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Lactone Carboxylic Acids. II.
Synthesis of α-Benzylideneparaconic Acids*

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The reaction of ethyl γ,γ-dialkylparaconate with aromatic aldehydes, i.e., benzaldehyde, anisaldehyde, *p*-chlorobenzaldehyde, and piperonal, has been investigated. The condensation took place at the α-position of the lactone ring. As the acidic components, α-benzylideneparaconic acids and α-benzylidene-ß-alkylidensuccinic acids were obtained in 25—48% and 7—15% yields, respectively. From the neutral portions small amount of ethyl benzylideneparaconates were separated. During the course of distillation ethyl α-benzylideneparaconate was partially converted into α-benzylidene-γ-methyl-γ-ethylbutyrolactone.

In continuation of our investigation on γ-lactone carboxylic acids[1-4], we examined the reaction of ethyl γ,γ-dialkylparaconates with aromatic aldehydes in the presence of sodium ethoxide in ethanol. Recently, similar attempt was briefly reported by Dallacker[5] who found that the reaction of methyl terebinate with piperonal in the presence of sodium methoxide in dry benzene afforded α-piperonylideneterebic acid. Homologues of the α-benzylideneparaconic acids have been separated during the course of Stobbe condensation[6,7]. The related compounds have become of considerable interest because of the structural resemblance to a lignans skeleton[8].

The reactions of equimolar amounts of γ,γ-dialkylparaconates[1] with aromatic aldehydes were carried out in the presence of sodium ethoxide in dry ethanol for overnight at 5—10°C. The condensation products were separated into acidic and neutral portions in the ratio of 75—80% to 25—20%. In the case of reaction with anisaldehyde, the dibasic acid (II, $R=C_2H_5$ and $R'=OCH_3$) crystallized out firstly from the acidic portion, and then crystalline α-anisylideneparaconic acid (I, $R=C_2H_5$ and $R'=OCH_3$) was separated. α-Benzylideneparaconic acid (I, $R=C_2H_5$ and $R'=H$), however, crystallized at the beginning. The structures of I and II have been established by means of infrared spectra as shown in Figure 1 (Chart A and D). I has a characteristic carbonyl band[1] at 1725-1730cm^{-1}, and II has two carbonyl bands at 1695 and 1680cm^{-1}. The NMR spectrum of I ($R=C_2H_5$ and $R'=H$) shows bands at 9.1τ (3H, triplet), 8.3τ (3H, singlet), 7.8τ (2H, quartet), 5.9τ (1H, singlet), and 2.82τ (1H, singlet) in chloroform as are illustrated by the chart in Figure 2. The α-substituted paraconic acids (I) obtained are listed in Table I.

Esterification of the acid (I) with diazomethane gave the corresponding methyl ester (IV), as shown in Table II, which have lactone carbonyl band at 1755cm^{-1} and ester carbonyl band at 1720cm^{-1}. The ethyl esters (V) were obtained successfully by treating I with ethyl orthoformate[9] instead of ethanol in the presence of *p*-toluenesulfonic acid. The ethyl paraconates (V) prepared by this method are summerized in Table III. The IR spectrum of V ($R=C_2H_5$ and $R'=H$) is given in Figure 1 (chart B).

Decarboxylation of I ($R=C_2H_5$ and $R'=H$) occurred, when I was heated to 220—235°C in the presence of small amount of potassium hydrogen sulfate[1], to afford corresponding α-benzylidenebutyrolactone (VI, $R=C_2H_5$ and $R'=H$). The IR spectrum of VI ($R=C_2H_5$ and $R'=H$) shows a band at 1760cm^{-1} due to lactone carbonyl. The structure of the dibasic acids (II) was elucidated by further conversion to methyl esters (III) by the action of diazomethane.

On the other hand, the distillation of the neutral portion obtained by the reaction of ethyl γ-methyl-γ-ethylparaconate with benzaldehyde gave two fractions: one boils at 140-145°C/0.03 mmHg and the other at 120-125°C/0.03mmHg.

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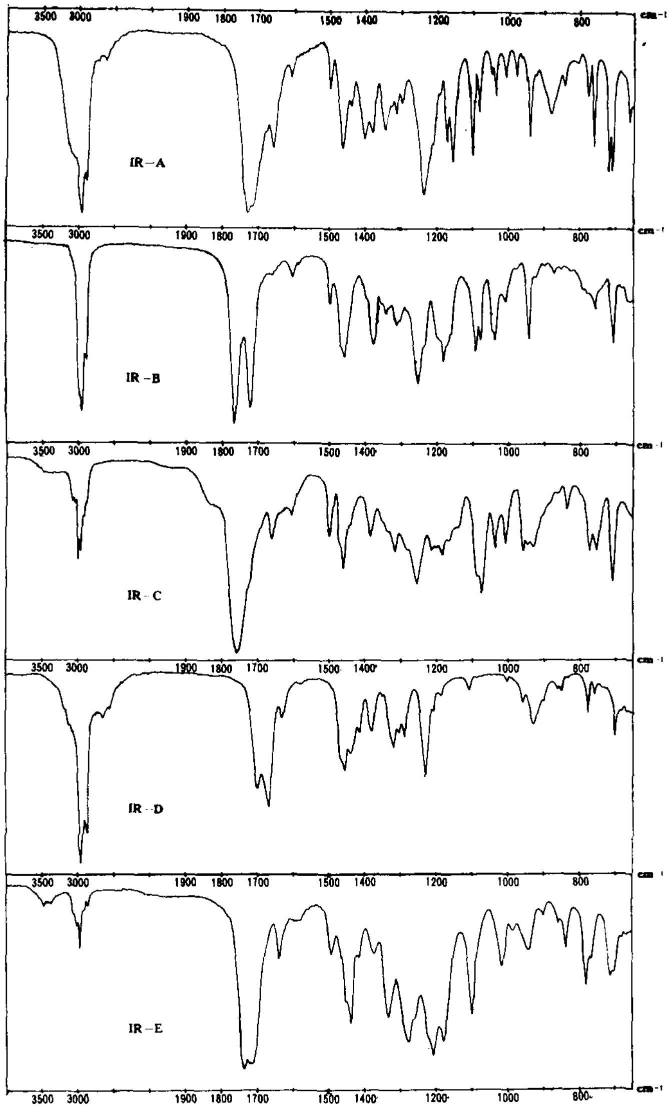
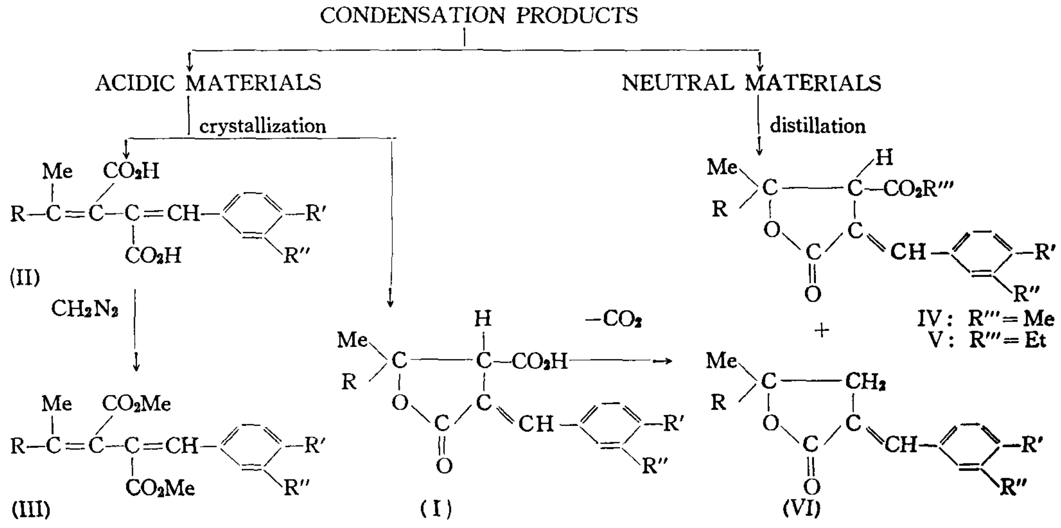


Fig. 1. IR spectra of I (A), V (B), VI (C), II (D), and III (E), (R = Me, R′ = R″ = H, and R‴ = Et, respectively).



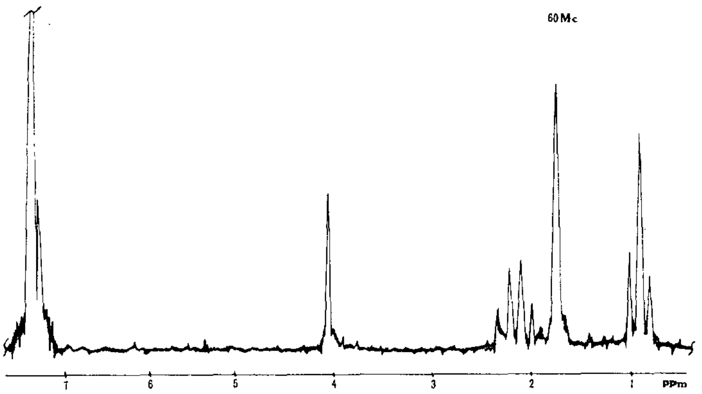


Fig. 2. NMR spectrum of α-benzylidene-γ-methyl-γ-ethylparaconic acid in the region of 0.5—7.5 ppm in chloroform.

Table I. α-Benzylidene-γ, γ-dialkylparaconic Acids (I)

R	R′	Yield, %	M. p., C°	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found
Ethyl	H	36	182	69.22	69.34	6.20	6.34
Ethyl	*p*-Methoxy	30	128.5	66.20	65.94	6.25	6.06
Ethyl	*p*-Chloro	43—48	131	61.13	61.51	5.13	5.08
Ethyl	3, 4-Methylenedioxy	25	126	63.15	63.36	5.30	5.35

Table II. Methyl α-Benzylidene-γ, γ-dialkylparaconates (IV)

R	R′	B. p., °C/mmHg	n_D^{20}	C, % Galcd.	C, % Found	H, % Calcd.	H, % Found
Ethyl	H	132–134/0.02	1.5305	70.09	70.27	6.61	6.68
Ethyl	*p*-Methoxy	182–184/0.01	1.5315	67.09	66.74	6.62	6.62
Ethyl	*p*-Chloro	139/0.03	1.5393	62.24	62.46	5.55	5.78
Ethyl	3,4-Methylenedioxy	170–173/0.01	1.5397	64.14	64.15	5.70	5.88
Isobutyl	*p*-Chloro	175/0.03	1.5363	64.18	63.93	6.28	6.25
Isobutyl	H	148–150/0.04	1.5202	71.50	71.63	7.33	7.37

Table III. Ethyl α-Benzylidene-γ-ethylparaconates (V)

R′	B. p., °C/mmHg	n_D^{20}	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found
H	139/0.02	1.5172	70.81	70.81	6.99	7.12
p-Methoxy	160/0.02	1.5213	67.91	67.65	6.79	7.00
p-Chloro	158/0.04	1.5261	63.26	63.09	5.93	5.98
3, 4-Methylenedioxy	180/0.03	1.5294	65.05	65.02	6.07	6.21

The infrared spectrum of the former compound was identical with that of the ethyl paraconate (V, R=C_2H_5 and R′=H) and the latter with that of the butyrolactone (VI, R=C_2H_5 and R′=H) (Figure 1, Chart C). Thin-layer chromatography reveals that the butyrolactone was absent in the original neutral portions, whereas the ethyl paraconate (V, R=C_2H_5 and R′=H) was clearly detected. This fact suggests that the butyrolactone (VI) might have been produced during

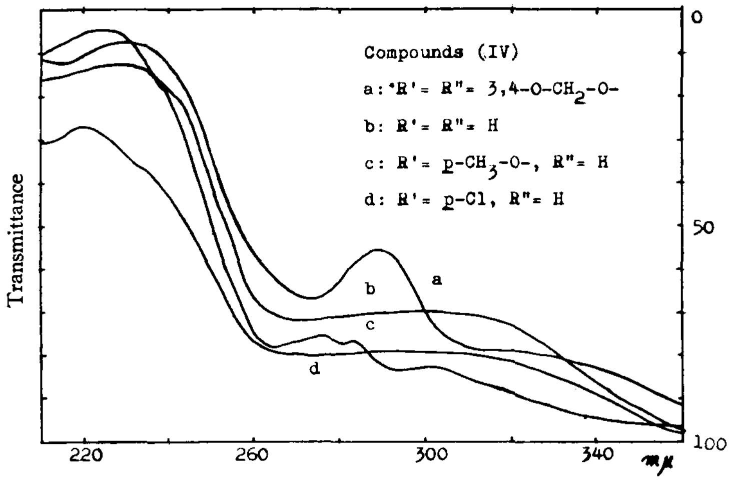


Fig. 3. Ultraviolet spectra of methyl α-benzylidene-γ-methyl-γ-ethylparaconates (IV).

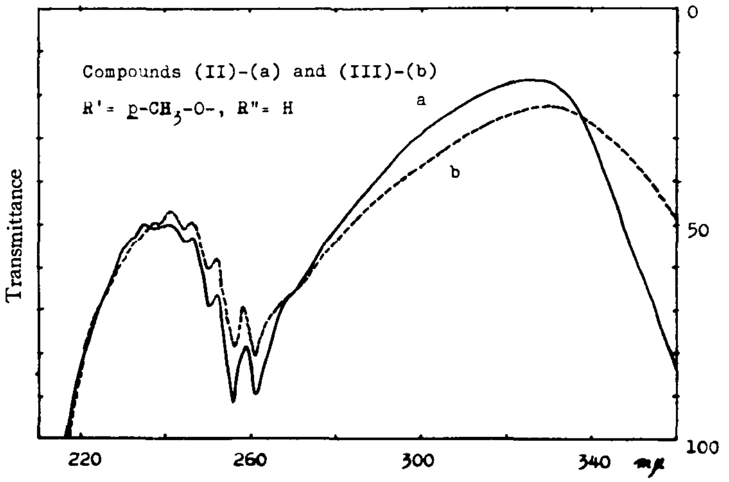


Fig. 4. Ultraviolet spectra of the compound II and III (R=Et).

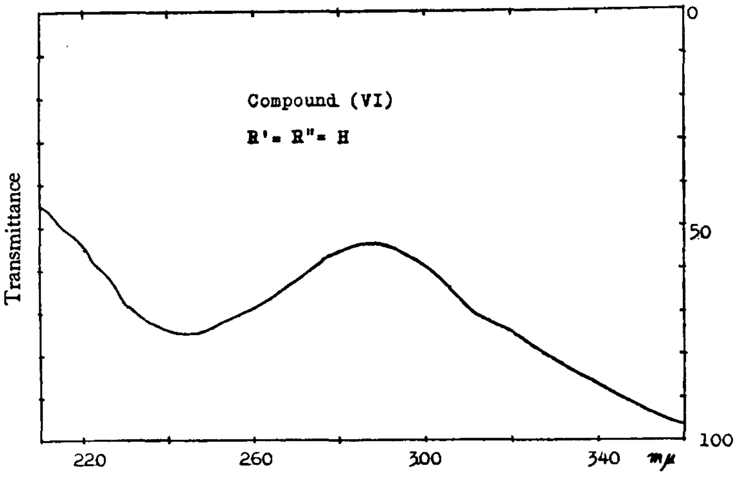


Fig. 5. Ultraviolet spectrum of α-benzylidene-γ-methyl-γ-ethylbutyrolactone (VI).

the distillation. Homologous neutral portions were checked by thin-layer chromatography similarly. The ultraviolet absorption spectra of the compounds, IV, II and III, VI, and I, are shown in Figures 3, 4, 5, and 6, respectively.

Experimental

NMR Spectra. — The spectra were taken with JNM-C-60 high resolution NMR spectrometer working at 60 Mc. in chloroform.

Ethyl Paraconates. — Esterification of γ-methyl-γ-isobutylparaconic acid[1] and γ-methyl-γ-ethylparaconic acid[10] was carried out in a mixed solution of ethanol and benzene in the presence of *p*-toluenesulfonic acid as a catalyst.

Ethyl γ-Methyl-γ-isobutylparaconate; 121°C/2 mmHg.

Found: C, 63.36; H, 8.78. Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83%.

Ethyl γ-methyl-γ-ethylparaconate; 113°C/2.5mmHg.

Found: C, 60.04; H, 8.10. Calcd. for $C_{10}H_{16}O_4$: C. 59.98; H, 8.05%.

Reaction of Ethyl γ-Methyl-γ-ethylparaconate with Anisaldehyde. Acidic Materials. — To a solution of 3.9g. (0.05 mole) of sodium ethoxide in 62 ml. of dry ethanol, 10.0 g. (0.05 mole) of anisaldehyde were added at 0—5°C with stirring and then kept overnight at 5—10°C in refrigerator. The mixture was acidified to pH 6.5—7, extracted with ether and then washed with saturated sodium chloride solution. The ethereal solution was extracted with sodium bicarbonate solution

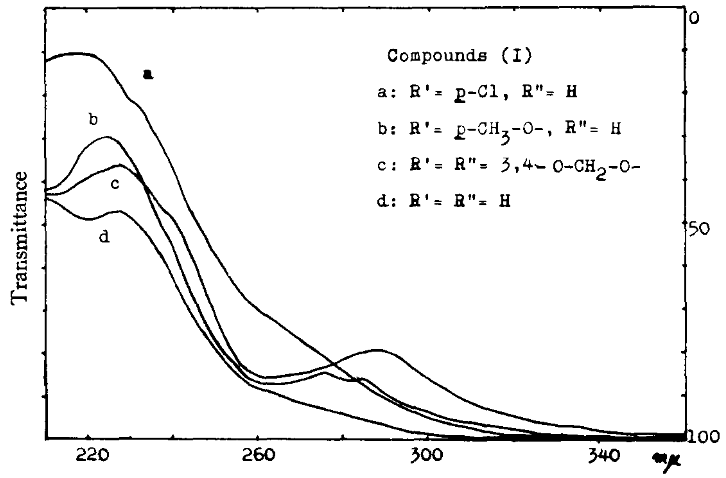


Fig. 6. Ultraviolet spectra of the compound I (R=Et).

and then the solvent was evaporated in diminished pressure to give 2.5—3.0 g. of neutral liquid which was further treated as described in next paragraph. The alkaline extracts were acidified with dilute sulfuric acid, the organic layer was taken up in ether, washed with water and then dried over anhydrous sodium sulfate. Upon evaporation of the solvent, there was obtained 12—13 g. of liquid material. This liquid, when triturated with xylene and kept at room temperature for a week, partially crystallized. The crystalline precipitate was filtered and was recrystallized from benzene-ethanol to give 1.3 g. (10%) of 2-anisylidene-4-methyl-3-carboxy-3-hexenoic acid (II, R = C_2H_5 and R′ = OCH_3), m. p. 157°C.

Found: C, 65.96; H, 6.34. Calcd. for $C_{16}H_{18}O_5$: C, 66.20; H, 6.25%.

λ_{max}^{EtOH} mμ (ε): 233 (8500), 237 (9200), 241 (9400), 246 (8100), 252 (5400), 259 (3300), 268 (5000), 327 (24900). IR: 1695, 1675 (acids ν C=O), 1650 (ν C=C), 1600, 1510, 830 cm^{-1} (phenyl group).

This dibasic acid (III, R = C_2H_5 and R′ = OCH_3), when treated with diazomethane, was converted into methyl esters, b. p. 156°C/0.04 mmHg, n_D^{20} 1.5441.

Found: C, 67.92; H, 7.00. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97%.

λ_{max}^{EtOH} mμ (ε): 233 (8900), 237 (1000), 241 (10600), 246 (10060), 252 (7900), 259 (5400), 268 (5800), 331 (21800). IR: 1730, 1700 cm^{-1} (diesters ν C=O).

On the other hand, the above filtrate, when further kept in cold storage for several days, crystallized massively. The precipitate was filtered and was recrystallized from benzene to give 3.9 g. (30%) of α-anisylidene-γ-methyl-γ-ethylparaconic acid, m. p. 128.5°C.

λ_{max}^{EtOH} mμ (ε): 224 (19500), 276 (2700), 283 (2500). IR: 1730 (paraconic acid[1]) ν C=O), 1650 (ν C=C), 1610, 1580, 1510 cm^{-1} (phenyl group).

Physical properties and microanalyses are given in Table I. The structures of these paraconic acids (I) are established by conversion into corresponding methyl and ethyl esters as described in the following paragraph.

The Neutral Materials.—Distillation of the neutral portion gave mostly starting materials, i. e., anisaldehyde and ethyl γ-methyl-γ-ethylparaconate which were confirmed by means of infrared spectra, together with small amount of high boiling material whose structure was established in comparison with the authentic specimen such as ethyl α-anisylidene-γ-methyl-γ-ethylparaconate by means of thin-layer chromatography on silica gel developed with benzene. Rf: 0.25—0.27.

In the case of the neutral portion derived from condensation of ethyl γ-methyl-γ-ethylparaconate with benzaldehyde, two high boiling materials were separated, i. e., one boiling at 120—125°C/0.03 mmHg, the other at 140—145°C/0.03 mmHg. The former was assigned to ethyl α-benzylidene-γ-methyl-γ-ethylparaconate whose infrared spectrum was identical with that of the specimen prepared by the esterification of the paraconic acid (I, R = C_2H_5 and R′ = H) with ethyl orthoformate, and the latter was assigned to α-benzylidene-γ-methyl-γ-ethylbutyrolactone (VI, R = C_2H_5 and R′ = H) whose infrared spectrum was superimposable with that of the authentic specimen obtained in the manners described in the following paragraph.

Methyl α-Anisylidene-γ-methyl-γ-ethylparaconate (IV, R = C_2H_5 and R′ = OCH_3).—The esterification was carried out by treating I (R = C_2H_5 and R′ = OCH_3) with diazomethane to give the ester IV (R = C_2H_5 and R′ = OCH_3) in quantitative yield, b. p. 172—184°C/0.01 mmHg, n_D^{20} 1.5315. λ_{max}^{EtOH} mμ (ε): 226 (18100), 276 (2500), 283 (2300), 300 (1500). IR: 1760 (lactone ν C=O), 1720 cm^{-1} (ester ν C=O).

Other methyl esters were prepared similarly.

The physical constants together with elemental analyses are listed in Table II.

Ethyl α-Anisylidene-γ-methyl-γ-ethylparaconate (V, R = C_2H_5 and R′ = OCH_3). — A mixture of 5.2 g. of the paraconic acid (I, R = C_2H_5 and R′ = OCH_3) and 4 ml. of ethyl orthoformate was refluxed for 5—6 hr. Then, excess ethyl orthoformate was removed in vacuo. Upon distillation of the residue, there was obtained 4.8 g. (90%) of the ester (V, R = C_2H_5 and R′ = OCH_3), b. p. 160°C/0.02 mmHg, n_D^{20} 1.5213. λ_{max}^{EtOH} mμ (ε): 225 (19500), 277 (2400), 283 (2200), 300 (1400). IR: 1755 (lactone ν C=O), 1715cm^{-1} (ester ν C=O).

In a similar manner, a number of V, as shown in Table III, were obtained, whereas usual acid-catalyzed esterification hardly afforded analytical pure samples.

Decarboxylation of the Paraconic Acid (I, R = C_2H_5 and R′ = H). — A mixture of 4.6 g. (0.02 mole) of α-Benzylidene-γ-methyl-γ-ethylparaconic acid and a portion of potassium hydrogen sulfate was heated to 220—235°C for 2 hr. After cooling to room temperature, the mixture was extracted with ether. The ethereal solution was washed with sodium bicarbonate solution, then with water, dried over anhydrous sulfate, and evaporated. Distilling the residue under diminished pressure, there was obtained 2.3 g. (63%) of α-benzylidene-γ-methyl-γ-ethylbutyrolactone (VI, R = C_2H_5 and R′ = H), b. p. 120—125°C/0.03 mmHg, n_D^{20} 1.5771.

Found: C, 77.63; H, 7.41. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46%.

λ_{max}^{EtOH} mμ (ε): 225 (7300), 275 (8600), 300 (7300), 325 (4500). IR: 1760 cm^{-1} (lactone ν C=O).

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