841		875	877
	856	892	894
	863		957
878	881	987	
	902		997
917	918	1022	1021
	955	1031	1033
966	963	1068	1065 (sh)[a]
	987		1072
	1009	1091	1093 (sh)[a]
1017			1097
	1022	1129	
1028		1142	1140
	1033	1172	1172 (sh)[a]
	1062	1211	
	1077	1225	1228
1085	1088		1235
	1116	1262	1260
	1130	1271	1271
1141			1280 (sh)[a]
	1180		1310
	1200	1316	
1210			1324
	1221		1335
	1237		1338 (sh)[a]
	1260	1352	1350
1267	1270		1377
	1281	1423	1423 (sh)[a]
	1316		1428
	1320	1451	1449
1328			1453 (sh)[a]
	1336	1461	1463
	1343		1694
	1356		1698
	1396	1701	1704
1416			
	1422		
1439			
	1444		
	1461		
1467	1470		
1685			
1695 (sh)[a]	1693		
	1698		
	1702		

[a] sh denotes shoulder.

we set the lower limit for comparison purposes at 250 cm^{-1}, the cutoff point of the infrared spectrometer. The final frequency measurements were obtained from slow scans of expanded traces.

Table IV summarizes the infrared and Raman spectra of three isophorone dimers. The complete structures of these dimers are unknown at present; however, **7** is known to be (h-h) while **8** and **9** are (h-t) dimers.

Discussion

As stated previously, the basis for using infrared and Raman spectra to distinguish between the presence or absence of an inversion center, or between C_i and C_1 symmetry in the photodimer examples, is the Mutual Exclusion Rule. An examination of the comparison for **1** and **2**, listed in Table I, clearly indicates that the Raman active bands in **1** do not appear in the infrared spectrum and vice versa, thus establishing a C_i symmetry for **1**. The situation with regard to **2** in the same table is quite different. In this case many of the Raman bands have an infrared counter-

TABLE III

COMPARISON OF THE RAMAN DISPLACEMENTS AND INFRARED FREQUENCIES FOR THE 3-METHYLCYCLOHEXENONE PHOTODIMERS

5, head-to-tail		**6**, head-to-head	
Raman, cm^{-1}	Infrared, cm^{-1}	Raman, cm^{-1}	Infrared, cm^{-1}
277		284	
320		308	
375		322	
402		366	367
	431	394	
467		407	407
485		425	
	496		438
	508	455	
	522	483	484
537		502	
575			508
609		545	
	634		566
712		603	602
	717	627	
751		676	677
	805	707	707
818		743	744
	853	765	
872			833
	877	847	
893		874	873 (sh)^a
	898 (sh)^a		876 (sh)^a
	903	899	901
915			904
940	943	929	932
	968		945
982		954	955
1009			963
1041		974	978
	1048		1005
1058		1018	
1099		1031	1033
	1144	1047	1050
1154		1058	1062
	1163	1094	1094
1169		1108	1109
	1188	1128	1127
	1194	1167	1168
1206	1210 (sh)^a		1187
1235		1205	1208
	1241 (sh)^a	1223	
1264			1247
1283	1279		1269 (sh)^a
	1297	1281	1277
1317			1289 (sh)^a
	1323	1307	1310
	1331 (sh)^a	1319	1321
	1341		1338
1353		1356	1354
	1362		1378
	1376		1382
1401	1402	1420	1419 (sh)^a
1434			1421 (sh)^a
	1438	1456	1453
	1448		1460
1454	1458	1466	1468
1471	1468	1690	1686
1681	1679		1698 (sh)^a
	1683		~1703

[a] sh denotes shoulder.

TABLE IV

COMPARISON OF THE RAMAN DISPLACEMENTS AND INFRARED FREQUENCIES FOR THE ISOPHORONE PHOTODIMERS

7, head-to-head		**8**, head-to-tail		**9**, head-to-tail	
Raman, cm^{-1}	Infrared, cm^{-1}	Raman, cm^{-1}	Infrared, cm^{-1}	Raman, cm^{-1}	Infrared, cm^{-1}
253		278			285
307	334	282	286	318	
342	344 (sh)^a	291	293		333
385	383	302		370	373
401		313	316	394	
416			338		418
447		360		423	
	473	370			449
486		409			483
510	513	424		492	
554		479	480	527	
	620	488 (sh)	489		542
627	628 (sh)^a	519	521		579
751		556	559	608	
	788		573	619	
812		605	607		656
828	825	626	629	688	
844		672		708	
880	879	706			756
892	894		756	789	
900		792 (sh)	793	818	814
	914	799			827
921		818	818	869	
936	937	857		900	900
945 (sh)^a	943 (sh)^a		892	907	
980	979	900			920
1023	1023	906	905 (sh)^a	928	
1063	1063	923		942	945
1086 (sh)^a	1086		929 (sh)^a		969
1093	1090 (sh)^a		931 (sh)^a		989
1102 (sh)^a	1101	947		998	
1108 (sh)^a	1108		957		1025
1130	1128	974	977	1030	
1170	1167		982	1055	
	1192		991		1081
	1222	998		1092	
1228	1229 (sh)^a	1010			1107
	1250		1017	1117	
1255		1038			1128
	1259		1046	1138	
	1278	1086			1163
	1298		1092	1169	
1313		1120			1179
	1319		1127		1189
	1353		1146	1228	1225
	1366	1170			1239
	1376		1177	1262	1262
	1388	1186		1280	
1417	1417		1192		1288
	1420 (sh)^a		1216		1315
1455	1458	1241		1326	
1466	1470		1233		1337
1685	1687		1240		1346
	1696		1252		1373
	1706	1261			1386
			1265		1392
			1286	1415	
			1300		1424
		1312		1454	1457 (sh)^a
			1319	1472 (sh)^a	1468
			1345		1477
			1353	1595	
			1376	1681	
			1387		1688
			1397		1698 (sh)^a
		1410			1714 (sh)^a
		1419	1420		
		1454			
			1461		
		1468 (sh)^a	1465 (sh)^a		
			1473		
			1482		
		1682			
			1687		
			1694		

[a] sh denotes shoulder.

part indicating that the Rule of Mutual Exclusion does not apply. The presence of only six coincidences for 1 compared with twenty-six for 2 (see Table V)

TABLE V
COMPARISON OF THE RAMAN AND
INFRARED FREQUENCY COINCIDENCES[a]

	Head-to-tail photodimer				Head-to-head photodimer		
Compd	R	ir	C[a]	Compd	R	ir	C
1	24	24	6	**2**	31	36	26
3	24	46	10	**4**	33	42	24
5	34	34	7	**6**	41	46	28
10	26	42	10	**11**	24	43	16

Compd	R	ir	C
7	37	42	23
8	41	48	16
9	33	41	9

[a] R, ir, and C denote Raman lines, infrared peaks, and coincidences, respectively.

is quite remarkable. Since each dimer contains twenty-four atoms, or a total of sixty-six vibrational fundamentals, and since overtone and combination bands commonly appear in the infrared spectrum, the strong possibility exists for accidental coincidences to occur between the infrared and Raman spectra. Other factors that may distort the frequency positions and hinder a valid spectral comparison are Fermi resonance and crystal field effects, although the latter, particularly, are probably small. Therefore, in examining the infrared and Raman frequency comparisons for these dimers, it is important to establish a trend rather than to require a strict mutual exclusion for the C_i molecules or a complete set of coincidences for C_1 molecules. Since nonplanar cyclobutane derivatives do not contain a center of symmetry, the conclusion that **1** contains a center of symmetry agrees with the X-ray determination, by Margulis,[8] which demonstrated the planarity of the cyclobutane ring for this species.

Table II lists the results for the 2-cyclohexenone dimers (**3** and **4**). Although the structure proofs for these dimers have not been published, Hammond, *et al.*,[5] report that the dimers were assigned as **3** and **4** by Eaton. The comparison for **3** (Table II) shows that there are ten coincidences (Table V) while twenty-four coincidences occur for **4**. The number of coincidences for **4** clearly suggests C_1 symmetry; however, the trend establishing a center of symmetry for **3** is less persuasive, although still indicative of C_i symmetry, than it was for **1**. In order to determine the complicating effects of increasing the size of the dimer with additional molecular groups, we examined the two photodimers of 3-methyl-2-cyclohexenone (Table III). Seven coincidences appear in the spectra of **5**, while twenty-eight coincidences occur in **6**. Again, differentiation between C_i and C_1 symmetry appears clear for these two dimers.

As the molecule increases in size through addition of various units, specific vibrational frequencies of the molecule can shift through coupling effects between the large number of vibrations of the same symmetry. These effects, in addition to the occurrence of accidental degeneracies, complicate the isophorone dimer spectra. The summary in Table V shows that **7** has twenty-three coincidences and therefore does not contain a center of symmetry. If we assume[9] that the two (h-t) alkali stable dimers are **8** and **9**, then, on the basis of the earlier arguments, it appears that the dimer with only nine coincidences has the center of symmetry and is therefore **9**. Unfortunately, the other compound, assigned as **8**, with sixteen coincidences is a borderline case for establishing either C_i or C_1 symmetry in the absence of **7** and **9**. The interpretation of the vibrational comparison for **8** or **9** must await the complete structure determination of these compounds.

Since the trends indicating the presence or absence of a center of symmetry were particularly clear with regard to **1** and **2**, we were interested in determining the effect upon the spectral comparisons of fusing an aromatic ring to this system. Compounds **10** and **11** were prepared by established synthesis[10,11] and the results, summarized in Table V, show that **10**, with a potential center of symmetry, has ten coincidences; **11**, which lacks a center, has sixteen. The greater number of coincidences in **10**, compared with **1**, for example, is understandable in that the opportunity for accidental coincidences becomes greater as the molecular size increases. An alternate possibility arises in that several conformers may coexist. Thus, the situation could be complicated by having a small percentage of the molecules in the puckered state. Greenberg and Post[12] summarize X-ray data for several cyclobutane derivatives that possess either a planar or puckered cyclobutane ring depending upon the nature of the substituent about the ring. The reason for **11** showing fewer coincidences as compared with **2** is probably related to these larger dimers usually exhibiting fewer Raman bands than expected. This phenomenon may result from the nature of the experiment. For example, since fluorescence, intrinsic or resulting from minute impurities, masks the weaker Raman signals, a decrease in the total number of observed Raman lines with compounds more difficult to purify is not surprising. In any event, the results for compounds **8** through **11** suggest that these dimers can not be unambiguously analyzed by this technique.

We conclude that, in cases where dimers can be compared, the compound possessing the center of symmetry can be confidently assigned. The method is rapid, nondestructive, and, in conjunction with laser Raman spectroscopy, requires only milligram samples of material. In addition, if other physical measurements, for example, dipole moment or nmr methods, indicate that dimerization occurs in an h-t fashion, then the converse information from the vibrational comparisons that the molecule does not contain a center of symmetry also becomes valuable in completing the structural analysis.

Experimental Section

Infrared spectra were recorded with a Perkin-Elmer Model 521 spectrophotometer at spectral slit widths of about 0.9 cm^{-1}. Samples were viewed in KBr disks, approximately 0.5 mm thick, in concentration ratios of about 1:300 for sample to KBr. Water

---

(8) T. N. Margulis, *Acta Crystallogr.*, **18**, 742 (1965).

(9) The assumption is somewhat arbitrary since Corey, *et al.*, have shown that *trans* six-four ring junctions adjacent to a carbonyl function are less stable than *cis* six-four junctions; however, the effect of steric repulsion between *cis* 1,3 methyl groups on the stability of the ring junction is unknown.

(10) E. H. White and H. C. Dunathan, *J. Amer. Chem. Soc.*, **78**, 6055 (1956).

(11) J. Bowyer and Q. N. Porter, *Aust. J. Chem.*, **19**, 1455 (1966).

(12) B. Greenberg and B. Post, *Acta Crystallogr.*, **B24**, 918 (1968).

vapor, ammonia, and carbon dioxide served as calibrating gases for the spectrometer.

Raman spectra of the solid samples (several milligrams) were obtained with a Cary Model 81 spectrophotometer equipped with a helium-neon CW laser source. Scattering from samples placed in a conical holder was viewed coaxially along the laser beam by the monochromator. Spectral slit widths varied from 2.5 to 3 cm^{-1}. Spectra were calibrated with atomic neon lines and are probably accurate to ±2 cm^{-1}.

A crucial point in obtaining quality Raman spectra is to eliminate all traces of fluorescing material from the samples. For the systems examined in this study, sublimation of the samples under vacuum appears to be most effective. Under some circumstances, repeated sublimation is necessary.

The dimers were prepared by previously published procedures as indicated in Table VI.

Table VI

Dimer	Mp, °C	Lit. mp, °C	Lit. reference
1	126–126.5	125–126.5	4
2	69–70	66–67	4
3	51–52	53–55	5
4	77–78	79–80	5
5	146–147	146–147	6
6	68–69	68–69	6
7	118.5–190	188.5–190	7
9[a]	112–113.5	112–113.5	7
8[a]	211–213	211–213	7
10	286–288	293	9
11	229–235	225–266	10

[a] The structural assignments of **8** and **9** are tentative.

Registry No.—**1,** 2065-43-2; **2,** 21876-87-9; **3,** 712-27-6; **4,** 21876-89-1; **5,** 21876-90-4; **6,** 21927-71-9; **7,** 21899-39-8; **8** and **9,** 21865-12-3; **10,** 21899-40-1; **11,** 17062-18-9.

Acknowledgments.—We wish to thank Miss Glenna Christie for her assistance in obtaining the Raman spectra. Also, we wish to thank Dr. O. Chapman for kindly supplying samples of isophorone dimers.

Studies in Alkylation. II. Reactions of Epoxyalkyl Bromides[1]

Philip A. Cruickshank and Morris Fishman

Central Research Department, Chemical Research and Development Center, FMC Corporation, Princeton, New Jersey 08540

Received May 20, 1969

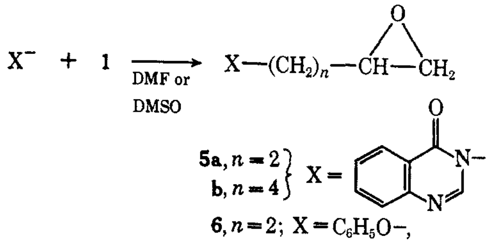
Alkylation reactions of the bifunctional ω-bromo-1,2-epoxyalkanes have been found to be markedly dependent upon the solvent and the nature of the nucleophile. In alcoholic media, compounds which generate an anion with a localized electron pair react by opening the oxirane ring to give β-hydroxy-ω-bromoalkyl derivatives. In aprotic solvents, these same compounds react by displacement of bromide ion to give epoxyalkyl derivatives. Compounds which generate anions with a delocalized electron pair react exclusively by displacement of bromide ion. Subsequent cyclization reactions may occur in alcohol if the initial product can be converted into an anion and if the proper spatial relationship exists between the epoxy group and the nucleophilic carbon.

As part of a program to prepare compounds for screening as antimalarial agents,[2] a series of amino alcohols of general structure **4** was required. Our approach to the synthesis of these compounds involved condensation of appropriate nucleophiles with the homologous ω-bromo-1,2-epoxyalkanes **1**, followed by aminolysis of the bromo alcohol **2** (Scheme I). During the course of this work novel solvent and nucleophile dependent reactions of the epoxyalkyl bromides **1** were encountered.

Results

The anions of 4(3H)-quinazolone and of phenol were found to react with an excess of 4-bromo-1,2-epoxybutane (**1a**) in alcohol to give the expected products, the 4-bromo-2-hydroxybutyl derivatives **2a** and **3** (Table I). A similar reaction with 6-bromo-1,2-epoxyhexane (**1c**) and 4(3H)-quinazolone gave the homologous product 3-(6-bromo-2-hydroxyhexyl)-4-quinazolone (**2b**). These compounds were characterized by infrared spectrometry (hydroxyl absorption at 3350 cm^{-1}), nmr chemical shifts and coupling constants (Table II), and mass spectrometry (Table III).

When the same anions were allowed to react with the ω-bromo-1,2-epoxyalkanes in dimethylformamide or dimethyl sulfoxide, bromine free products were obtained. Elemental and spectrometric analyses identified the products as the epoxyalkyl derivatives **5** and **6**



5a, $n = 2$; **b**, $n = 4$

6, $n = 2$; X = C_6H_5O–,

(Table IV). The infrared spectra were free of hydroxyl absorption. The nmr spectra established that the oxirane ring has been retained; chemical shifts and coupling constants (Table V) were in close agreement with published values for mono substituted epoxides.[3] Prominent molecular ions were observed in the mass spectra as well as daughter ions corresponding to known fragmentation mechanisms for structures of this type (Table VI).[4]

Diethyl sodiomalonate (**7**, R = H) and diethyl sodiomethylmalonate (**7**, R = CH_3) also were found to react with the epoxyalkyl bromides in dimethylformamide to give the corresponding epoxyalkylmalonates **8** (Table IV), as evidenced by the nmr chemical

---

[1] This paper was presented before the Division of Organic Chemistry, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., September 1968, Abstract ORGN 71.

[2] M. Fishman and P. A. Cruickshank, *J. Heterocycl. Chem.*, **5**, 467 (1968).

[3] E. Lippert and H. Prigge, *Ber. Bunsenges. Phys. Chem.*, **67**, 415 (1963).

[4] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, pp 450–458.