INVESTIGATIONS ON THE NATURE OF ADDITION OF ALIPHATIC DIAZO-COMPOUNDS TO CONJUGATED DOUBLE BONDED SYSTEMS : ACTION OF DIAZOMETHANE AND ETHYL DIAZO ACETATE UPON CYCLOPENTA- AND CYCLOHEXA-DIENES AND THEIR DERIVATIVES.*

By P. C. Guha and G. D. Hazra.

No systematic investigation with a view to elucidating the nature of the addition of aliphatic diazo-compounds upon compounds possessing a system of conjugated double bonds is on record. Muller and Roser (*J. pr. Chem.*, 1932, [2], **133**, 291) studied the action of aliphatic diazo compounds upon butadiene ; Heide (*Ber.*, 1904, **37**, 2101) studied the action of ethyl diazoacetate upon phenyl butadiene. Ruzicka and Staudinger (*Helv. Chim. Acta.*, 1924, **7**, 390) studied the action of ethyl diazoacetate upon methyl-butadienes and all these authors observed the addition of the diazo-compounds to 1 : 2-carbon atoms of the conjugated double bonded systems. The action of diazo-acetic ester (addition in 1 : 2 positions) upon benzene and its homologues was studied by Buchner (*Ber.*, 1900, **33**, 3453 ; 1901, **34**, 982 ; 1903, **36**, 3502 ; 1904, **37**, 931 ; *Annalen*, 1908, **358**, 1) and upon zingiberene by Ruzicka and Veen (*Annalen*, 1929, **468**, 143).

It is clear from the instances cited above that the action of aliphatic diazo-compounds have been studied in a few isolated cases with hydrocarbons containing conjugated double bonded system taking place only in 1 : 2 positions in preference to 1 : 4. Moreover, no work seems to have been on record in literature on the addition of aliphatic diazo-compounds to conjugated double bonded systems, with the 1 : 4-carbon atoms activated by attachment with negative groups like Ph, CO, CN, CO_2Et, etc. As the first experiment tried on the possibility of addition of aliphatic diazo-compounds to the 1 : 4 carbon atoms activated

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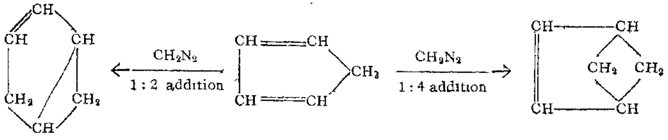
*Preliminary notes appeared in the Proceedings of the Indian Science Congress, Chemical Abstracts, 1938, paper No. 110 ; 1939, paper No. 117.

by attachment with negative groups, dimethyl diazomethane has been found to add on to diethyl muconate to yield diethyl isodehydroapocamphorate (Guha and Sankaran, *Ber.*, 1937, **70**, 2109).

Buchner's experiments with benzene and its homologues (loc. cit.) cannot, strictly speaking, be regarded as instances representing real conjugated double bonded systems. It was considered desirable, therefore, that a systematic investigation should be undertaken with cyclic compounds possessing conjugated double bonded systems, e.g., with *cyclo*pentadiene (I), $\Delta^{1:3}$-dihydrobenzene (II), and 2 : 3-dimethyl-$\Delta^{1:3}$-dihydrobenzene (III) (cantharene). The study of these reactions was of additional importance in view of the fact that in whichever manner the addition (1 : 2 or 1 : 4) takes place, the products (IV, V, VI, VI-a, VII and VII-a) would be compounds of great synthetic significance ; (IV) representing bi*cyclo*-(0 : 1 : 3)-hexane, a skeleton present in compounds of the thujane series ; (V) representing bi*cyclo*-(1 : 1 : 2)-hexane, a bridged system hitherto unknown perhaps due to its great instability ; (VI and XIII) representing bi*cyclo*-(0 : 1 : 4)-heptane, a ring skeleton present in compounds of the carane series ; and (VII) representing bi*cyclo*-(1 : 2 : 2)-heptane, a skeleton present in compounds of the camphane-fenchane series.



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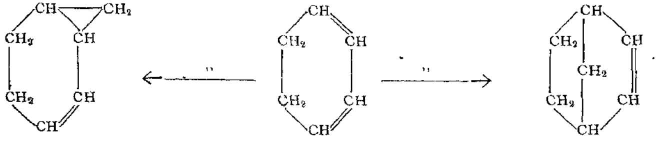

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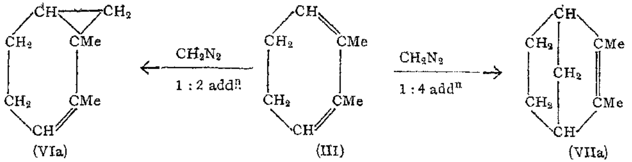
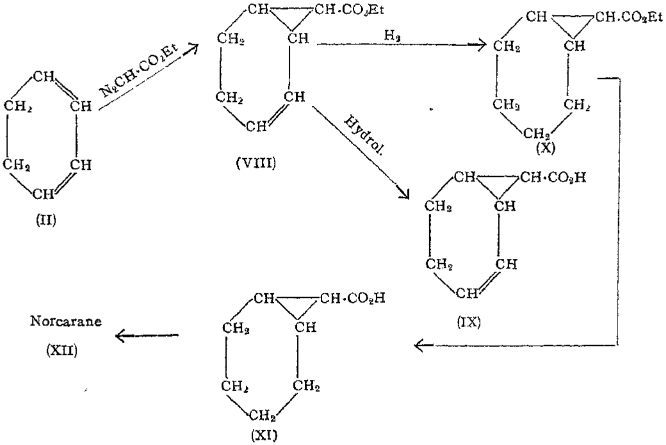


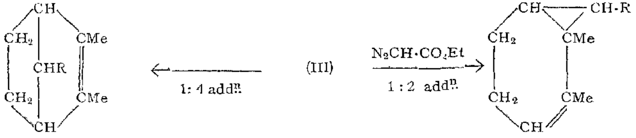
Compounds (I), (II) and (III) have been found not to react with diazomethane although the reactions were tried under various experimental conditions. *Cyclo*pentadiene reacts with ethyl diazoacetate at 0°, but the reaction mixture could not be worked up as it exploded when allowed to attain the room temperature.

$\Delta^{1 \cdot 3}$-Dihydrobenzene reacts with ethyl diazoacetate to yield ethyl norcarene carboxylate (VIII) yielding norcarene carboxylic acid (IX) on hydrolysis; anilide, m.p. 195-96°. The structure of the compound (VIII) has been established by reducing it catalytically to ethyl norcarane carboxylate (X), b.p. 112-14°/10 mm. Compound (X) yielded norcarne carboxylic acid (XI), m.p. 97°. The Ba-salt of (XI)



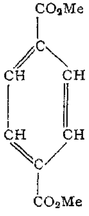
when distilled with ZnO gave norcarane (XII). All of these compounds (X, XI, and XII) are identical with the corresponding samples of Ebel, Brunner and Mangeli (*Helv. Chim. Acta.*, 1929, **12**, 19).

2 : 3-Dimethyl- $\Delta^{1\,3}$-dihydrobenzene (III) reacts quite readily with ethyl diazoacetate to yield dimethyl-norcarene carboxylic ester (XIII). This formula (XIII) is attributed to the compound in preference to (XIIIa) formed if the addition had taken place in 1 : 4-positions, by analogy with the formation of (VIII).



(XIIIa, R = CO_2Et)   (XIII)

Considerable amount of difficulty had to be overcome before methyl $\Delta^{1:3}$-dihydro-terephthalate (XIX) could be successfully prepared, there being no detail available in Baeyer's papers (*Annalen*, 1888, **245**, 103 ; 1890, **258**, 39 ; 1889, **251**, 298). This has now been prepared starting from dimethyl terephthalate (XIV) via dimethyl hexahydro-terephthalate (XV), hexahydro-terephthalic acid (XVI), methyl 1 : 4-dibromo-hexahydro-terephthlate (XVII) and $\Delta^{1\cdot3}$-dihydro terephthalic acid (XVIII). Successful preparation of compound (XV) from (XIV) and the conversion of compound (XVII) into (XVIII) necessitated adoption of new or altered methods. Baeyer (loc. cit.) reduced terephthalic acid to Δ^{1}- and Δ^{2}- tetrahydro-terephthalic acids by sodium amalgam both of which on reduction with hydriodic acid yielded hexahydro-terephthalic acid. Willstätter (*Ber.*, 1918, **51**, 776) obtained hexahydro-terephthalic acid from terephthalic acid by reducing with hydrogen in presence of platinum black at 40°C. Dimethyl terephthalate (XIV) has now been reduced directly to the hexahydro compound (XV) in presence of Adam's catalyst during 1½ hours at ordinary temperature in an yield of about 85 per cent.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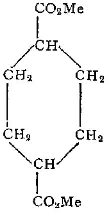
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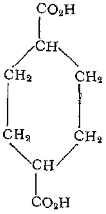
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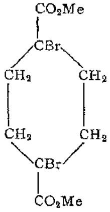
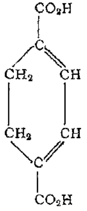
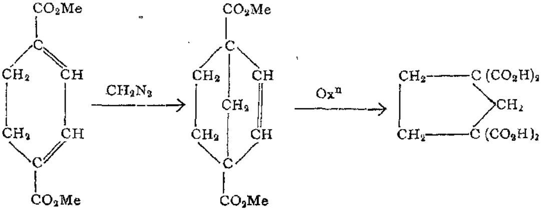
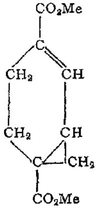

(XVII)


(XVIII)

Methyl $\Delta^{1:8}$-dihydro-terephthalate (XIX) reacts with diazomethane in ethereal solution at 0° during 48 hours to yield an oily product, b.p. 130–34°/3 mm. which could either be compound (XX) if the addition had taken place in 1 : 4-position, or compound (XXa) the addition taking place in 1 : 2 positions. To know the correct structure of the compound (XX or XXa), the product was treated with 3 per cent. potassium permanganate when *cyclo*pentane-(1 : 1 : 3 : 3)-tetracarboxylic acid, m. p. 187° (XXI) was obtained. This can only happen if the preceding compound possesses the structure (XX).



(XIX) (XX) (XXI)


(XXa)

From the results described above it can be concluded that (i) diazomethane does not react with 5 and 6 membered cyclic hydrocarbons containing a system of conjugated double bonds, (ii) ethyldiazoacetate reacts with them giving 1 : 2 addition products ; (iii) when the carbon atoms in positions 1 and 4 are attached with negative groups like CO_2Et, the addition of diazomethane takes place in 1 : 4 positions.

EXPERIMENTAL.

Action of diazomethane on cyclo*pentadiene* (I).—*Cyclo*pentadiene (I) was prepared by distilling bi*cyclo*pentadiene at the rate of 4 g. per hour in a Claisen flask having the side tube fitted with two perforated platinum discs. The distillate consisted mostly of *cyclo*pentadiene; pure *cyclo*pentadiene, b. p. 41.5°, was obtained by another distillation (Hanstobbe, *Annalen*, 1912, **391**, 151). A mixture of molecular proportion of *cyclo*pentadiene and diazomethane in dry ether was kept at 0° for a month without any reaction taking place. The reaction could not be induced to take place even with the addition of methyl alcohol as catalyst, and trying the reaction at room temperature.

Action of ethyl diazoacetate on cyclo*pentadiene.*—A mixture of molecular proportion of *cyclo*pentadiene and ethyl diazoacetate, was kept at 0° for 7 days, the dull yellow colour of ethyl diazoacetate disappearing within 24 hours. The reaction product could not be worked up, as it exploded when allowed to attain the room temperature. The reaction when tried with the addition of copper bronze as catalyst in presence of air, carbon dioxide or nitrogen, was found to take place at ordinary temperature. The product after staying overnight was heated under reflux for one hour and on being worked up yielded only a tarry product.

$\Delta^{1:3}$*-Dihydrobenzene* (II) *and diazomethane.*—$\Delta^{1:3}$-Dihydrobenzene was prepared starting from *cyclo*hexanol via. *cyclo*hexene and 1 ; 2-dibromo-*cyclo*hexane according to the method described in Organic Synthesis (vol. 5, p. 33 ; vol. 12, p. 26). In the last step viz. in the conversion of 1 ; 2-dibromo-*cyclo*hexane into $\Delta^{1:3}$-dihydrobenzene on treatment with quinoline, the yield has been considerably improved (42 g. of the dibromo compound gave 12 g. of the *cyclo*hexadiene) by allowing the temperature to rise from 140° to 160° very slowly during 3 hours (Crossley, *J. C. S.*, 1904, **85**, 1416).

Diazomethane and $\Delta^{1\cdot 3}$-cyclo*hexadiene.*—As in the case of *cyclo*pentadiene, there was no reaction between *cyclo*hexadiene and diazomethane, even when the reaction was tried at room temperature.

Action of ethyl diazoacetate on $\Delta^{1:3}$*-dihydrobenzene: Formation of ethyl norcarene carboxylate* (VIII).—To a slightly warmed mixture of $\Delta^{1:3}$-dihydrobenzene (16 g.) and copper bronze (1.5 g.) contained in a flask fitted with a reflux condenser, ethyl diazo-acetate (22.5 g.) was added drop by drop during 4 hours with frequent shaking. The mixture was then heated on water-bath for 6 hours. After filtration, the product was distilled under reduced pressure and the fraction coming at 84°/2.5 mm. collected; yield 64 per cent. (Found: C, 71.24; H, 9.2. $C_{10}H_{14}O_2$ requires C, 72.29; H, 8.43 per cent.).

Norcarene carboxylic acid (IX).—The above ester was hydrolysed with 5 per cent. alcoholic potassium hydroxide at ordinary temperature by keeping for two days and then working up as usual. The acid crystallised from 25 per cent. methyl alcohol, m. p. 82.5° (Found: Eq. Wt., 136.9. $C_8H_{10}O_2$ requires Eq. Wt., 138).

Catalytic reduction of the ester (VIII) *into ethyl norcarane carboxylate* (X).—The unsaturated ester (VIII, 10 g.), platinic oxide (0.05 g.) and methyl alcohol (200 c.c.) were taken in a sodawater-bottle placed on a shaking machine. The apparatus was exhausted by suction and then hydrogen was introduced at 2.5 atmospheric pressure. The reduction was complete under shaking within an hour. The reaction mixture after filtration was freed from methyl alcohol by distillation and the residue was distilled under reduced pressure, the fraction coming at 112–14°/19 mm. was collected. The boiling point is identical with that given by Ebel, Brunner and Mangeli (loc. cit.).

Hydrolysis of compound (X) *to norcarane carboxylic acid* (XI).—The reduced ester (X) was hydrolysed with 5 per cent. alcoholic potash in the cold during 48 hours and worked up as usual. The acid melted at 97°, m.p. as given by Ebel, Brunner and Mangeli (loc. cit.) is 97°. The identity of compound (XI) was also established by preparing norcarane (XII), b.p. 111-112° by heating the Ba-salt with zinc oxide (Ebel, Brunner and Mangeli, loc. cit.).

1 : 2-Dimethyl-Δ^1-*cyclo*hexene was prepared starting from methyl *cyclo*hexanol via. 1 : 2-dimethyl*cyclo*hexanol, according to the

method of Signaigo and Cramer (*J. Amer Chem. Soc.,* 1933, **55**, 3332). 1 : 2-Dimethyl- $\Delta^{2\ 6}$-dihydrobenzene (cantharene) was prepared from dimethyl-*cyclo*hexene as follows : Dimethyl*cyclo*hexene (33 g.) was dissolved in dry chloroform (60 c.c.) in a flask fitted with a calcium chloride guard tube and cooled to 0°. Bromine (48 g.) dissolved in chloroform (60 c.c.) was added drop by drop under stirring not allowing the temperature to rise above 0°. After the addition of bromine was over, chloroform was removed quickly from the reaction mixture under suction on a water-bath at 80°. The thick residue on cooling with freezing mixture mostly solidified and was pressed on a porous plate, the latter kept in a vacuum desiccator at 0° overnight. Next day the crystalline white powder was crystallised from 50 per cent. alcohol in colourless needles, m.p. 150° ; yield 50 g. It possesses a peculiar camphoraceous odour. This experiment is described in detail here as Meerwein does not give any detail in his paper (Annalen, 1914, **405**, 147).

*Conversion of dimethyldibromo*cyclo*hexane into* 1 : 2-*dimethyl-* $\Delta^{2\cdot 6}$ *dihydrobenzene* (*cantharene*).— Dimethyldibromo*cyclo*hexane (40 g.) was heated with freshly distilled quinoline (90 g.) as in the case of the preparation of $\Delta^{1\ 3}$-dihydrobenzene. From 85 g. of the dibromo compound, 26 g. of dimethyl *cyclo*hexadiene (III) was thus obtained. It was purified by distilling once more with little quinoline, washing the product with dilute hydrochloric acid and then with water, drying over calcium chloride and finally distilling thrice over sodium, b.p. 135°. The yield does not suffer much by this extra method of purification.

Action of diazomethane and ethyl diazoacetate upon 1:2-*dimethyl*-2 : 6-*dihydrobenzene* (*cantharene,* III).—Just as in the case of *cyclo*pentadiene (I) and *cyclo*hexadiene (II), the compound (III) have been found not to react with diazomethane. To a mixture of 1:2-dimethyl-$\Delta^{2:6}$-dihydrobenzene (III, 23 g.) and copper bronze (0.5 g.) heated to 70° in a flask, was added ethyl diazoacetate (24.2 g.) drop by drop during 4 hours and allowed to stand at that temperature for 17 hours. After filtration, the reaction product was freed from the unreacted starting materials by distilling up to 135-40° under ordinary pressure, the distillate by fractionation yielded about 9 g. of the unreacted hydrocarbon. The residual liquid on being fractionally distilled under reduced pressure gave an oil, b.p. 91-95°/2.5 mm.; yield 11 g. The recovered hydrocarbon (10 g.) yielded by reacting with ethyl diazoacetate 3 more grams of the product (XIII) (Found: C, 73.45; H, 10.1. $C_{12}H_{18}O_2$ requires C, 74.26; H, 9.77 per cent.). This ester decolorised bromine water and permanganate solution indicating unsaturation.

The ester (XIII, 9.5 g.) was hydrolysed with 5 per cent. alcoholic potash, by keeping at the room temperature for 2 days. After being worked up as usual, an acidic substance was obtained which did not melt sharp. A portion of this acid mixture was found to be readily soluble in could benzene, from which solution an acid melting sharply at 140° was isolated. The benzene insoluble portion was easily cryatallised from dilute methyl alcohol, m.p. 282° (Found: Eq. Wt., 162.34. $C_{10}H_{14}O_2$ requires Eq. Wt. 166). As the yield of the acids obtained by hydrolysis of (XIII) is very poor (0.5 g. from 9.5 g. of the ester) perhaps due to ring fission, the acids (m.p. 282° and 140°) could not be further examined.

Dimethyl hexahydroterephthalate.— Dimethyl terephthalate (XIV, 40 g.), platinic oxide (5 g.) and pure glacial acetic acid (250 c.c.) were taken in a soda-water bottle fitted in a shaking machine. After removal of air by suction, the bottle was connected with an aspirator containing hydrogen under 3 atmospheric pressure and the shaking machine started. The absorption was slow at the beginning but after about 15 minutes the absorption proceeded quite quickly and the temperature rose. It is better at this stage to stop the shaking for some time. When the temperature came down a little, shaking was started again. The absorption of hydrogen is mostly complete during 1½ hours' shaking; but for completion of the reaction, the shaking was continued for one hour more. The reaction mixture after filtration was freed from acetic acid, first by distillation and later by washing with water. From the residual oily liquid methyl hexahydroterephthalate (XV 37 g.), boiling at 137°/10-11 mm. or at 132-33°/2mm. was obtained.

Hydrolysis of (XV): *Formation of* cis *and* trans *hexahydroterephthalic acid* (XVI).—Dimethyl hexahydroterephthalate (146 g.) was heated under reflux with 8 per cent. hydrochloric acid (1.5 litres) during 6 hours when a clear solution was obtained. The solution was evaporated almost to dryness, cooled, filtered and the solid residue consisting of a mixture of the *cis* and *trans* acids was extracted with chloroform in a soxhlet apparatus when the *cis* acid went into solution. Out of 125 g. of the mixture of acids 85 g. of the *cis* acid was obtained, m.p. 168-70°. The *trans* acid left insoluble in chloroform weighed about 42 g., m.p. 308°.

Dimethyl 1 : 4-*dibromohexahydro-terephthalate* (XVII).—*Cis*hexahydro-terephthalic acid (20 g.) was converted into the acid chloride by treating with more than 2 molecular proportions of thionyl chloride. After removing the excess of thionyl chloride under suction, the residual diacid chloride was heated with bromine (40 g.) on an oil-bath at 150° during 4 hours when the absorption of bromine was complete. After cooling in a freezing mixture, excess of absolute methyl alcohol was added, allowed to stand overnight and then heated under reflux on water-bath during 3 hours. After removing methyl alcohol by distillation, the residual liquid was poured into ice-cold sodium bicarbonate solution when a mixture of the *cis* and *trans* dibromo esters separated out. The solid *trans* dimethyl ester was separated by filtration, and crystallised from methyl alcohol, m.p. 150°; yield 10 g. The liquid *cis*-ester was purified by distillation under reduced pressure, the distillate soon solidified, m.p. 68°, yield 11 g.

$\Delta^{1:3}$-*Dihydroterephthalic acid* (XVIII).—A mixture of the above *trans* bromo ester (81g.) and *cis*-bromo ester (69g.) was treated with 50 per cent. alcoholic potash (750g.), and the mixture allowed to stand for 48 hours, with frequent trituration in a mortar.

It is to be noted that application of heat at this stage tends to the formation of $\Delta^{1,4}$-dihydroterephthalic acid (cf. Baeyer, loc. cit.). The pasty alkaline liquid was acidified with dilute sulphuric acid under ice-cooling when $\Delta^{1,3}$-dihydroterephthalic acid (XVIII) separated out. The acid was converted into the acid chloride by thionyl chloride, and the latter converted into the methyl ester by heating under reflux with methyl alcohol for 3 hours, and then poured into water, and the mono-ester removed by sodium carbonate solution. Dimethyl $\Delta^{1,3}$-dihydroterephthalate (XIX) was purified by crystallisation from dilute methyl alcohol, m.p. 85°, yield 25g.

Action of diazomethane upon dimethyl-$\Delta^{1:3}$*-dihydrotherephalate: Formation of bi*cyclo-(1 : 2 : 2)*-heptene-dicarboxylic ester* (XX).—Dimethyl $\Delta^{1:3}$-dihydroterephthalate (20g.) was mixed with diazomethane (4.2g.) in ethereal solution, and kept at 0°C for 2 days when the dull yellow colour of the diazomethane disappeared. After removal of ether, nitrogen was removed from the reaction product by heating at 140°. The temperature of the bath should be raised slowly from 135-40°, as otherwise there is the danger of an explosion, The nitrogen free ester distilled at 132-34°/3 mm, yield 13g. (Found; C, 62.6; H, 7.3. $C_{11}H_{14}O_4$ requires C, 62.8; H, 6.7 per cent.).

Oxidation of (XX) *to* cyclo*pentane*-(1 : 1 : 3 : 3) *tetracarboxylic acid* (XXI).—The cyclic ester (XX, 5g.) was hydrolysed by boiling with 10% HCl during 12 hours under reflux and the clear solution thus obtained was evaporated to dryness. The white solid acid was crystallised from water, m. p. 255°, yield 3 g. This acid (3 g.) was dissolved in dilute sodium carbonate solution at 0°, and 3% permanganate solution was added drop by drop under ice-cooling till the pink coloration persisted. After standing for 12 hours the reaction product was gently warmed and then filtered. The clear colourless solution was acidified under ice-cooling and evaporated to dryness. The semi-solid residue being hygroscopic was thoroughly dried in a vacuum desiccator. The dry solid was extracted in a soxhlet apparatus with dry ether, the extract yielded an acid, m. p. 188°, which was proved to be identical with *cyclo*pentane-(1 : 1 : 3 : 3)-tetracarboxylic acid by taking mixed melting point with a genuine sample (Guha and Ranganathan, *Ber.*, 1936, **69**, 1199), the m.p. remaining undepressed.

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[Received 25–10–1939.]

Printed at the Hosali Power Press, Ulsoor, Bangalore, by D. N. Hosali, Proprietor.