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RING-EXPANSION OF AROMATIC COMPOUNDS BY METHYLCARBENOID OF ZINC AND CADMIUM

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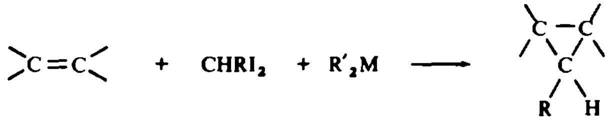
Abstract—Several 7-methylcyclohepta-1,3,5-triene derivatives have been prepared in 11–44% yield by the reaction of alkylbenzene and methylcarbenoid generated from ethylidene iodide with diethylzinc or diethylcadmium. The relative reactivity of alkylbenzene in this reaction was as follows: Benzene (0·4), toluene (1·0), ethylbenzene (1·2), cumene (1·0), *o*-xylene (2·1), *p*-xylene (2·0), and *m*-xylene (2·8). The relative reactivity showed a good correlationship with that in the Friedel–Crafts alkylation. Partial rate factors evaluated for the ring-expansion of toluene satisfied the selectivity relationship, $\log p_f^{Me} = 1{\cdot}310 \times \log(p_f^{Me}/m_f^{Me})$. Based on these results, the rate of the ring-expansion reaction was concluded to be determined by the σ-complex formation step. A stepwise mechanism was proposed for the reaction.

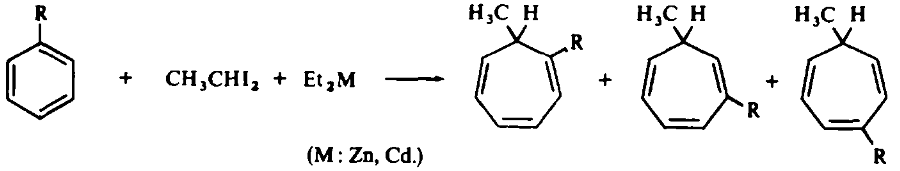
THE authors previously reported the preparation of cyclopropanes by the reaction of organozinc or organocadmium compounds with *gem*-diiodoalkanes and olefins.[1]



(i)

(R: H, CH_3, C_6H_5. M: Zn, Cd.)

The nature and the synthetic utility of this reaction were discussed[1] in comparison with Simmons–Smith reaction.[2] In this paper the authors would like to describe the ring-expansion of alkylbenzene by methylcarbenoid generated from ethylidene iodide with diethylzinc or diethylcadmium.



(ii)

(M: Zn, Cd.)

Ring-expansion of aromatic compounds by carbene, carbethoxycarbene and chlorocarbenoid has been well-known.[3] Müller *et al.*[4] reported the reaction of aromatic compounds with carbene generated from a catalytic decomposition of diazomethane with copper salts, and proposed a bimolecular two-step mechanism involving inverse ylid for the reaction.

Miller[5] proposed another bimolecular two-step mechanism for the reaction of benzene with alkylcarbenoid of aluminum.

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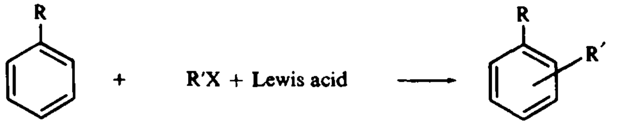
Baldwin and Smith[6] proposed a concerted mechanism for the reaction of aromatic compounds with carbethoxycarbene. The reaction (ii) is of interest in connection with these ring-expansion reactions. Since the reaction (ii) is concerned with aromatic compounds, metal alkyl (a Lewis acid) and alkyl halide, some similarity of this reaction to the Friedel–Crafts alkylation may be conceivable.



(iii)

The similarity between reactions (ii) and (iii) was investigated in order to elucidate the mechanism of the reaction (ii).

RESULTS AND DISCUSSION

Reaction of alkylbenzene with methylcarbenoid of zinc gave 7-methylcyclohepta-1,3,5-triene derivatives in 31–44% yield.

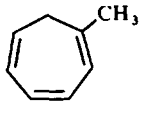
Table 1. Synthesis of 7-methylcyclohepta-1,3,5-trienes by reaction (ii)[a]

R	Yield[b] (%)	Isomer distribution of 7-methylcyclohepta-1,3,5-trienes[c] (%)
H	31[d] (11)[e]	———
CH_3	36 (19)	**1**-, 17[d](14)[e]; **2**-, 37[d](34)[e]; **3**-, 46[d](52)[e]
CH_3CH_2	39 (26)	**1**-, 12 (13); **2**-, 33 (35); **3**-, 55 (52)
$(CH_3)_2CH$	35 (26)	**1**-, 8 (11); **2**-, 30 (31); **3**-, 62 (57)
$(CH_3)_3C$	34 (27)	**1**-, 7(9); **2**-, 25·(27): **3**-, 68 (64)
o-$(CH_3)_2$	44	**1,2**-, 19; **2,3**-, 43; 3,4-, 38
m-$(CH_3)_2$	42	**1,3**-, 53; **2,4**, 47
p-$(CH_3)_2$	37	**1,4**-, 53; **2,5**-, 47
1,3,5-$(CH_3)_3$	46	———

[a] Reaction condition: CH_3CHI_2 (0·20 mole), Et_2M (0·15 mole) and RC_6H_5 (100 ml) at 80° for 10 hr.
[b] Based on CH_3CHI_2.
[c] Position of alkyl group shown in bold letter.
[d] With Et_2Zn.
[e] With Et_2Cd.

The corresponding reaction with methylcarbenoid of cadmium showed lower (11–27%) yield.

The relative reactivity of aromatic compounds in the reaction (ii) was investigated in relation to the Friedel–Crafts reaction (iii). The competitive reaction was performed with equimolar mixture of two aromatic compounds at 50°. No isomerization of products was observed, i.e., reaction (ii) with benzene gave **4**, but no isomeric product like **1**, **2** and **3** was detected in the reaction mixture.



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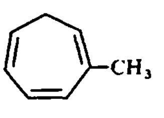

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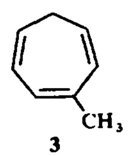

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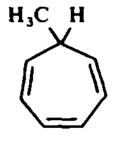

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Relative reactivity of alkylbenzenes and isomer distribution of 7-methylcyclohepta-1,3,5-triene derivatives in the reaction (ii) are summarized in Table 2.

TABLE 2. RELATIVE REACTIVITY OF ALKYLBENZENE AND ISOMER DISTRIBUTION FOR REACTION (ii)[a]

R	$k_{ArH}/k_{CH_3C_6H_5}$		Isomer ratio of 7-methyl-cyclohepta-1,3,5-triene (%)[b,d]
	Ring-expansion[b]	Friedel–Crafts alkylation[b,c]	
H	0·40	0·40	———
CH_3	1·0	1·0	1-, 22; 2-, 32; 3-, 46
CH_3CH_2	1·2	—	1-, 16; 2-, 32; 3-, 52
$(CH_3)_2CH$	1·0	—	1-, 7; 2-, 32; 3-, 61
o-$(CH_3)_2$	2·1 (1·8)	(1·9)	1,2-, 18 (18); 2,3-, 50 (50); 3,4-, 32 (32)
m-$(CH_3)_2$	2·8 (2·6)	(3·0)	1,3-, 52 (47); 2,4-, 48 (53)
p-$(CH_3)_2$	2·0 (1·3)	(1·2)	1,4-, 53 (50); 2,5-, 47 (50)

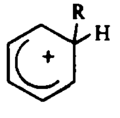
[a] Reaction condition: $Et_2Zn:CH_3CHI_2:ArH = 3:2:50$; 50°, 5 hr.

[b] These values in parenthesis were calculated by means of partial rate factors.

[c] By $EtBr–GaBr_3–ArH$ at 25°. Reference 8.

[d] Position of alkyl group shown in bold letter.

The rate determining step of Friedel–Crafts reaction has been discussed in terms of either the σ-complex (5)-formation or the π-complex (6)-formation.[7]



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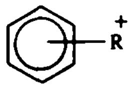

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The σ-complex formation step was concluded to determine the rate of the Friedel–Crafts ethylation of aromatic compounds by $GaBr_3$ and ethyl bromide.[8,9] The relative reactivity of alkylbenzenes in the reaction (ii) shows a good correlation with that in the Friedel–Crafts ethylation[8,9] (Table 2). As is shown in Fig 1, the relative reactivity was also correlated with the relative basicity of the alkylbenzenes toward such a σ-complex-forming agent as hydrogen fluoride–boron trifluoride mixture.[10] These findings suggest that the rate of the reaction (ii) is determined in a σ-complex formation step.

On the other hand, the following empirical relationship is known for Friedel–Crafts reaction,[7]

$$\log p_f^{Me} = 1{\cdot}310 \times \log\left(p_f^{Me}/m_f^{Me}\right) = 1{\cdot}310 \times S_f \qquad \text{(iv)}$$

where p_f^{Me}, m_f^{Me} are para and meta partial rate factors for toluene. In order to examine the adaptability of the above equation to the reaction (ii), the partial rate factors were evaluated as follows from isomer ratios of dimethylcycloheptatrienes obtained in the reaction (ii) with toluene.

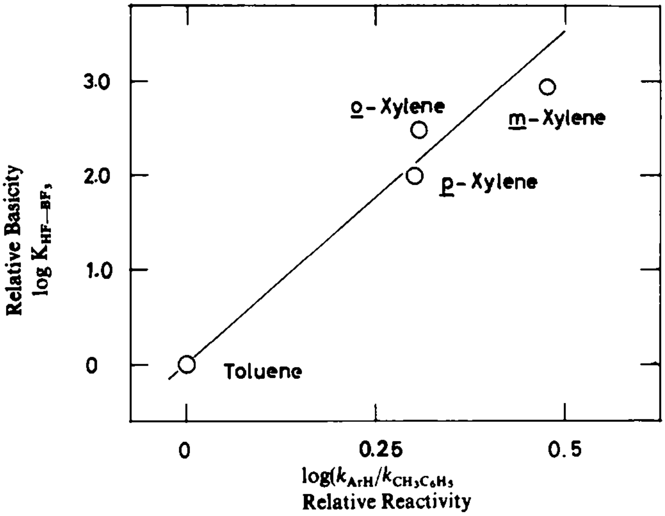
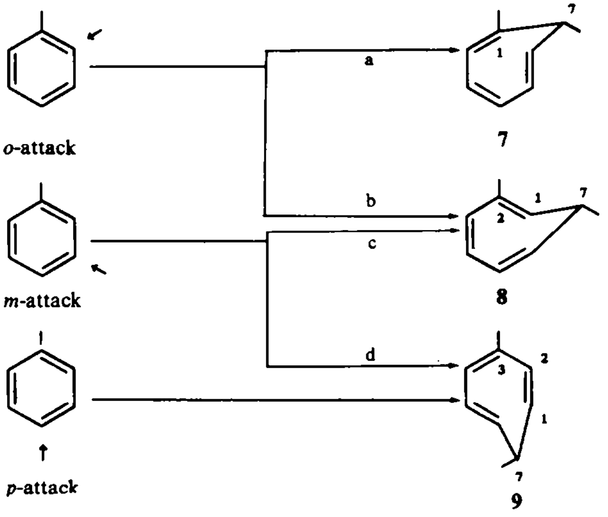


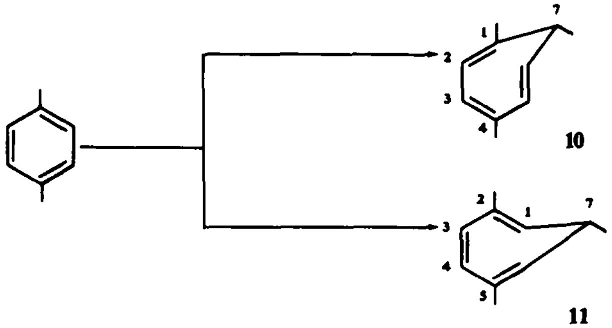
Fig 1. Relative reactivity of alkylbenzene in reaction (ii) vs. relative basicity

The *ortho* attack on toluene by the carbenoid is to produce 1,7-(7) and 2,7-dimethylcyclohepta-1,3,5-triene (8). The *meta* attack is to give 2,7- (8) and 3,7-dimethylcyclohepta-1,3,5-triene (9), while the *para* attack only the 3,7-dimethyl isomer (9).



The reaction of *p*-xylene with ethylidene iodide and diethylzinc was found to yield a nearly 1:1 mixture of 1,4,7-(10) and 2,5,7-trimethylcyclohepta-1,3,5-triene (11). Consequently, the a/b ratio is close to unity and it would be a reasonable estimation that the c/d ratio is also nearly equal to unity.

Then, the probability of attacking at *o*-position (P_o) is taken to be two times as much as the fraction of isomer 7 ($R_{1,7}$) in the isomer mixture. The probability of *m*-attack (P_m) and that of *p*-attack (P_p) can be calculated from $R_{1,7}$, together with the fraction of



isomer **8** ($R_{2,7}$) and that of isomer **9** ($R_{3,7}$) using the following equations.

$$P_o = 2R_{1,7}$$
$$P_m = 2(R_{2,7} - R_{1,7})$$
$$P_p = R_{3,7} - R_{2,7} + R_{1,7}$$

The probabilities of attacking at *o*-, *m*- and *p*-position of toluene were thus calculated and are listed in Table 3. The partial rate factors (p_f^{Me}, m_f^{Me} and o_f^{Me}) and the selectivity factor (S_f) were calculated with the equations defined in literature[7] and are summarized in Table 3 together with the factors for the Friedel–Crafts alkylation[8,9] and the ring-expansion by inverse ylid.[4d] Relative reactivity and isomer ratio of *o*-, *m*- and *p*-xylene in the reaction (ii) were calculated by the usual method[7] from the partial rate factors obtained. Good agreement between calculated and observed values of the relative reactivity and the isomer ratio for xylenes indicates the reasonableness of the assumption that a/b and c/d ratios are nearly equal to unity (Table 2).

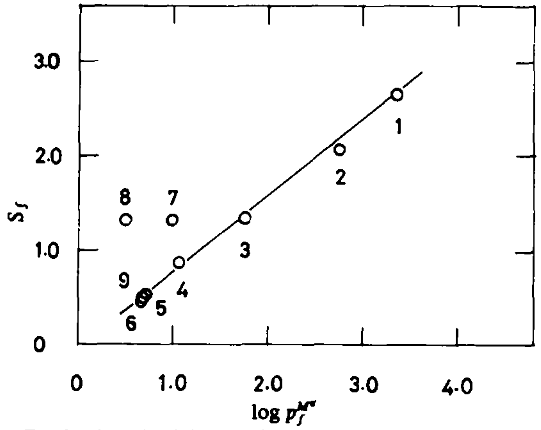


Fig 2. The selectivity relationship in aromatic electrophilic substitution[7]

1. Bromination by Br_2 in $HOAc–H_2O$ at 25°
2. Benzoylation by PhCOCl and $AlCl_3$ in ArH at 25°
3. Bromination by HOBr and $HClO_4$ in 50% dioxane at 25°
4. Methylation by MeBr and $GaBr_3$ in ArH at 25°
5. Ethylation by EtBr and $GaBr_3$ in ArH at 25°
6. Isopropylation by *i*-PrBr and $GaBr_3$ in ArH at 25°
7. Benzylation by $PhCH_2Cl$ and $AlCl_3$ in $MeNO_2$ at 25°
8. Nitration by $NO_2–BF_4$ in $C_4H_8SO_2$ at 25°
9. Ring-expansion by CH_3CHI_2 and Et_2Zn in ArH at 50°

TABLE 3. PARTIAL RATE FACTORS AND SELECTIVITY FACTOR FOR TOLUENE

No.	Reaction, conditions[a]	k_T/k_B[b]	Attacking part			Partial rate factor			S_f
			o	*m*	*p*	o_f	m_f	p_f	
1	Ring-expansion CH_3CHI_2–Et_2Zn, ArH, 50°C	2·5	44	20	36	3·3	1·5	5·4	0·56
2	Ethylation CH_3CH_2Br–$GaBr_3$, ArH, 25°[d]	2·47	38·4	21·0	40·6	2·84	1·56	6·02	0·59
3	Isopropylation $(CH_3)_2CHBr$–ZnI_2, $CH_3C_6H_5$, 25°[e]	—	42	21	37	—	—	—	—
4	Isopropylation $(CH_3)_2CHBr$–$AlCl_3$, CH_3NO_2, 25°[f]	1·65	47·7	18·2	35·1	2·36	0·90	3·47	0·59
5	Ring-expansion CH_2N_2–CuBr, ArH, 80–140°[g]	1·0	64	0	36	—	—	—	—

[a] The reaction is given first, followed by reagents, solvent and temp

[b] T and B mean toluene and benzene, respectively

[c] CH_3CHI_2:Et_2Zn:ArH = 2:3:50, 50°, 5 hr

[d] Ref 9

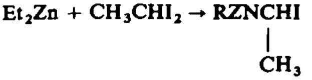
[e] G. A. Olah, S. H. Flood, S. J. Kuhn, M. E. Moffatt and N. A. Overchuck, *J. Am. Chem. Soc.* **86**, 1046 (1964)

[f] G. A. Olah and N. A. Overchuck, *Ibid.* **87**, 5786 (1965)

[g] Ref 4*d*

Partial rate factors and selectivity factor in reaction (ii) are close to those in the Friedel–Crafts alkylation[8,9] (Table 3). The selectivity factor and para partial rate factor for the reaction (ii) also obey the linear relationship (iv) as shown in Fig. 2. This finding supports the estimation that the rate determining step of the reaction (ii) is the σ-complex formation.*

Thus, the following stepwise mechanism is proposed for the ring-expansion of aromatic compounds by methylcarbenoid.



$$Et_2Zn + CH_3CHI_2 \rightarrow \underset{\displaystyle CH_3}{RZnCHI}$$

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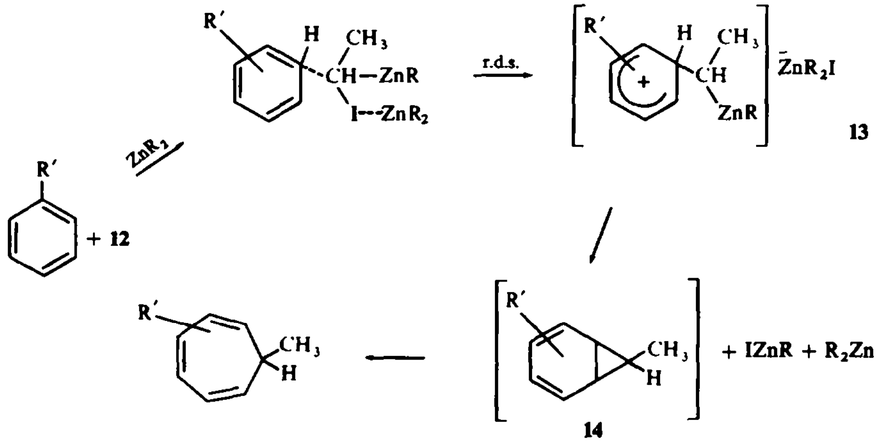
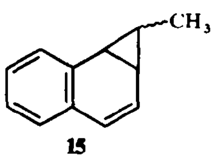


The formation of norcaradiene derivatives (14) as a transient intermediate is not clear. However, 7-methyl-2,3-benzobicyclo[4.1.0]hepta-2,4-diene (15) was obtained when naphthalene was reacted with methylcalbenoid of zinc.[13]



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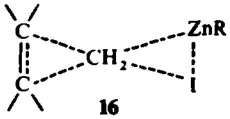
The mechanism proposed for the reaction (ii) resembles a bimolecular two-step process of the mechanism suggested by Hoberg for the reaction of chloromethylaluminum compound with olefin.[14] On the other hand, a bimolecular, one-step methylene transfer mechanism was proposed for the cyclopropane formation by the reaction of iodomethylzinc compound with olefin, where the iodomethylzinc reagent reacts with the olefin through a multi-center transition state (16).[2]



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* Olah discovered two major discrepancies from equation (iv), i.e., nitration with nitronium fluoroborate[11] and benzylation[12] as is shown in Fig 2, and suggested that in these cases, the rate is determined by a slow formation of a π-complex followed by a rapid isomerization to benzenium ion.

This difference between the mechanism proposed for cyclopropane formation from olefin and that for the ring-expansion of aromatic compounds may be ascribable to the difference in stability of intermediates; benzenium ion (13) may be more stable than alkylcarbonium ion.

EXPERIMENTAL

Analyses were performed at the Elemental Analysis Center of Kyoto University. IR spectra were recorded on a Hitachi EPI-G spectrophotometer. NMR spectra were taken on a Varian Model A-60 or Japan Electron Optics Lab. Model C60H spectrometer, in CCl_4 using TMS as internal standard. VPC were obtained on a Shimadzu GC-2C gas chromatograph. All b.ps were uncorrected.

Materials. t-Butylbenzene was prepared according to a conventional procedure.[15] Other alkylbenzenes were commercial products of high purity and were purified by usual methods before use.[16] Other reagents were prepared as described in previous papers.[1]

*7-Methylcyclohepta-*1,3,5-*triene derivatives from alkylbenzene (general procedure).* A 3-necked, round-bottomed flask equipped with thermometer, dropping funnel, 3-way cock and magnetic stirring bar was evacuated and filled with dry N_2. Alkylbenzene (100 ml) and diethylzinc or diethylcadmium (0·14 mole) were added by use of hypodermic syringes. Ethylidene iodide (0·20 mole) was added through dropping funnel over a period of ½ hr while stirring at about 80°. An exothermic reaction took place immediately. After the addition was completed, the reaction mixture was allowed to stand at 80° for 10 hr, and cooled mixture was successively washed with NH_4OHaq. The aqueous layer was extracted 3 times with ether. The combined organic soln was dried over $MgSO_4$. After the solvent was evaporated, the residue was fractionally distilled through a packed column. Analytical data and physical properties of cycloheptatriene derivatives were given in Table 4. Structures of 1-, 2- and 3-substituted 7-methhlcyclohepta-1,3,5-triene were confirmed by comparing their NMR spectra in the region of τ 3 to τ 5 with those of 1-, 2- and 3-methylcyclohepta-1,3,5-triene reported by Egger.[17] Retention time of isomers in VPC analysis increased in the order, 2-, 3- and 1-substituted compound. 1-Isopropyl-7-methylcyclohepta-1,3,5-triene and 1-t-butyl-7-methylcyclohepta-1,3,5-triene were identified only by VPC, because their yields were too poor to be isolated.

TABLE 4. ANALYTICAL DATA FOR 7-METHYLCYCLOHEPTA-1,3,5-TRIENES

Starting alkylbenzene	B.p.	n_D^{20}	Anal. (Found)	
			C	H
Benzene[a]	131–132°	1·5030	——	——
Toluene[b]	100°/136	1·5049	89·94 (89·66)	10·06 (10·31)
Ethylbenzene[b]	115–116°/123	1·5027	89·49 (89·20)	10·51 (10·58)
Cumene[b]	102–103°/50	1·4989	89·12 (88·94)	10·88 (10·85)
t-Butylbenzene[b]	81–90°/16	1·4965	88·82 (88·75)	11·18 (11·40)
o-Xylene[b]	55–60°/8	1·5102	89·49 (89·27)	10·51 (10·57)
m-Xylene[b]	52–57°·10	1·5055	89·49 (89·35)	10·51 (10·48)
p-Xylene[b]	54–57°/8	1·5057	89·49 (89·34)	10·51 (10·62)
Mesitylene	60°/7	1·5082	89·12 (88·88)	10·88 (10·89)

[a] G. L. Closs and L. E. Closs (*Tetrahedron Letters* **10**, 38 (1960)), reported b.p. 132·5° and n_D^{20} 1·5030

[b] For isomer mixtures

Competitive reaction. Competitive reactions were carried out in a round-bottomed 100 ml-flask equipped with magnetic stirrer, reflux condenser, dropping funnel, thermometer and gas-inlet with 3-way cock under N_2 at 50°. Two alkylbenzenes (0·25 mole each) and diethylzinc (0·03 mole) were placed in the flask with use of hypodermic syringes and stirred. Ethylidene iodide (0·02 mole) was added dropwise within ½ hr. The reaction proceeded homogeneously. After stirring at 50° for 5 hr, the reaction mixture was washed with

NH_4Claq and analyzed. Relative reactivity was calculated by the following equation

$$k_a/k_b = P_a A_b / P_b A_a$$

where, P and A are moles of cyclohepta-1,3,5-triene and alkylbenzene, respectively. Results are given in Table 5.

TABLE 5. RELATIVE REACTIVITY OF ALKYLBENZENE IN REACTION (ii)

Alkylbenzene		A/B	$k_A/k_{toluene}$
A	B		
Benzene	Toluene	1:1	0·40
Benzene	Toluene	2:1	0·39
Ethylbenzene	Toluene	1:1	1·2
Cumene	Benzene	1:1	1·0
o-Xylene	Benzene	1:1	2·1
m-Xylene	Benzene	1:1	2·8
p-Xylene	Benzene	1:1	2·0

The first-order dependence of reaction (ii) with respect to alkylbenzene was ascertained in the competitive reaction of benzene and toluene (Table 5). Two runs showed nearly the same relative reactivity.

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