401. *Infrared Spectra of Natural Products. Part XII.* Triterpenoid and Diterpenoid Carboxylic Acids.*

By A. R. H. COLE and A. J. MICHELL.

The infrared spectra of a group of triterpenoid and diterpenoid carboxylic acids have been measured in carbon tetrachloride and chloroform and a few in carbon disulphide and dioxan solutions. Hydroxyl and carbonyl frequencies are given for the monomeric and the dimeric acids, and the distribution of the acids between monomer and dimer is studied in the different solvents. Most of the acids exist as monomer in dioxan, predominantly as monomer in chloroform, and predominantly as dimer in carbon disulphide and tetrachloride. In the carbonyl region the change from mostly dimer (~1695 cm.$^{-1}$) in carbon tetrachloride to mostly monomer (~1735 cm.$^{-1}$) in chloroform can be useful in identifying an unknown compound as an acid since all other types of carbonyl function absorb at lower frequencies in chloroform. Dicarboxylic acids and polyhydroxy-acids might exist as dimers in all solvents if the substituent groups are favourably oriented for the formation of more than one hydrogen-bond system.

CARBOXYLIC ACIDS in the polyterpenoid field can often be isolated and purified more readily than alcohols and hydrocarbons but, in general, they are not so convenient for infrared structural analysis. They form very strong intermolecular hydrogen-bonds and hence are usually sparingly soluble in the non-polar solvents which are best for infrared work, and their spectra[1-4] are complicated by the presence of various proportions of dimeric and monomeric molecules. It is usual to overcome these difficulties in degradative work by converting acids into methyl esters, but, as part of a programme based on correlations of

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* Part XI, *J.*, 1959, 1224.

[1] Davies and Sutherland, *J. Chem. Phys.*, 1938, **6**, 755.

[2] Shreve, Heether, Knight, and Swern, *Analyt. Chem.*, 1950, **22**, 1948.

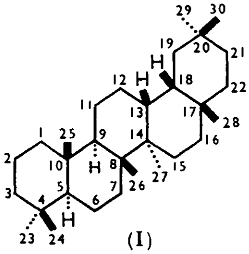
[3] Flett, *J.*, 1951, 962.

[4] Hadži and Sheppard, *Proc. Roy. Soc.*, 1953, *A*, **216**, 274; Harris and Hobbs, *J. Amer. Chem. Soc.*, 1954, **76**, 1419; Bratož, Hadži, and Sheppard, *Spectrochim. Acta*, 1956, **8**, 249; Wenograd and Spurr, *J. Amer. Chem. Soc.*, 1957, **79**, 5844.

triterpenoid structures with infrared spectra, we have investigated the spectra of dilute solutions of the acids themselves in a number of solvents.[5]

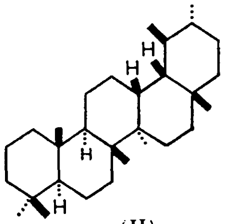
Experimental.—The experimental conditions were as in Parts V and VIII of this series.[6] Cells of 10 mm. path length were often necessary because of the low solubility of some of the compounds.

Results and Discussion.—Most of the acids studied in this work are triterpenoids based on oleanane (I), ursane (II), or lupane (III). Of the others one is a degradation product of lanosterol, one is coprostan-27-oic acid,[7] and four [(IV)—(VII)] are diterpenoids. Propionic and benzoic acid are included for comparison.



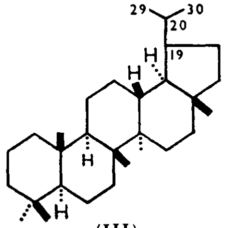
(I)

Oleanane



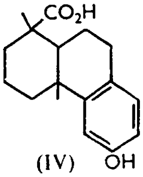
(II)

Ursane



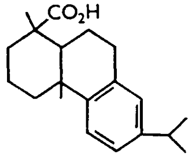
(III)

Lupane



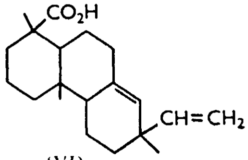
(IV)

Podocarpic acid



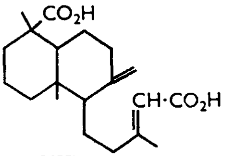
(V)

Dehydroabietic acid



(VI)

Dextropimaric acid



(VII)

Agathenedicarboxylic acid

Their hydroxyl and carbonyl stretching frequencies in carbon tetrachloride and chloroform solutions are given in Table 1, where maximum values of the apparent molar extinction coefficients are given for those compounds soluble enough for quantitative measurements.

Hydroxyl absorption. Carboxylic acids exist in these solvents in varying proportions of monomer and dimer (see below). The carboxyl-hydroxyl absorption of the monomer (in CCl_4) occurs at about 3535 cm.$^{-1}$ and is easily distinguished from alcoholic-hydroxyl absorption near 3630 cm.$^{-1}$, while that of the dimer is extremely broad and underlies the C–H stretching absorption at much lower frequencies[4] (Fig. 1). Alcoholic-hydroxyl frequencies are lowered by about 10 cm.$^{-1}$ in chloroform while the monomer carboxyl-hydroxyl frequency falls by 15—25 cm.$^{-1}$. Absorption of chloroform interferes with hydroxyl measurements on the dimer.

The absorption frequency of the equatorial secondary 3-hydroxyl group (3630 cm.$^{-1}$) for a number of the compounds is consistent with previous measurements on triterpenoid alcohols,[8,9] while the high frequency for β-boswellic acid (3638 cm.$^{-1}$) shows that this hydroxyl group is axial. The absence of absorption due to intramolecular hydrogen-bonding[10] means that the 4-carboxylic group is also axial, thus establishing the structure

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[5] Michell, Thesis, W. Australia, 1956.
[6] Cole and Thornton, *J.*, 1956, 1007; Cole and Willix, *J.*, 1959, 1212.
[7] Bridgwater and Haslewood, *Biochem. J.*, 1952, **52**, 588.
[8] Allsop, Cole, White, and Willix, *J.*, 1956, 4868.
[9] Cole, Müller, Thornton, and Willix, *J.*, 1959, 1218.
[10] Cole and Müller, *J.*, 1959, 1224.

TABLE 1. *Hydroxyl and carbonyl frequencies (cm.$^{-1}$) of carboxylic acids in various solvents. Apparent molar extinction coefficients are given in parentheses.*

					Carbonyl							
	Alcoholic OH		Carboxyl OH		CCl_4		$CHCl_3$		CS_2		Dioxan	
Compound	CCl_4	$CHCl_3$	CCl_4	$CHCl_3$	Monomer	Dimer	Monomer	Dimer	Monomer	Dimer	Monomer	Complex
3β-Hydroxyolean-12-en-28-oic acid (oleanolic acid)	3630(60)	3621(80)	3537(45)	3512(65)	1744(140)	1696(590)	1734(225)	1696(190)	1743	1694	1727	1644
3β-Hydroxyolean-19-en-28-oic acid (morolic acid)	3630	3621(90)	3532	3507(65)	1743(275)	1696(490)	1734(290)	1696(135)				
3β-Hydroxyolean-13(18)-en-28-oic acid (δ-oleanolic acid)	3629(50)	3617(80)	3530(30)	3515(55)	1742(150)	1693(380)	1732(255)	1693(220)				
3β-Hydroxyurs-12-en-28-oic acid (ursolic acid)					1742	1691	1731	1694				
3α-Hydroxyurs-12-en-24-oic acid (β-boswellic acid)	3638 [a] (70)	3631 [a] (65)	3524(35)	3509(45)	1737(165)	1694(455)	1731(345)	1694(145)	1736(95)	1692(585)	1718	1650
Olean-12-en-30-oic acid (deoxydeoxoglycyrrhetic acid)			3535(30)	3518(70)	1747(160)	1699(535)	1738(400)	1698(275)				
3-Oxolupan-28-oic acid (dihydrobetulonic acid)			3528(35)	3513(50)	1742(220)	1697 [b]	1737(355)	1699 [e] (570)			1726	1644
3β-Hydroxyoleana-11 : 13(18)-dien-28-oic acid (dehydro-oleanolic acid)	3630	3615	3531	3508	1743	1695	1736	1695				
3β : 23-Dihydroxyolean-12-en-28-oic acid (hederagenin)	*	*	*	*	*	*	1733	1697 1682				
3β-Acetoxyolean-12-en-28-oic acid (acetyloleanolic acid)			3534(25)	3520(40)	1745 [b]	1696	1731 [b]	1695 [b]	1745 [b]	1696(575)	1731 [b]	1637
3β-Acetoxy-18α-olean-12-en-28-oic acid (acetyl-18-*iso*-oleanolic acid)					1752 [b]	1700	1741 [b]	1700 [b]				
3β-Acetoxy-23-oxo-olean-12-en-28-oic acid (gypsogenin acetate)			3532(15)	3515(50)	1747 [b]	1697(565)	— [c] (1730)	1698				
3β-Acetoxylup-20(29)-en-28-oic acid (acetylbetulic acid)			3533(35)	3516(50)	1745 [b]	1694	1733 [b]	1695 [b]				
3β-Hydroxyurs-12-ene-27 : 28-dioic acid (quinovic acid)	*	*	*	*	No. abs.	1693 [b] 1678	No abs.	1693 [b] 1678				
3β-Hydroxy-(25–27)-trisnor-lanost-8-en-24-oic acid					*	*	1745	1710 [b]				
Coprostan-27-oic acid (coprostanic acid)			3530(40)	3518(45)	1755	1708	1742(310)	1706(220)				
Dehydroabietic acid			3537(50)	3522(55)	1743(175)	1695(565)	1734(425)	1695(385)				
Podocarpic acid	3618 [d]	3603 [d]	3528	3514	1743	1696	1735	1696				
Dextropimaric acid			3534(40)	3512(50)	1742(150)	1696(575)	1732(250)	1694(180)				
Agathenedicarboxylic acid			*	3512	1740	1693	1725(450)	1693(332)				
Propionic acid			3535(10)		1760(71)	1716(600)	1747(303)	1715(223)	1760(67)	1714(595)	1739	1640
Benzoic acid			3535(20)		1742(85)	1697(710)	1732(360)	1697(350)	1741(110)	1697(590)	1723	1636

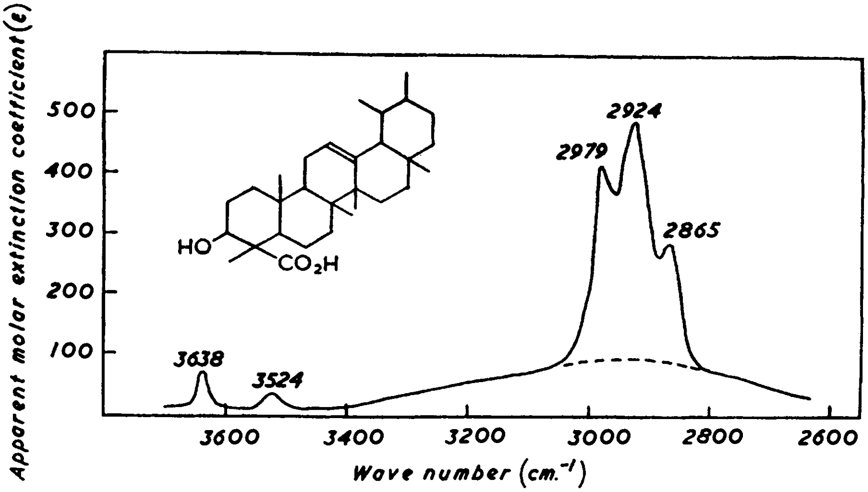
* Measurement impossible because of low solubility.

[a] Axial hydroxyl. [b] Partially resolved shoulder on side of stronger band. [c] Indistinguishable from acetate-carbonyl absorption (maximum in parentheses). [d] Phenolic OH. [e] Includes 3-ketone absorption.

of this region of β-boswellic acid[5] in agreement with the chemical evidence of Beton, Halsall, and Jones.[11]

The phenolic-hydroxyl frequency of podocarpic acid (3618 cm.$^{-1}$ in CCl_4) is also readily distinguished from those of the secondary alcoholic compounds. The apparent molar extinction coefficients of the hydroxyl absorption may be inaccurate because of low solubility, but they indicate the order of magnitude of the intensities, and the increase in the intensity of the monomeric carboxyl-hydroxyl band on change from carbon tetrachloride to chloroform is consistent with the measurements in the carbonyl region (see below). However, the proportions of monomer and dimer are not identical for the two regions since the solutions used for the hydroxyl absorption were, of necessity, much more concentrated.

FIG. 1. *Spectrum of β-boswellic acid in the hydroxyl and* C–H *stretching regions* (CCl_4 *solution*).



C–H *Stretching absorption.* All terpenoids show strong absorption near 2900 cm.$^{-1}$ due to the stretching vibrations of the alphatic C–H bonds (Fig. 1). However, this absorption is not very sensitive to small changes in molecular structure and provides very little useful information. Ethylenic C–H stretching absorption on the high-frequency side of the main band is often useful in identifying unsaturated centres, but the absorption is relatively weak and is obscured by the broad hydrogen-bonded dimer absorption in the spectra of the acids. Even the vinylidene band at 3070 cm.$^{-1}$ ($\varepsilon \sim 40$) which is usually easy to find was not visible in the spectrum of dextropimaric acid. The spectra of the acids were all measured in this region, but since no new information was obtained they will not be considered further.

Carbonyl absorption. The physical state in which carboxylic acids are examined has a direct effect on the carbonyl frequency. The carbonyl bands of monomer and dimer are easily resolved (Table 1) and their intensity ratio indicates the degree of association under different conditions.* Table 1 shows that the monomer carbonyl frequency measured in chloroform is approximately 10 cm.$^{-1}$ lower than in carbon tetrachloride and carbon disulphide, while that of the dimer is the same for all solvents. In dioxan the acids are

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* A broad band centred near 1714 cm.$^{-1}$ reported by Cole and Thornton[6] for a few triterpenoid acids in chloroform is now known to be due to hydrogen-bonding to ethanol (0·5%) present in the solvent as stabiliser. Most types of carbonyl group can be studied in the presence of the ethanol, but for the carboxylic acids with their much greater tendency to form hydrogen-bonds it must be removed. For the present work this was done with silica gel.[12]

[11] Beton, Halsall, and Jones, *J.*, 1956, 2904.

[12] Cole, *Fortschr. Chem. org. Naturstoffe*, 1956, **13**, 17.

mainly monomeric (see below) and the carbonyl frequency is 7—13 cm.$^{-1}$ lower than in chloroform. These (monomer) solvent effects are similar to those reported for simpler carbonyl compounds,[13] although here the greater lowering in dioxan should be noted. The absence of a differential solvent shift in the case of the dimer must be due to the difficulty of approach of solvent molecules to the " internal " carbonyl groups, an effect similar to that reported by Bayliss, Cole, and Little [13] for the C–C bond of acetonitrile in a variety of solvents.

There is a marked increase in the proportion of monomer to dimer in changing from carbon tetrachloride to chloroform. This is in the expected direction since the polar solvent would stabilise the more polar monomeric form. The proportion of monomer is about the same in carbon disulphide as in carbon tetrachloride, while in dioxan the acids exist almost completely as monomer.[3] However, in the latter solvent there is some tendency to form a hydrogen-bond to a dioxan-oxygen, as shown by the small broad band near 1640—1650 cm.$^{-1}$.

FIG. 2. *Carbonyl region of the spectrum of β-boswellic acid in* CCl_4–$CHCl_3$ *mixtures* (*see Table* 2).

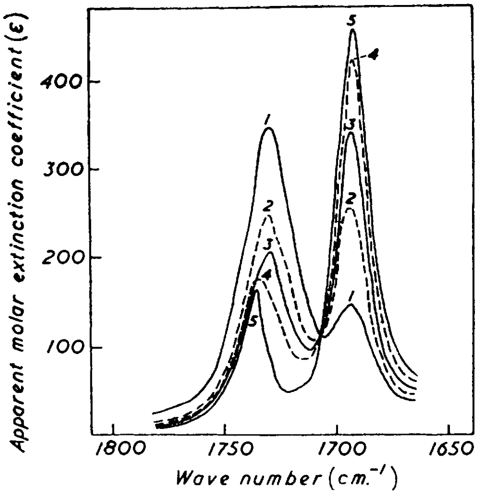
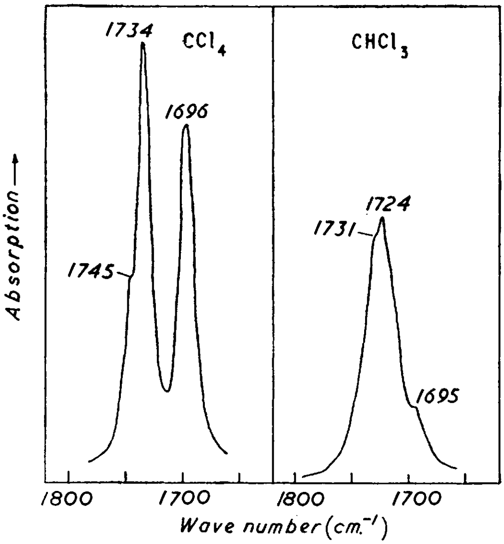


FIG. 3. *Carbonyl region of the spectrum of acetyl-oleanolic acid in* CCl_4 *and* $CHCl_3$.



The change from predominantly dimeric in carbon tetrachloride to monomeric in chloroform was followed quantitatively for β-boswellic acid in mixtures of the two solvents (Table 2 and Fig. 2). The isosbestic point for the system is at 1708 cm.$^{-1}$ (ε 110). These curves also show clearly the constant frequency of the dimer, the solvent shift of the monomer, and the broader shape of the bands in chloroform.

TABLE 2. *Carbonyl frequencies* (*cm.*$^{-1}$), *and apparent molar extinction coefficients* (*in parentheses*), *for β-boswellic acid in carbon tetrachloride–chloroform mixtures* (*see Fig.* 2).

Curve no. (Fig. 2)	Mole fractions CCl_4	Mole fractions $CHCl_3$	Monomer	Dimer
1	1	0	1737(165)	1694(455)
2	0·75	0·25	1736(170)	1694(415)
3	0·52	0·48	1731(190)	1694(340)
4	0·16	0·84	1731(250)	1694(255)
5	0	1	1730(345)	1694(145)

In structural analysis the monomer–dimer change can be useful in showing that carbonyl absorption is due to the presence of a carboxyl group, since the more intense part of the absorption appears to move to a higher frequency in chloroform whereas other types

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[13] Josien and Lascombe, *Compt. rend.*, 1954, **238**, 2414; Bayliss, Cole, and Little, *Austral. J. Chem.*, 1955, **8**, 26.

of carbonyl function move to lower frequencies. It can also be helpful in separating overlapping absorption if quantitative measurements are not used to determine the number of carbonyl groups in a compound.[14] For example, in the spectrum of acetyloleanolic acid (Fig. 3) the acetate-carbonyl band lies between that of the monomer and the dimer and, in chloroform, the slightly resolved shoulders at 1731 (monomer) and 1695 cm.$^{-1}$ (dimer) could easily be missed, especially if a sodium chloride prism is used, whereas the carbon tetrachloride solution shows conclusively that two types of carbonyl function are present.

The fact that the degree of association is approximately equal in carbon tetrachloride and carbon disulphide is important since the former solvent is the best (most transparent) for infrared work between 2·5 and 8 μ while the latter is the best liquid for the range 8—15 μ. It is thus possible to obtain the complete spectrum in solution between 2·5 and 15 μ with the acid in approximately the same state of association.

The low solubilities of hederagenin and quinovic acid, which prevented measurements in the hydroxyl region in either solvent and in the carbonyl region of the former in carbon tetrachloride, can be explained in terms of hydrogen-bond formation. Hederagenin has the possibility of dimerisation involving carboxyl–carboxyl, carboxyl–alcohol, or alcohol–alcohol hydrogen-bonds. The existence of the first two of these types is indicated by the two dimer carboxyl bands (1697, 1682 cm.$^{-1}$) in chloroform solution. Of these, that with the higher frequency must belong to the carboxyl–carboxyl system since it occurs in all the other acids, and the band at 1682 cm.$^{-1}$ to the carboxyl–alcohol bond. The intensity and appearance of the hydroxyl absorption of the monohydroxy-acids and absence of such low-frequency carbonyl absorption shows that they have none of this type of bonding in solution, although it could occur in the solids.

Quinovic acid exhibits similar absorption, but is sufficiently soluble in carbon tetrachloride to allow qualitative carbonyl measurements. The spectrum shows that it exists completely in the hydrogen-bonded form even in chloroform solution.

Trisnorlanostenolic acid, with a primary carboxyl group, also forms very strong hydrogen-bonds and is not soluble enough in carbon tetrachloride for measurement. In chloroform, its monomeric carbonyl absorption is very broad, probably because of easy access of solvent molecules to the primary group, and the dimer absorption at 1710 cm.$^{-1}$ could not be properly resolved from it.

TABLE 3. *Miscellaneous absorption frequencies (cm.$^{-1}$).*

In CCl_4		In $CHCl_3$	In CCl_4		In $CHCl_3$
	Acetate-carbonyl groups			3-*Ketones*	
1734	Acetyloleanolic acid	1724	1707	Dihydrobetulonic acid	1699[a]
1734	Acetyl-18-*iso*oleanolic acid	1725	1707	Methyl dihydrobetulonate	
1737	Gypsogenin acetate	1730		*Vinylidene* C=C *frequency*	
1735	Acetylbetulic acid	1723	1643	Acetylbetulic acid	1642
			1644	Agathenedicarboxylic acid	1644

[a] Indistinguishable from dimeric acid absorption.

A number of miscellaneous band frequencies which were recorded are given in Table 3. They are consistent with those previously reported for similar triterpenoids.[6,12]

Other characteristic carboxylic acid absorption bands. (i) Near 1400 cm.$^{-1}$. Flett[3] and Hadži and Sheppard[4] have described a band between 1395 and 1440 cm.$^{-1}$ in a large number of acids. This is a region of strong methyl and methylene absorption in terpenoid and steroid spectra, and although bands undoubtedly associated with the carboxyl group were found for some of the present compounds (coprostanic acid 1418 cm.$^{-1}$, β-boswellic acid 1410 cm.$^{-1}$) it does not appear to be a useful region for structural information in this field.

(ii) Near 1250 cm.$^{-1}$. A band near 1250 cm.$^{-1}$ appeared in the spectra of all the acids examined by Flett,[3] and Shreve *et al.*[2] and Freeman[15] described a doublet near 1280 and

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[14] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72; Jones, Ramsay, Keir, and Dobriner, *ibid.*, p. 80.

[15] Freeman *ibid.*, p. 2523.

1240 cm.$^{-1}$. Of the acids in the present work which were studied beyond the calcium fluoride region, most show this doublet strongly, with some variation in the intensity ratio of the peaks (Table 4).

TABLE 4. *Absorption frequencies* (*cm.*$^{-1}$) *near* 1250 *cm.*$^{-1}$ *Apparent molar extinction coefficients* (CS_2 *solutions*) *are given for the more soluble acids.*

Oleanolic acid	1270, 1237	Acetyloleanolic acid	1270(200), 1241 [b]
β-Boswellic acid	1262(175), 1240 [a]	Coprostanic acid	1288, 1236
δ-Oleanolic acid	1266, 1228	Propionic acid	1280(95), 1234(135)
Dihydrobetulonic acid	1273(330), 1240(525)	Benzoic acid	1283(370)

[a] Partially resolved shoulder. [b] Mostly acetate absorption.

(iii) O–H Deformation absorption. A band near 935 cm.$^{-1}$ has been assigned (Hadži and Sheppard [4]) to the OH out-of-plane deformation mode of the dimeric acids. This appeared as a broad, fairly intense band in the spectra of benzoic (933 cm.$^{-1}$), propionic (932 cm.$^{-1}$), β-boswellic (946 cm.$^{-1}$), and coprostanic acid (984 cm.$^{-1}$) in this work. For some of the other acids, particularly those with tertiary carboxyl groups and those containing other oxygenated groups with fairly intense bands in the range 900—1100 cm.$^{-1}$ it did not stand out and might not always be of use in structure determinations.

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