# Kinetics and Mechanism of 1,3-Dioxolane Formation from Substituted Benzaldehydes with Ethylene Oxide in the Presence of Tetrabutylammonium Halides

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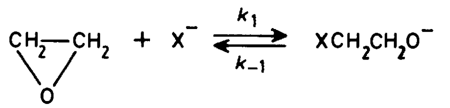
Kinetic measurements of the reaction among eight substituted benzaldehydes and ethylene oxide in the presence of catalytic amounts of tetrabutylammonium halides have been performed. With poor electrophilic aldehydes the rate-determining step of the reaction is the nucleophilic attack of the halogeno ethoxide anion to the carbonyl group while with rich electrophilic aldehydes the rate-determining step becomes the ring opening of ethylene oxide by the halide ion. Hammett correlations and kinetic results confirm these proposed mechanisms.

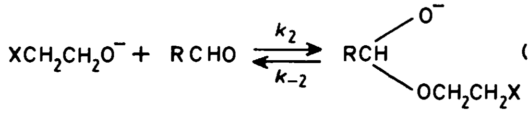
The use of ethylene oxide, in the presence of catalytic amounts of halide ions, as a base has been thoroughly studied by Buddrus and is well documented.[1] Kinetic measurements have shown that even in aprotic solvents the intermediate in the reaction of oxirane and halide ions is the 2-halogenoethoxide ion which is in fact the true base present in the system.[2,3]

One of the reactions in which the basic behaviour of ethylene oxide has had a major use is the one-pot Wittig condensation with triphenylphosphine, alkyl halides, and carbonyl compounds. We have used this technique in the preparation of polymeric phosphonium ylides, mainly stabilized ones, *e.g.* Ⓟ-$PPh_2$=CHCOOMe,[4] and their condensation with carbonyl compounds. However, in these reactions a competition was observed between the Wittig olefination and the formation of the ethylene acetal of the carbonyl compound. Buddrus had already described this secondary reaction and reported[5] that 1,3-dioxolanes can be prepared from aldehydes and ethylene oxide at high temperature if catalytic amounts of a quaternary ammonium halide were present in the medium. However, no kinetic measurements have been reported and hence the relative rates of the series of reactions (1)—(3) have not been evaluated.

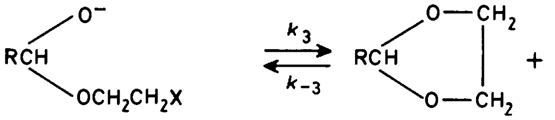
We thought that it would be worthwhile to examine this reaction kinetically, using several benzaldehydes with different electronic requirements and in the presence of three different tetrabutylammonium halides (chloride, bromide, and iodide). The proposed mechanism involves a nucleophilic attack of the 2-halogenoethoxide ion to the carbonyl compound and an entropically favourable ring closure of the intermediate (**4**) with recovery of the halide. Therefore the reaction can be understood as catalysed by halide ions.


(1)

**(1)** (2)


(2)

**(2)** **(3)** **(4)**


(3)

**(4)** **(5)**

## Experimental

Substituted benzaldehydes (4-$OCH_3$, 4-$CH_3$, 4-H, 4-Cl, 4-CN, 4-$NO_2$) and the ammonium salts were purchased from Fluka, A. G. and distilled or crystallized before use. 4-Trifluoromethylbenzaldehyde was purchased from Fluorochem and used without further purification. 3-Nitro-4-trifluoromethylbenzaldehyde was obtained in 23% yield by treatment of 4-trifluoromethylbenzaldehyde with fuming nitric acid in concentrated sulphuric acid for 2 h at 40 °C followed by neutralization, extraction, and purification on silica gel column chromatography with hexane–chloroform (1:4).

The corresponding 1,3-dioxolane were alternatively prepared from substituted benzaldehydes by reaction with ethylene glycol in toluene with toluene-*p*-sulphonic acid as catalyst, purified by distillation, and identified by n.m.r., i.r., and mass spectra.

Kinetic measurements were conducted as follows: a 0.1M solution both in aldehyde and tetrabutylammonium salt was prepared by dissolving the required amounts of these substances in dichloromethane (65 ml) and ethylene oxide (35 ml), at 0 °C. For these aldehydes which showed a fast reaction, smaller amounts of the tetrabutylammonium salts were used in order to permit analysis; however, the $k_{obs}$ values given in this work are homogeneous and referred to 0.1M solutions as above. The solution was transferred in 5 ml portions to 18 cooled (−30 °C) tubes which were rapidly sealed. The reaction was carried out in a thermostatted bath which was heated to the desired temperature (45, 60, 75, 90, or 105 ± 0.1 °C). At intervals three tubes were cooled, opened, concentrated, and analysed by g.l.c. A HP-5830A chromatograph was used with a 10% UCW-982F14 2 m × 1/4 in column and the analysis conditions were characteristic of each aldehydes. The mean values (for the three tubes) of measured areas (formed acetal and unchanged aldehyde) were corrected by interpolation on a calibration curve. The operation was carried out at six time intervals. For each aldehyde the measurements were made at three different temperatures.

This procedure was repeated three times using different tetrabutyalammonium halides (chloride, bromide, or iodide), in order to find the influence of the halide.

Determination of the equilibrium constant for the ring opening of ethylene oxide in the presence of tetrabutylammonium halides in dichloromethane solution was carried out as follows: 0.1M solution of tetrabutylammonium halide* (chloride, bromide, or iodide) and 10M solution of ethylene oxide in dichloromethane was sealed in a Pyrex tube (3 tubes for each halide containing 5 ml solution). The tubes were heated in different runs at 45, 60, or 75 °C respectively, for 1 h. The reaction was quenched by cooling the tubes at −12 °C, opening, and throwing the solution on water. Fast titration with 0.0241M-HCl gave a close measurement of the concentration of 2-halogenoethoxide ion, from which $K_{eq}$ can be calculated. The analysis of kinetic data was carried out according to ref. 6.

## Results

The reaction is first order in the aldehyde as shown by the linear relation observed between the initial concentration of the reactant and the concentration of the acetal formed after a specific time. Similar linear relations were obtained for the three different ammonium salts, when plotting the initial concentration of halide *versus* the logarithm of the concentration of the unchanged aldehyde or *versus* the concentration of formed acetal. From this preliminary work we obtained the concentrations that defined the work limits in the determination of the rate constants, and the best experimental conditions to perform the reaction: initial concentration of aldehyde 0.1M, initial concentration of halide 0.1M, with a big excess of ethylene oxide. Also in this preliminary work we observed that 3-nitro-4-trifluoromethylbenzaldehyde (NTB) did not give a linear correlation with the acetal formed: the final concentration of acetal is independent of the initial concentration of this aldehyde.

For the proposed mechanism based on reactions (1)—(3), the following equations can be established, keeping in mind that the reaction is first order in aldehyde, first order in halide [although its concentration remain constant since it is regenerated after cyclization of (**4**)] and that the concentration of ethylene oxide is also constant due to the experimental conditions. We assume also that reaction (3) is totally shifted to the right, *i.e.* the acetal would be stable under the experimental conditions ($k_3 \gg k_{-2}$).

$$\begin{aligned}d[XCH_2CH_2O^-]/dt = {} & k_1[X^-][C_2H_4O] \\ & - k_{-1}[XCH_2CH_2O^-] + k_{-2}[(4)] \\ & - k_2[XCH_2CH_2O^-][Ald]\end{aligned} \quad (4)$$

If the steady-state principle is taken into account for the concentration of the 2-halogenoethoxide anion, then we have equation (5). Since the concentration of the intermediate (**4**) is assumed to be small, equation (5) becomes (6).

$$-d[Ald]/dt = \frac{k_1k_2[X^-][C_2H_4O][Ald]}{k_{-1} + k_2[Ald]} - \frac{k_{-2}k_{-1}[(4)]}{k_{-1} + k_2[Ald]} \quad (5)$$

$$-d[Ald]/dt = \frac{k_1k_2[X^-][C_2H_4O][Ald]}{k_{-1} + k_2[Ald]} \quad (6)$$

Two extreme cases can be considered for equation (6). (i) When $k_2 \ll k_{-1}$, *i.e.* when the back reaction for the formation of oxirane is much faster than nucleophilic attack by the 2-halogenoethoxide anion to the carbonyl group. In this case we have relationship (7). (ii) When $k_2 \gg k_{-1}$, *i.e.* when the formation of intermediate (**4**) is faster than the reclosing of the 2-halogenoethoxide anion to give the oxirane, equation (8) holds.

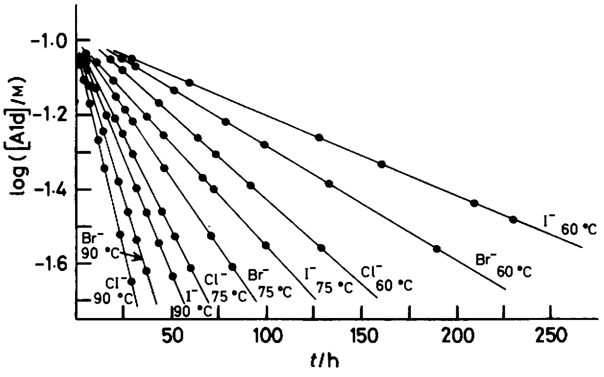


**Figure 1.** Plots for the determination of *k* on the reaction of 4-chlorobenzaldehyde (0.1M initial concentration), ethylene oxide (big excess, 6M), and tetrabutylammonium halides (0.025M) at three different temperatures. The value of *k* in Table 1 are homogeneous and referred to 0.1M concentration of the ammonium halide

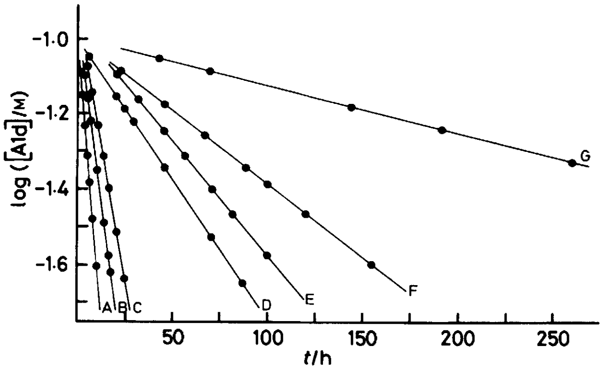


**Figure 2.** Determination of *k* on the reaction of different *p*-R-benzaldehydes (0.1M initial concentration), ethylene oxide, and tetrabutylammonium bromide (0.025M): (R and reaction temperature are given), A ($NO_2$, 60 °C), B (CN, 60 °C), C ($CF_3$, 60 °C), D (Cl, 75 °C), E (H, 75 °C), F ($CH_3$, 90 °C), G ($OCH_3$, 90 °C)

$$-d[Ald]/dt \simeq k_{obs.}[Ald] \quad (7)$$

$$-d[Ald]/dt = k_{obs.} \quad (8)$$

All the observed rate constants ($k_{obs.}$) with the exception of that for NTB were deduced from plots log[Ald] − log$[Ald]_i$ = 2.3 $k_{obs.}t$ which fitted equation (7) with errors of *ca.* 2.5%. Figures 1 and 2 give some of these plots, and Table 1 gives values of $k_{obs.}$ for all the aldehydes used, at three different temperatures each, and for the three tetrabutylammonium halides. 3-Nitro-4-trifluoromethylbenzaldehyde has a kinetic behaviour that fits only equation (8), *i.e.* only straight lines are obtained when $[Ald] - [Ald]_i = k_{obs.}t$ (see Figure 3).

The activation parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were obtained from the above kinetic data through the Eyring equation and the usual graphical methods and are given in Table 2.

The equilibrium constant for equation (1) has also been determined. Brönsted *et al.*[7] and Porret[8] have given values for this reaction when water is used as solvent. We have somewhat modified the experimental method reported by Brönsted to find the equilibrium constants at different temperatures and halides

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* A 0.025M concentration of halide was used in the plots since it gives lower slopes although much longer kinetic runs were needed when using this concentration.

**Table 1.** Experimental rate constants[a] ($k_{obs.}$/s$^{-1}$) for the formation of ethylene acetals of several benzaldehydes in the presence of tetrabutylammonium halide [$N^+(C_4H_9)_4X^-$]. The values of $k_{obs.}$ are referred to 0.1M initial concentration of both aldehyde and ammonium salt. The last column refers to zeroth-order rate constants ($k_{obs.}$/mol l$^{-1}$ s$^{-1}$)

| R-$C_6H_4$-CHO | | 4-MeO | 4-Me | 4-H | 4-Cl | 4-$CF_3$ | 4-CN | 4-$NO_2$ | 3-$NO_2$-4-$CF_3$ |
|---|---|---|---|---|---|---|---|---|---|
| $X^-$ | [$T$/°C] | ($10^6k$) | ($10^6k$) | ($10^6k$) | ($10^5k$) | ($10^5k$) | ($10^4k$) | ($10^4k$) | ($10^5k$) |
| $Cl^-$ | 45 | | | | | 3.85 ± 0.01 | 0.57 ± 0.01 | 0.81 ± 0.01 | 0.55 ± 0.01 |
| | 60 | | | | 1.17 ± 0.01 | 9.78 ± 0.02 | 1.55 ± 0.01 | 2.52 ± 0.03 | 2.01 ± 0.03 |
| | 75 | 0.52 ± 0.02 | 1.54 ± 0.01 | 5.52 ± 0.07 | 2.64 ± 0.02 | 22.8 ± 0.7 | 3.87 ± 0.04 | 7.07 ± 0.09 | 6.51 ± 0.07 |
| | 90 | 1.20 ± 0.02 | 3.45 ± 0.02 | 11.8 ± 0.1 | 5.60 ± 0.02 | | | | |
| | 105 | 2.59 ± 0.07 | 7.24 ± 0.04 | 23.7 ± 0.1 | | | | | |
| $Br^-$ | 45 | | | | | 2.72 ± 0.02 | 0.44 ± 0.02 | 0.64 ± 0.01 | 0.94 ± 0.02 |
| | 60 | | | | 0.80 ± 0.01 | 7.43 ± 0.02 | 1.31 ± 0.02 | 2.12 ± 0.12 | 3.19 ± 0.01 |
| | 75 | 0.36 ± 0.01 | 1.12 ± 0.01 | 3.88 ± 0.04 | 1.93 ± 0.02 | 18.5 ± 0.2 | 3.53 ± 0.03 | 6.30 ± 0.06 | 9.74 ± 0.12 |
| | 90 | 0.80 ± 0.02 | 2.50 ± 0.01 | 8.83 ± 0.03 | 4.35 ± 0.05 | | | | |
| | 105 | 1.67 ± 0.01 | 5.23 ± 0.02 | 18.7 ± 0.1 | | | | | |
| $I^-$ | 45 | | | | | 1.80 ± 0.02 | 0.30 ± 0.01 | 0.47 ± 0.01 | 1.45 ± 0.01 |
| | 60 | | | | 0.56 ± 0.01 | 5.09 ± 0.05 | 0.92 ± 0.01 | 1.62 ± 0.01 | 4.61 ± 0.04 |
| | 75 | 0.26 ± 0.01 | 0.63 ± 0.01 | | 1.40 ± 0.02 | 13.1 ± 0.1 | 2.53 ± 0.03 | 5.02 ± 0.03 | 13.2 ± 0.2 |
| | 90 | 0.55 ± 0.01 | 1.39 ± 0.03 | | 3.26 ± 0.02 | | | | |
| | 105 | 1.10 ± 0.04 | 2.88 ± 0.03 | | | | | | |

[a] 90% Confidence limit.

**Table 2.** Activation energy parameters[a] ($\Delta H^{\ddagger}$/kcal mol$^{-1}$ and $\Delta S^{\ddagger}$/cal K$^{-1}$ mol$^{-1}$) for the reaction of several substituted benzaldehydes with ethylene oxide in the presence of tetrabutylammonium halides

| R-$C_6H_4$-CHO | 4-MeO | 4-Me | 4-H | 4-Cl | 4-$CF_3$ | 4-CN | 4-$NO_2$ |
|---|---|---|---|---|---|---|---|
| $\Delta H^{\ddagger}_{Cl^-}$ | 13.2 ± 0.4 | 12.7 ± 0.2 | 12.0 ± 0.2 | 11.8 ± 0.2 | 12.3 ± 0.2 | 13.3 ± 0.2 | 15.1 ± 0.2 |
| $\Delta H^{\ddagger}_{Br^-}$ | 12.7 ± 0.3 | 12.7 ± 0.2 | 13.0 ± 0.2 | 12.8 ± 0.2 | 13.3 ± 0.2 | 14.5 ± 0.4 | 16.0 ± 0.5 |
| $\Delta H^{\ddagger}_{I^-}$ | 11.9 ± 0.4 | 12.6 ± 0.1 | | 13.4 ± 0.3 | 13.8 ± 0.2 | 14.9 ± 0.4 | 16.7 ± 0.3 |
| $\Delta S^{\ddagger}_{Cl^-}$ | −48.7 ± 1.5 | −47.5 ± 0.8 | −47.7 ± 0.7 | −44.8 ± 0.8 | −39.7 ± 0.8 | −35.0 ± 0.7 | −28.7 ± 0.4 |
| $\Delta S^{\ddagger}_{Br^-}$ | −50.7 ± 1.3 | −48.2 ± 0.8 | −45.5 ± 0.7 | −42.5 ± 0.8 | −37.2 ± 0.6 | −31.8 ± 1.1 | −26.2 ± 1.0 |
| $\Delta S^{\ddagger}_{I^-}$ | −53.7 ± 1.9 | −49.8 ± 1.1 | | −41.5 ± 0.9 | −36.5 ± 0.7 | −31.3 ± 0.9 | −24.7 ± 0.6 |

[a] 90% Confidence limit.

**Table 3.** Equilibrium constants ($10^3$ $K_{eq}$/l mol$^{-1}$) for the reaction of ethylene oxide with tetrabutylammonium halides in water as solvent

| $N^+(C_4H_9)_4X^-$ | 45 °C | 60 °C | 75 °C |
|---|---|---|---|
| $Cl^-$ | 0.80 | 0.44 | 0.08 |
| $Br^-$ | 1.85 | 1.47 | 0.89 |
| $I^-$ | 3.77 | 3.26 | 2.80 |

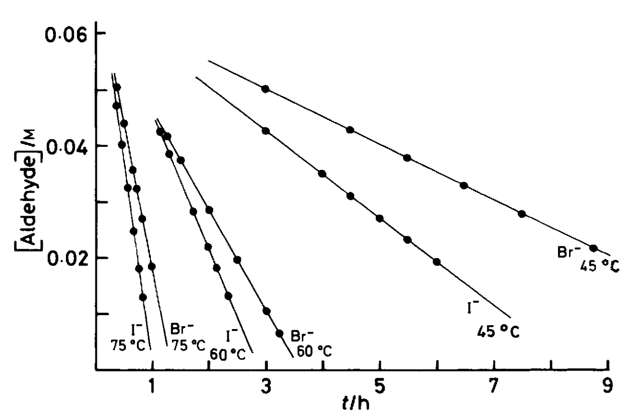

**Figure 3.** Determination of $k$ for the reaction of 3-nitro-4-trifluoromethylbenzaldehyde (0.06M initial concentration), ethylene oxide, and tetrabutylammonium halides (0.025M) at three different temperatures

using dichloromethane as solvent and water as quencher of the reaction. The values for those constants are given in Table 3 and are in agreement with those reported by Brönsted.

## Discussion

From the kinetic data given in Table 1 it can be observed that the reaction under study has a strong dependence on the electrophilic capacity of the carbonyl carbon atoms. Thus, while $k_{obs.}$ for 4-methoxybenzaldehyde, when tetrabutyammonium chloride is used as the source of halide ions, has a value of $5.26 \times 10^{-7}$ s$^{-1}$ at 75 °C, 4-nitrobenzaldehyde under the same conditions has $k_{obs.}$ $1.4 \times 10^{-4}$ s$^{-1}$, *i.e.*, 4-nitrobenzaldehyde reacts 1 500 times faster than 4-methoxybenzaldehyde at 75 °C. This indicates that the rate-determining step for this reaction is represented by equation (2), *i.e.* nucleophilic attack of the 2-chloroethoxide anion on the carbonyl group of the aldehyde.

The effect of the halide ion is quite unexpected. From the kinetic data of Table 1, and taking the two extreme aldehydes mentioned above, at 45 °C, the ratio of $k_{obs.}Cl^-$:$k_{obs.}I^-$ is 1.7, more or less the same for other aldehydes.

Therefore using chloride seems to enhance the reaction, which is not compatible with the pre-equilibrium (1). The equilibrium constants for this equation (see Table 3) are in agreement with the known order of nucleophilicity $I^- > Br^- > Cl^-$ which means that the 2-iodoethoxide anion has to be present in higher concentration than the 2-chloroethoxide anion by a factor of 4. However, steric factors can play a role

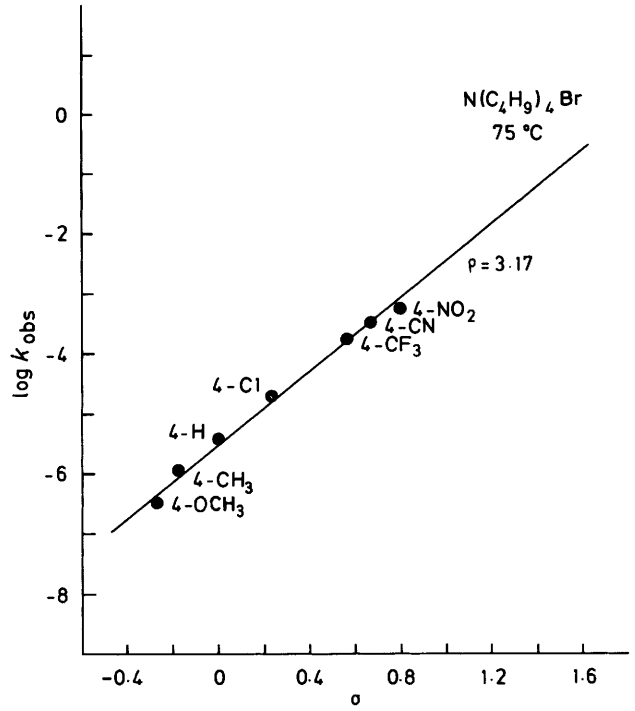

**Figure 4**. Hammett representation of log $k_{obs.}$ *versus* σ, at 75 °C in the case of tetrabutylammonium bromide

sufficient to produce the observed kinetic rates in favour of the smallest 2-chloroethoxide anion.

In fact, for the extremely activated 3-nitro-4-trifluoromethylbenzaldehyde, which follows pseudo-zero-order kinetics, $k_{obs.}$ follows the order $I^- > Br^- > Cl^-$ since the rate-determining step is the pre-equilibrium (1). In this reaction the aldehyde has the effect of an internal probe or scavenger of the 2-halogenoethoxide ion formed.

The change of mechanism can also be seen by a Hammett representation of log $k_{obs.}$ *versus* σ. Normal values of the substituent constants have been taken, since in the transition state, although some negative charge is created, it is not directly conjugated with the substituent groups. Figure 4 shows a linear Hammett correlation at 75 °C for tetrabutylammonium bromide. Similar correlations have been obtained for the other halides and temperatures. NTB, with pseudo-zero-order kinetics, does not fit and cannot be compared in this correlation. A positive ρ value (mean value 3.20) also indicates that in the transition state electrons are captured and that acceleration of the reaction takes place with electron-withdrawing groups. This value is in agreement with well known reactions such as semicarbazide formation[9] (ρ 2.36 at pH 3.9) and the saponification of ethyl benzoate (ρ 2.54).[10]

The values of the activation parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are also consistent with the behaviour of similar substances under nucleophilic attack: $\Delta H^\ddagger$ increases with the increasing electron-withdrawing power of the substituent and $\Delta S^\ddagger$ becomes much less negative.

We think, therefore, that we have verified the proposed mechanism for the formation of 1,3-dioxolanes or ethylene acetals by reaction of aldehydes and ethylene oxide in the presence of tetrabutylammonium halides. The mechanism involves the generation of 2-halogenoethoxide anions, a rate-determining step for nucleophilic attack of this anion on the carbonyl group of the aldehyde, and catalytic action by the halide since it is recovered at the end of the reaction. Very activated aldehydes react through the same steps but a change in the rate-determining step is observed; in those cases the rate-determining step is the formation of the 2-halogenoethoxide ion which reacts with the substrate as soon as it is formed.

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