Registry No.—I, 1871-53-0; II, 1002-35-3; III (all *trans*), 15192-80-0; III (*cis,trans,trans*), 14947-19-4; III (*cis,cis,cis*), 14947-20-7; IVb, 14947-21-8; IVc, 14947-22-9; VI, 15077-07-3.

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Aldehyde and Ketone Condensation Reactions Catalyzed by Boric Acid

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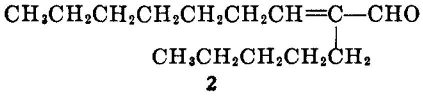
Aldol condensation and dehydration reactions using boric acid, boron oxide and 10-hydroxy-10,9-boroxarophenanthrene as catalysts were studied. Heptanal (**1**) gave 2-pentyl-2-nonenal (**2**) nearly quantitatively. Acetophenone (**3**) gave *trans*-1,3-diphenyl-2-buten-1-one (**4**). Benzaldehyde (**5**), 4-methoxybenzaldehyde (**6**), and 4-nitrobenzaldehyde (**7**) each reacted with **3** to give 1,3-diphenyl-2-propen-1-one (**8**) and substituted derivatives. Acetophenone **3** reacted at equal rates with both components of mixtures of **5** with **6** and **5** with **7**, suggesting that the rate-determining step involved only **3**. Competitive reactions of nonanal (**10**) with heptanal-2,2-d_2 (**12**) showed a deuterium isotope effect of 4. An enol borate or a partial enol borate is suggested as an intermediate, the formation of which is rate determining.

Wayne and Adkins[2] have cited a variety of acids and bases which catalyze the aldol condensation of ketones and subsequent dehydration to form α,β-unsaturated ketones. They further observed that aluminum *t*-butoxide had advantages over many of these reagents. Both the condensation and dehydration occurred in one step, the alkoxide acting both as catalyst for the condensation and as dehydrating agent. In the latter step, inactive products are formed from the catalyst. They generally obtained high yields of the desired products. In some cases, however, small amounts of high molecular weight products were formed. Further, they found it necessary to use at least 1 mole of the alkoxide for 3 moles of the ketone.

Kuivila and coworkers,[3] in a study of the reduction of carbonyl compounds with isopropyl borate, reported, in the case of heptanol (**1**), that 2-pentyl-2-nonenal (**2**) was formed through condensation and dehydration in greater yield (20.5%) than that of the reduced product, heptanal (17.5%). A large amount of higher molecular weight "condensation product" was also reported.

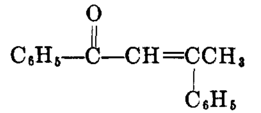
Now, a convenient and efficient method has been found for condensing aldehydes and ketones using boric acid or boron oxide as catalyst. The α,β-unsaturated aldehydes and ketones produced did not react further. This resulted in high yields of the primary condensation products.

Heptanal **1** under dehydrating conditions which existed (1) when boric acid was used and water was azeotropically removed or (2) when a molar quantity of "porous" boron oxide[4] was used gave nearly quantitative yields of 2-pentyl-2-nonenal **2**. Acetophenone (**3**) reacted slowly by the first method to give only *trans*-1,3-diphenyl-2-buten-1-one (**4**). Benzaldehyde (**5**), 4-methoxybenzaldehyde (**6**), and 4-nitrobenzaldehyde (**7**) each reacted with **3** to give 1,3-diphenyl-2-propen-1-one (**8**) and substituted derivatives in high yield.



$$\underset{CH_3CH_2CH_2CH_2CH_2}{CH_3CH_2CH_2CH_2CH_2CH_2CH{=}C{-}CHO}$$

2



$$C_6H_5{-}\overset{\overset{O}{\|}}{C}{-}CH{=}\underset{C_6H_5}{C}CH_3$$

4

Most of the work involved the use of boric acid and a solvent such as *m*-xylene which allowed water removal through the use of a Dean–Stark trap. Boric acid was only slightly soluble in this system. Varying the amount of the catalyst used had little, if any, effect on the reaction rates, suggesting that only the soluble portion was effective as a catalyst.

Increasing the concentration of **1** relative to the solvent markedly increased the rate of reaction. In several experiments with **1** using no solvent, but a stream of nitrogen to remove the water formed, the rate of formation of **2** was increased greatly. Conversion of **1** was complete in 2 hr as opposed to about 18–20 hr when *m*-xylene was used as solvent. It seems probable that the rate in these cases was limited by the efficiency of water removal. Boric acid was completely soluble in the medium in these experiments. In the absence of a solvent, however, a variety of products were formed from **1** in addition to **2**. Similarly, **3** when heated with boric acid in the absence of a solvent reacted much more rapidly to give the expected **4**, but again yielded a by-product.

The selectivity of the catalyst is demonstrated by an attempt to react the unsaturated aldehyde **2** with cyclohexanone (**9**). At the termination of the reaction, all of the **9** had disappeared to form a complicated mixture of products. At the same stage, none of the aldehyde **2** had undergone reaction.

The use of boron oxide as both catalyst and dehydrating agent potentially increases the versatility of the reaction by allowing the use of reactants such as acetone, etc., from which it is difficult to remove water. Knowledge of this variation to date is limited to **1** which gave a quantitative yield of **2** in 24 hr in refluxing dioxane.

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(1) Author to whom inquiries should be directed.

(2) W. Wayne and H. Adkins, *J. Am. Chem. Soc.*, **62**, 3401 (1940).

(3) H. G. Kuivila, S. C. Slack, and Pentti Siiteri, *ibid.*, **73**, 123 (1951).

(4) Willy Lange, *Inorg. Syn.*, **2**, 22 (1946).

TABLE I

REACTIONS OF BENZALDEHYDES WITH ACETOPHENONE

Time, hr	Vpc peak areas, %							
	Benzaldehyde	Acetophenone	Product	4-Methoxybenzaldehyde	Acetophenone	Product	4-Nitrobenzaldehyde[a]	Acetophenone
0 (theory)	8.6	9.8		10.8	9.6		11.9	9.4
0 (found)	7.4	9.2		8.9	9.4		8.7	8.7
17	2.6	3.6	6.5	5.0	4.9	5.5	6.5	6.7
41	1.1	1.2	10.5	2.5	2.6	9.0	5.8	5.4
65	0.5	0.5	11.4	1.0	1.1	10.1	4.5	3.9
∞ (theory)			17.2			19.2		

[a] The 4-nitrobenzalacetophenone was insoluble in the cooled samples, therefore did not appear in the vpc.

TABLE II

COMPETITIVE REACTIONS OF BENZALDEHYDE AND 4-METHOXYBENZALDEHYDE WITH ACETOPHENONE

Time, hr	Vpc peak areas, %				
	Benzaldehyde	4-Methoxybenzaldehyde	Acetophenone	Benzalacetophenone	4-Methoxybenzalacetophenone
0 (theory)	4.3	5.5	9.7		
0 (found)	4.1	4.6	9.1		
6	2.4	2.9	6.2	1.9	1.9
24	0.5	1.0	2.1	6.8	6.8

10-Hydroxy-10,9-boroxarophenanthrene[5] also converts heptanal into 2-pentyl-2-nonenal quantitatively.

The effect on the over-all rate of deuterating aldehyde **1** in the α positions was determined. It was felt, since the reactor used was not suited to precise studies of rate, that an internal competition would be most meaningful. Accordingly, the condensation of a mixture of **1** with nonanal (**10**) was studied by the same method used for **1** alone. Analysis of the products by vapor phase chromatography (vpc) gave three peaks. The first was **2**. The last was 2-heptyl-2-undecenal (**11**) identified by comparison of its vpc retention time with the same material prepared by condensation of aldehyde **10** alone. The intermediate peak was assumed to be an equimolar mixture of the two possible mixed condensation products. The per cent peak areas of 3.1:6.7:3.8 checked very closely to those expected from completely random reaction; *i.e.*, 1:2:1 on a molar basis. Heptanal-2,2-d_2 (**12**) was then condensed similarly with **10**. Three peaks were again obtained, but not in a 1:2:1 ratio. Determination of the ratio of **11** to the 2-pentyl-2-nonenal-4,4-d_2 (**13**) produced from **12** was made at several reaction times. Extrapolation of the ratio back to zero time showed a 4:1 initial preference for inclusion of **10** rather than **12** in the condensation products.

Further information was obtained from the reaction of benzaldehyde **5**, 4-methoxybenzaldehyde **6**, and 4-nitrobenzaldehyde **7** with acetophenone **3**. Table I shows the results. Both **6** and **7** reacted measurably slower than did the unsubstituted **5**. In competitive condensations between **5** and **6** and between **5** and **7** using molar ratios of **5** to **6** to **3** and of **5** to **7** to **3** of 1:2:1, each aldehyde disappeared at very nearly the same rate as its competitor, the over-all rate being nearly the same as when **5** alone was used. These results are shown in Tables II and III.

The results with the deuterated aldehyde **12** showed a step involving scission of the α-hydrogen–carbon bond to be rate controlling. Making the reasonable assumption that this would also hold true for the aldehyde–ketone condensations, these results with the benzaldehydes eliminate the dehydration step as being rate controlling since the rate of dehydration would almost certainly be influenced by the polar groups. Further, they suggest that the rate-controlling step involves only acetophenone **3**. These results are consistent with the possibility that an enol borate or partial enol borate is an intermediate and that the formation of the enol borate is the rate-controlling step in this condensation. There is, however, no direct evidence for this proposed intermediate.

TABLE III

COMPETITIVE REACTIONS OF BENZALDEHYDE AND 4-NITROBENZALDEHYDE WITH ACETOPHENONE

Time, hr	Vpc peak areas, %			
	Benzaldehyde	4-Nitrobenzaldehyde[a]	Acetophenone	Benzalacetophenone
0 (theory)	4.2	6.1	9.6	
0 (found)	3.7	4.3	8.6	
1.5	3.4	3.5	7.8	
5	2.6	2.6	6.2	
22	1.1	0.6	1.1	9.6

[a] 4-Nitrobenzalacetophenone was insoluble, not determined.

Simple enol borates (except some tetrahedral coordinate compounds) have not been reported.[6a] A related product, dibromovinyl diethylborate, has, however, been reported by Meerwein.[6]

Experimental Section

All melting points are corrected. Vpc analyses were run on a 10 ft × 1/8 in. silicone rubber column in an F & M Model 720 chromatograph. Boric acid was from J. T. Baker and was recrystallized from water before use. All other chemicals were from Matheson Coleman and Bell. Heptanal, nonanal, and benzaldehyde were purified by forming the sodium bisulfite addition compounds, washing with ether, decomposing the adduct with cold NaOH, and distilling in a rotary evaporator. Acetophenone was distilled in the rotary evaporator. Other chemicals were used as obtained. Dioxane was Chromatoquality Reagent grade.

Condensation of Heptanal (1). 1.—A stirred mixture of 37.6 g (0.33 mole) of heptanal (**1**), 12.4 g of boric acid (0.2 mole),[7] and 220 g of *m*-xylene was refluxed using a Dean–Stark

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[5] M. J. S. Dewar and R. Dietz, *Tetrahedron Letters*, **14**, 21 (1959).

[6] (a) H. Steinberg, "Organoboron Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1964, pp 27, 523–525. (b) H. Meerwein, G. Hinz, H. Majert, and H. Sönke, *J. Prakt. Chem.*, **147**, 226 (1936).

[7] Far less boric acid could be used. In another experiment, identical except that only 0.02 M of catalyst was used, a nearly quantitative yield of **2** was formed at the same rate as when the larger amount of boric acid was used. No attempt was made to determine the minimum amount of catalyst that could be used.

trap to remove water. The volume of water collected agreed with vpc in every case as a method for following the degree of completion of reaction. Vpc showed that a small amount of **2** had been formed after 1 hr. After 18 hr, the **1** had disappeared and conversion to product was complete.[8] By comparison with a standard sample of the product in *m*-xylene, the yield of **2** was shown to be nearly quantitative. No higher boiling products were formed. The product was isolated by filtering to remove boron oxides and distilling the filtrate in a 45 cm × 0.6 cm spinning band column. The fraction boiling at 86–87° (1 mm) was identified by comparison of its infrared spectrum with a reported spectrum[9] and formation of its 2,4-dinitrophenylhydrazone, mp 129.5–130.5°. The 2,4-dinitrophenylhydrazone of **2** reported by Fuller and King[10] had mp 129°.

2.—An 18.6-g (0.3 mole) sample of boric acid was dehydrated by heating over several hours up to 192° (1 mm) in a rotating evaporator. This treatment produced 10.1 g (*ca.* 0.15 mole) of "porous" boron oxide. Traces of boron compounds were lost through entrainment. A solution of 50 g of dioxane and 22.8 g (0.2 mole) of **1** was added and refluxed with stirring for 22 hr. At this point a translucent brown solid adhered to the sides of the flask. Vpc analysis of the supernatant liquid showed it to be pure dioxane. To the cooled mixture, 2 ml of H_2O was added. A voluminous colorless solid formed. Vpc of the liquid portion showed, by comparison with a standard solution of the product, that a nearly quantitative yield of **2** had been formed.

3.—A solution of 3.8 g of **1**, 10 g of *m*-xylene, and 0.5 g of 10-hydroxy-10,9-boroxarophenanthrene[5] was refluxed using a Dean–Stark trap. After 12 hr, **1** had disappeared and conversion into **2** as measured by vpc was complete. By comparison with a standard sample of the product in *m*-xylene, the yield of **2** was shown to be nearly quantitative.

Condensation of Acetophenone (3). 1.—A stirred mixture of 2.4 g (0.02 mole) of **3**, 10.0 g of *m*-xylene, and 0.5 g (0.01 mole) of boric acid was refluxed for 47 hr using a Dean–Stark trap. Vpc showed that **4** was formed in 18% yield. The yield was determined by comparison with a standard solution. Identification was made by trapping a sample from the vpc and comparing its infrared spectrum with that of a reported spectrum.[11]

2.—A stirred mixture of 10.0 g (0.08 mole) of **3** and 0.5 g (0.01 mole) of boric acid was refluxed. After 10 hr, three products were present in the following amounts calculated from vpc per cent peak areas: **3**, 31% at a retention time of 6.6 min, an unknown, 6% at 11.1 min, and **4**, 63% at 12.2 min. The last was identified as above. By comparison with a known infrared spectrum,[12] the unknown product was shown *not* to be *cis*-1,3-diphenyl-2-buten-1-one.

Attempted Reaction of 2-Pentyl-2-nonenal (2) with Cyclohexanone (9).—A mixture of 19.6 g (0.2 mole) of **9**, 5.0 g of **2**, 1.2 g of boric acid, and 100 g of toluene was refluxed for 24 hr. Vpc showed that all of the **9** had reacted forming a complicated spectrum of products, but none of the **2** had reacted.

Deuteration of Heptanal (1).[13]—A solution of 25 g of **1**, 250 g dioxane, 625 mg of 1,2-dihydro-1-methyl-2-methyliminopyridine (**14**),[14] and 50 g of D_2O was refluxed for 18 hr. The solution was cooled; 40 g of $MgSO_4$ was added to remove water and D_2O, and it was stirred for 1 hr and filtered. Vpc showed that very little loss of **1** had occurred. Another 50 g of D_2O and 200 mg of **14** were added and refluxing was continued for 20 hr. After cooling, 20 g of Amberlyst 15,[15] which had been swelled with water and washed with dioxane was added, stirred for 6 min, and filtered. This treatment had been shown to remove effectively the amine and not to destroy heptanal. Water and D_2O were again removed by stirring with 40 g of $MgSO_4$ for 1 hr and filtering. Vpc showed the filtrate to contain (neglecting the dioxane) 85% of **1** and/or **12** and 15% of **2**. Distillation in a 45 cm × 0.6 cm spinning-band column afforded 9.9 g of product, bp 56–57° (25 mm). From the nmr spectrum, it was estimated that this product was a **1–12** mixture containing a minimum of 93% of the deuterated species.

Condensation of Nonanal (10).—Condensation of **10** in xylene solution in the presence of boric acid was carried out in the same way as was the condensation of **1**. The product, **11**, was identified by the similarity of its infrared spectrum with that of **2** and by the method used in its preparation. The vpc retention time was 8.7 min under conditions which gave a retention time of 7.2 min for **2**.

Condensation of Heptanal (1) with Nonanal (10).—A mixture of 1.14 g (0.01 mole) of **1**, 1.42 g (0.01 mole) of **10**, 10 g of *m*-xylene and 0.5 g (0.009 mole) of boric acid was stirred and refluxed for 24 hr. Vpc analysis (by peak areas) showed 3.1% of a product at a retention time of 9.4 min, 6.7% at 10.4 min, and 3.8% at 11.4 min. These correspond, respectively, very closely to the expected ratios for **2**, the two mixed condensation products, and **11**.

Condensation of Heptanal-2,2-d_2 (12) with Nonanal (10).—A mixture of 1.93 g (0.017 mole) of **12**, 2.38 g (0.017 mole) of **10**, 0.81 g (0.013 mole) of boric acid, and 20 g of toluene was stirred and refluxed. The ratio of per cent peak areas by vpc of **11–13** were at 1.5 hr, 4; at 3 hr, 3.5; at 7 hr, 2.8; at 13 hr, 2.4; and at 24 hr, 1.8. Correcting by multiplying by the inverse of the **11** to **2** ratio or $^{3.1}/_{3.8}$ from the preceding experiment to convert from a weight to a molar basis and extrapolating to 0 time gives an isotope effect of about 4.

Reaction of Benzaldehyde (5) with Acetophenone (3).—A mixture of 10.6 g (0.1 mole) of **5**, 12.0 g (0.1 mole) of **3**, 6.2 g (0.1 mole) of boric acid and 100 g of *m*-xylene was stirred and refluxed. Results of vpc analyses (% peak areas) at various times are shown in Table I. After 65 hr the product was cooled and treated with water and ether. The organic layer was evaporated *in vacuo* and the solid product triturated with petroleum ether (bp 30–60°). Benzalacetophenone (**8**) (15.4 g, 74.0%) was obtained, mp 60–62°.

Reaction of 4-Methoxybenzaldehyde (6) with Acetophenone (3).—This reaction was carried out in a fashion identical with that for **5**. Results of vpc analyses are given in Table I. The product was 18.4 g (77.3%) of 4-methoxybenzalacetophenone (**15**), mp 76–78°.

Reaction of 4-Nitrobenzaldehyde (7) with Acetophenone (3).—This reaction was carried out as above. Results of vpc analyses are given in Table I. The product was only partially soluble in ether. The insoluble portion was filtered and combined with the soluble portion obtained from the filtrate by evaporation of the solvents and trituration with a small quantity of ether. 4-Nitrobenzalacetophenone (**16**) (9.8 g, 39%) was obtained, mp 163–166°.

Competitive Condensation. Benzaldehyde (5) *vs.* 4-Methoxybenzaldehyde with Acetophenone (3).—A mixture of 5.3 g (0.05 mole) of **5**, 6.8 g (0.05 mole) of **6**, 12.0 g (0.1 mole) of **3**, 6.2 g (0.1 mole) of boric acid, and 100 g of *m*-xylene was stirred and refluxed. Results of vpc analysis at various times are shown in Table II.

Competitive Condensation. Benzaldehyde (5) *vs.* 4-Nitrobenzaldehyde (7) with Acetophenone (3).—This reaction was run in the same way as the preceding one except that 7.6 g (0.05 mole) of **7** was used instead of **6**. Results appear in Table III.

Registry No.—**1**, 111-71-7; **2**, 3021-89-4; **3**, 98-86-2; **5**, 100-52-7; **6**, 123-11-5; **7**, 555-16-8; **8**, 94-41-7; **9**, 108-94-1; **10**, 124-19-6; **12**, 15040-89-8; **15**, 959-33-1; boric acid, 10043-35-3.

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[8] A curious observation was made on several occasions during runs similar to that described. The vpc peaks of the products increased regularly with time, then gradually disappeared. At the time when all of the aldehyde had undergone reaction, the only product appearing in the vpc was the solvent. At this point, addition of enough water to dissolve the boron oxides caused the expected amount of products to reappear in the vpc. One attempt was made to isolate the presumed unsaturated aldehyde–boron oxide combination by filtration. No special precautions were taken to exclude moisture. The precipitate was washed with pentane. The resulting boron oxide was free of organic material and the product **2** was found in the filtrate. It is not understood at this time in what way the "normal" runs differ from those few runs in which the product did not appear in the vpc.

[9] Sadtler Research Laboratories, Philadelphia, Pa., Infrared Spectrum No. 652.

[10] A. T. Fuller and H. King, *J. Chem. Soc.*, 963 (1947).

[11] Sadtler Research Laboratories, Philadelphia, Pa., Infrared Spectrum No. 8687.

[12] R. E. Lutz and L. T. Slade, *J. Org. Chem.*, **26**, 4888 (1961).

[13] D. N. Kursanov and Z. N. Parnes, *Dokl. Akad. Nauk SSSR* **103**, 847 (1955); *Chem. Abstr.*, **50**, 932e (1956).

[14] A. E. Tschitschibabin and R. A. Konowalowa, *Ber.*, **59**, 2055 (1926).

[15] The acid form of a highly porous sulfonated polystyrene cation exchange resin obtained from Rohm and Haas Co., Philadelphia, Pa.