170. *Acetylene Reactions. Part V. Reactions of Phenylacetylene with Secondary Amines.*

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Interaction of phenylacetylene and morpholine in the presence of cuprous chloride gives 3-*morpholino*-1 : 4-*diphenylbut*-1-*yne* (VI) and a second isomeric *base*, probably 1-morpholino-1 : 4-diphenylbut-3-yne (III). The structure of (VI) is confirmed by unambiguous synthesis, and the structure of (III) is made probable by the synthesis of the other two of the four possible isomers, with neither of which (III) is identical.

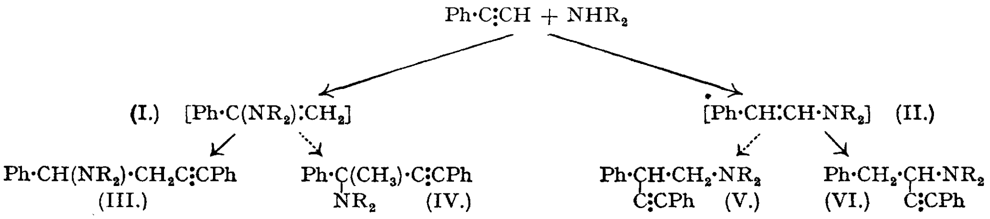
The investigation of the reactions of phenylacetylene was initiated to determine to what extent this substance could be used as a laboratory model for the reactions of acetylene itself. In work on the use of acetylene under pressure in organic synthesis, the sensitivity of such reactions to the surface conditions of the pressure vessel used greatly impeded the progress of the investigations. No reaction could be abandoned with confidence as a failure until three successive fruitless attempts had been made; reactions which failed on the first attempt frequently proceeded, if badly, on the second, and gave good results in the third and successive experiments. Since each experiment requires a considerable time it was thought that much effort might be saved if phenylacetylene could be used as a laboratory model for preliminary investigations to indicate what reactions would be most likely to succeed using acetylene itself.

It was first necessary to establish some parallelism between the reactions of acetylene and those of phenylacetylene, and the formation of 3-alkyl- or 3-dialkyl-aminobut-1-ynes from acetylene and amines (cf. Part I, this vol., p. 780) was chosen as a comparison case.

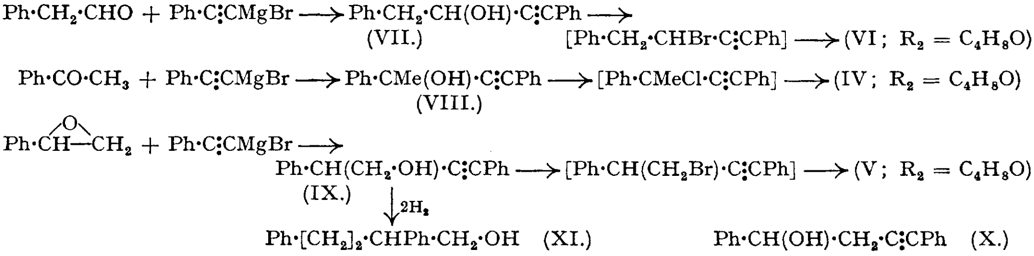
The interaction of acetylene and a primary or secondary amine is considered to proceed *via* the formation of an unstable and reactive intermediate vinylamine, which adds a further molecule of acetylene giving the aminobutyne, thus :

$$CH{\vdots}CH + NHR_2 \longrightarrow [CH_2{:}CH{\cdot}NR_2] \xrightarrow{C_2H_2} CH{\vdots}C{\cdot}CH(CH_3){\cdot}NR_2$$

If analogous reactions occur with phenylacetylene, there are two possibilities, (I) and (II), for the intermediate vinylamine, and four, (III), (IV), (V), and (VI), for the final product.



Morpholine (1 mol.) and phenylacetylene (2 mols.) reacted vigorously in the presence of a cuprous chloride catalyst, giving a mixture of basic products from which two isomeric bases, $C_{20}H_{21}ON$, m. p.s 70° and 88°, could be separated by fractional crystallisation from alcohol. The base, m. p. 70°, was identified as 3-*morpholino*-1 : 4-*diphenylbut*-1-*yne* (VI; $R_2 = C_4H_8O$) by unambiguous synthesis. Phenylacetaldehyde was caused to react with phenylacetylenylmagnesium bromide, and the resulting 1 : 4-*diphenylbut*-1-*yne*-2-*ol* (VII) was converted *via* the bromide into (VI; $R_2 = C_4H_8O$), identical with the product obtained directly from phenylacetylene and morpholine. Identification of the base, m. p. 88°, isolated in much lower yield than its isomeride, proved more difficult; although its structure cannot be regarded as definitely established, it is probably 1-*morpholino*-1 : 4-*diphenylbut*-3-*yne* (III; $R_2 = C_4H_8O$), since the remaining two isomerides (IV and V; $R_2 = C_4H_8O$) have been synthesised and are different from this base. 1 : 3-Diphenylbut-1-yn-3-ol (VIII) was prepared from acetophenone and phenylacetylenylmagnesium bromide, giving a product identical with that obtained by Nef (*Annalen*, 1899, **308**, 264) by long interaction of sodium phenylacetylide and acetophenone in ether. This was converted *via* its chloride into 3-*morpholino*-1 : 3-*diphenylbut*-3-*yne*, which had m. p. 99° and depressed the m. p. of the base, m. p. 88°, to 65—75°. The remaining isomeride was prepared as follows. Phenylacetylenylmagnesium bromide reacted vigorously with styrene oxide to give, in good yield, 1 : 3-*diphenylbut*-1-*yn*-4-*ol* (IX). This structure and mode of addition of the Grignard to the epoxide was made probable by the work of Kharasch and Clapp (*J. Org. Chem.*, 1938, **3**, 355) who established that addition of styrene oxide to phenylmagnesium bromide gives 2 : 2-diphenylethyl alcohol, whereas reversal of this order by addition of the Grignard solution to the styrene oxide gives the isomeric 1 : 2-diphenylethyl alcohol. There was, therefore, a probability that addition of styrene oxide to phenylacetylenylmagnesium bromide would give 1 : 3-diphenylbut-1-yn-4-ol (IX), and not the isomeric 1 : 4-diphenylbut-1-yn-4-ol (X). This was confirmed by hydrogenation of the product to 2 : 4-*diphenylbutanol* (XI), a liquid which could not be induced to crystallise and was different from the 1 : 4-diphenylbutanol described by Stoermer and Schenk (*Ber.*, 1928, **61**, 2320).



The acetylenic alcohol (IX) was converted *via* its bromide, in very low yield, into 4-*morpholino*-1 : 3-*diphenylbut*-1-*yne*, which had m. p. 126° and was different from the base, m. p. 88°. By elimination, therefore, it is considered probable that the structure of the base, m. p. 88°, is (III; $R_2 = C_4H_8O$), and this implies, in turn, that the primary condensation of phenylacetylene and morpholine does, in fact, proceed in both possible ways, giving (I) and (II).

At attempt to hydrogenate the base, m. p. 88°, in the hope of synthesising the hydrogenated product for comparison was unsuccessful; hydrogenation with Raney nickel and hydrogen at ordinary temperature and pressure disrupted the molecule completely.

The behaviour of piperidine was parallel with that of morpholine, but the only product isolated was 3-*piperidino*-1 : 4-*diphenylbut*-1-*yne* (VI; $R_2 = C_5H_{10}$), which was identified by comparison of its *picrate* and *methiodide* with the same derivatives formed from the product obtained by interaction of 3-bromo-1 : 4-diphenylbut-1-yne and piperidine.

EXPERIMENTAL.

Interaction of Phenylacetylene and Morpholine.—Morpholine (16 g.) and cuprous chloride (2 g.) were warmed together, giving partial solution. Phenylacetylene (40 g.) was added and the mixture warmed on the steam-bath, a thermometer being immersed in the liquid. At 98°, an exothermic reaction set in, and the mixture was kept at 100—105° by alternate warming and cooling. After 1½ hours the temperature fell, and was kept at 97° for 30 minutes. A yellow amorphous precipitate of copper phenylacetylide separated. The cooled mixture was diluted with ether (250 c.c.), filtered, and the ethereal solution shaken with 2N-hydrochloric acid (100 c.c.). An oily hydrochloride layer, insoluble in water and ether, was brought into solution by addition of alcohol, the acid layer separated, and the extraction repeated (50 c.c. of 2N-HCl). The combined acid solutions were basified with 10N-sodium hydroxide, and the precipitated oil collected in ether, dried, and distilled, giving a pale yellow viscous oil (21·5 g.), b. p. 154—160°/0·06 mm. This was dissolved in hot alcohol (40 c.c.), cooled, and scratched; a crystalline mass then separated. The crystals were collected, washed with ice-cold alcohol (5 c.c.), and dried. Yield 10·15 g., m. p. 56—60°. Recrystallisation from alcohol (20 c.c.) gave 6·6 g., m. p. 68—70°, which after a further crystallisation from alcohol gave 3-*morpholino*-1 : 4-*diphenylbut*-1-*yne* as colourless prisms, m. p. 70° (Found : C, 82·3; H, 7·2; N, 4·8. $C_{20}H_{21}ON$ requires C, 82·4; H, 7·2; N, 4·8%). The *picrolonate* formed yellow prisms from butyl alcohol, m. p. 220° (Found : C, 65·0; H, 5·25; N, 12·7. $C_{20}H_{21}ON,C_{10}H_8O_5N_4$ requires C, 64·9; H, 5·2; N, 12·6%). The *picrate* had m. p. 151° (Found : C, 59·65; H, 4·55; N, 11·0. $C_{20}H_{21}ON,C_6H_3O_7N_3$ requires C, 60·0; H, 4·6; N, 10·7%). The *perchlorate* formed white prisms from alcohol, m. p. 191° (Found : N, 3·4. $C_{20}H_{21}ON,HClO_4$ requires N, 3·5%). The *methiodide* formed white prisms from ether–alcohol, m. p. 186° (decomp.) (Found : C, 58·2; H, 5·6; N, 3·4. $C_{21}H_{24}ONI$ requires C, 58·2; H, 5·55; N, 3·25%). The mother liquors from crystallisation of this base were concentrated, and the residue fractionally crystallised. A little more of the above base, m. p. 70°, was obtained as the least soluble fraction, and a second *base* (2·9 g.), m. p. 88°, was obtained as white crystals from alcohol (Found : C, 82·4; H, 7·5; N, 4·7. $C_{20}H_{21}ON$ requires C, 82·4; H, 7·2; N, 4·8%). The *picrate* separated from alcohol in yellow plates, m. p. 144° (Found : C, 59·65; H, 4·45; N, 10·5. $C_{20}H_{21}ON,C_6H_3O_7N_3$ requires C, 60·0; H, 4·6; N, 10·7%). The *picrolonate* formed pale yellow prisms from alcohol, m. p. 163° (decomp.) (Found : C, 64·85; H, 5·15; N, 12·75. $C_{20}H_{21}ON,C_{10}H_8O_5N_4$ requires C, 64·9; H, 5·2; N, 12·6%).

The ethereal solution from which the basic products had been isolated was dried and distilled; some phenylacetylene was recovered, and a little acetophenone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. with an authentic specimen 249°) distilled at 10 mm. High-vacuum distillation gave (i) a yellow oil, b. p. 140—146°/0·2 mm. (2·15 g.), which solidified on cooling, and (ii) a yellow solid, b. p. 164—165°/0·2 mm. On crystallisation from alcohol, fraction (i) gave a *substance* as white needles, m. p. 74° (Found : C, 90·05; H, 5·9. $C_{32}H_{26}O$ requires C, 90·1; H, 6·1). Fraction (ii) gave a *ketone*, m. p. 89° (Found : C, 85·9; H, 6·6. $C_{16}H_{14}O$ requires C, 86·4; H, 6·3%). The 2 : 4-*dinitrophenylhydrazone* formed orange-yellow needles from alcohol, m. p. 190° (Found : C, 66·2; H, 4·25; N, 14·2. $C_{22}H_{18}O_4N_4$ requires C, 65·7; H, 4·5; N, 13·9%).

2-*Morpholino*-1 : 4-*diphenylbutane.*—3-Morpholino-1 : 4-diphenylbut-1-yne (2·92 g.) was dissolved in methyl alcohol (50 c.c.) and hydrogenated at ordinary temperature and pressure, using Raney nickel catalyst. Absorption (450 c.c.; calc. for $2H_2$: 448 c.c.) was complete in 20 minutes. The filtered solution was distilled, giving the *base* as a colourless viscous oil, b. p. 152°/0·1 mm. (Found : C, 81·35; H, 8·2; N, 5·0. $C_{20}H_{25}ON$ requires C, 81·35; H, 8·45; N, 4·75%). The *hydrochloride* separated from acetone in white needles, m. p. 158° (Found : N, 4·6; Cl, 11·2. $C_{20}H_{25}ON,HCl$ requires N, 4·2; Cl, 10·7%). The *picrolonate* formed yellow needles from alcohol, m. p. 198° (Found : C, 64·9; H, 5·6; N, 12·5. $C_{20}H_{25}ON,C_{10}H_8O_5N_4$ requires C, 64·9; H, 5·6; N, 12·5%).

1 : 4-*Diphenylbut*-1-*yn*-3-*ol.*—To a Grignard solution prepared from ethyl bromide (25·3 g.) and magnesium (7 g.) in ether (100 c.c.), phenylacetylene (38 g.) dissolved in ether (90 c.c.) was added dropwise, and the mixture refluxed for 2 hours. After cooling, a solution of phenylacetaldehyde (32 g.) in ether (90 c.c.) was added slowly, and the mixture was stirred and refluxed for 30 minutes and poured into an ice-cooled solution of ammonium chloride. The product, isolated with ether, gave on distillation 1 : 4-*diphenylbut*-1-*yn*-3-*ol* as a pale yellow viscous oil (31·5 g.), b. p. 144—145°/0·2 mm. (Found : C, 86·3; H, 6·1. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *a-naphthylurethane* formed white wax-like crystals from alcohol, m. p. 94° (Found : C, 82·3; H, 5·3; N, 3·5. $C_{27}H_{21}O_2N$ requires C, 82·8; H, 5·3; N, 3·6%). The 3 : 5-*dinitrobenzoate* formed pale yellow needles from light petroleum or alcohol (Found : C, 66·3; H, 3·8; N, 6·9. $C_{23}H_{16}O_6N_2$ requires C, 66·3; H, 3·8; N, 6·75%). The *a-naphthylamine* salt of the 3 : 5-dinitrobenzoate formed orange-brown needles from alcohol (Found : N, 7·6. $C_{23}H_{16}O_6N_2,C_{10}H_7NH_2$ requires N, 7·4%).

The alcohol above (20 g.) was dissolved in benzene (120 c.c.), and phosphorus tribromide (20 c.c.) added dropwise with stirring. The solution became dark, but at the end of the addition had turned pale green; it was heated on the steam-bath for 30 minutes, poured on ice, collected in ether, and distilled, giving the crude bromide (21·2 g.), b. p. 160—170°/0·4 mm. This bromide (5 g.) was heated with morpholine (3·5 g.) at 100—110° for 30 minutes, cooled, diluted with dry ether, and filtered from morpholine hydrobromide. From the ethereal solution, basic material was isolated by 2N-acid, and the base was regenerated, extracted with ether and distilled. The yellow oil, b. p. 150—155°/0·02 mm., crystallised on cooling, and after recrystallisation from alcohol had m. p. 70°, undepressed by admixture with 3-morpholino-1 : 4-diphenylbutyne prepared directly from phenylacetylene and morpholine. Identity was further established by the picrate, m. p. and mixed m. p. 151°, and the perchlorate, m. p. and mixed m. p. 191°.

1 : 3-*Diphenylbut*-1-*yn*-3-*ol.*—This alcohol has been prepared by Nef (*loc. cit.*) by interaction of

sodium phenylacetylide and acetophenone in ether. The following procedure is preferable. To a Grignard solution prepared from magnesium (4·7 g.), ethyl bromide (17·5 g.), and ether (90 c.c.), phenylacetylene (25 g.) was added slowly and the mixture refluxed with stirring for 2 hours. To the cooled solution, acetophenone (20 g.) in ether (60 c.c.) was added dropwise, and the mixture stirred overnight. After decomposition with ice and hydrochloric acid, the ether was distilled and the reddish viscous residue (40 g.) was crystallised from light petroleum (b. p. 40—60°), giving 1 : 3-diphenylbut-1-yn-3-ol (25 g.) as white needles, m. p. 75° (Nef, *loc. cit.*, gives m. p. 77°) (Found : C, 86·3; H, 6·35. Calc. for $C_{16}H_{14}O$: C, 86·5; H, 6·3%).

3-*Morpholino*-1 : 3-*diphenylbut*-1-*yne*.—The diphenylbutynol (above; 18·5 g.) was dissolved in benzene (50 c.c.) and cooled to 0°. A solution of phosphorus trichloride (2·4 c.c.) in benzene (20 c.c.) was added slowly with shaking, and the mixture left without external cooling for 45 minutes. After dilution with ether, the solution was washed successively with water, saturated sodium hydrogen carbonate, and water, and dried ($MgSO_4$), and the ether removed below 30°. The product was a dark viscous oil (20 g.) which was not further purified. A mixture of this chloride (3 g.) and morpholine (3 g.) was kept at ordinary temperature for 4 days. Crystals of morpholine hydrochloride separated. The mixture was diluted with ether and filtered, and the basic product isolated by extraction with 2N-hydrochloric acid, regeneration with sodium hydroxide, and extraction with ether. After distillation of the ether the residue, a dark viscous oil, was heated at 100°/20 mm. for 1 hour, and dissolved in alcohol (1 c.c.). White crystals separated which after recrystallisation from alcohol gave 3-*morpholino*-1 : 3-*diphenylbut*-1-*yne* as white needles, m. p. 99° (Found : C, 82·35; H, 7·1; N, 4·75. $C_{20}H_{21}ON$ requires C, 82·4; H, 7·2; N, 4·8%). The *picrate* formed yellow needles from alcohol, m. p. 156° (decomp.) (Found : C, 59·6; H, 4·6; N, 11·2. $C_{20}H_{21}ON,C_6H_3O_7N_3$ requires C, 60·0; H, 4·6; N, 10·7%).

1 : 3-*Diphenylbut*-1-*yn*-4-*ol*.—To a Grignard solution prepared from ethyl bromide (18 g.), magnesium (4 g.), and a crystal of iodine, in anhydrous ether (30 c.c.), was added dropwise during 30 minutes a solution of phenylacetylene (17 g.) in ether (30 c.c.). The mixture was boiled under reflux for 30 minutes with stirring, and a solution of styrene oxide (20 g.) in ether (30 c.c.) was then added during 30 minutes. The mixture was stirred under reflux for 1 hour, cooled, and cautiously decomposed with ice and dilute sulphuric acid. Distillation of the ethereal layer afforded 1 : 3-*diphenylbut*-1-*yn*-4-*ol* as a colourless viscous oil, b. p. 145—150°/0·2—0·25 mm., $n_D^{20^\circ}$ 1·6085 (Found : C, 86·55; H, 6·25. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *phenylurethane* formed prisms from alcohol, m. p. 99—100° (Found : C, 81·25; H, 5·75; N, 4·5. $C_{23}H_{19}O_2N$ requires C, 80·95; H, 5·6; N, 4·1%). The 3 : 5-*dinitrobenzoate* formed pale yellow needles from benzene, m. p. 142° (Found : C, 66·5; H, 3·8; N, 6·7. $C_{23}H_{16}O_6N_2$ requires C, 66·3; H, 3·8; N, 6·7%).

2 : 4-*Diphenylbutanol*.—The diphenylbutynol (above, 10 g.) dissolved in methyl alcohol (50 c.c.) was hydrogenated at ordinary temperature and pressure over Raney nickel catalyst. Absorption (1990 c.c. at N.T.P. Calc., 2010 c.c.) was complete in 75 minutes. The product, isolated by distillation in 90% yield, had b. p. 120°/0·03 mm., $n_D^{17^\circ}$ 1·5717 (Found : C, 84·7; H, 7·6. $C_{16}H_{18}O$ requires C, 84·9; H, 7·9%). The 3 : 5-*dinitrobenzoate* formed needles from alcohol, m. p. 96° (Found : C, 65·9; H, 4·9; N, 6·9. $C_{23}H_{20}O_6N_2$ requires C, 65·7; H, 4·8; N, 6·7%).

4-*Morpholino*-1 : 3-*diphenylbut*-1-*yne*.—1 : 3-Diphenylbut-1-yn-4-ol (10 g.) was treated with phosphorus tribromide (4 c.c.). After the initial exothermic reaction had subsided the mixture was heated on the steam-bath for 1 hour, diluted with ether, washed successively with water, sodium hydrogen carbonate, and water, dried, and evaporated. To the cold residue morpholine (5 c.c.) was added, and the mixture set aside for 3 days. Morpholine hydrobromide was collected after dilution with ether, and the basic material isolated. Evaporation of the ether solution of the basic portion left a very small amount of a brown oil which slowly crystallised and was recrystallised from alcohol, giving white needles of 4-*morpholino*-1 : 3-*diphenylbut*-1-*yne*, m. p. 126° (Found : N, 4·8. $C_{20}H_{21}ON$ requires N, 4·8%).

1-*Morpholino*-2 : 4-*diphenylbutane*.—2 : 4-Diphenylbutanol (12·7 g.) was brought into reaction with phosphorus tribromide (10 g.). When the initially vigorous reaction had subsided the mixture was heated on the steam-bath for 1 hour, cooled, poured into water, and extracted with ether. The ethereal solution, after successive washing with water, saturated aqueous sodium hydrogen carbonate, and water, was dried and evaporated, giving a colourless oil (12·1 g.). Morpholine (8 c.c.) was added, and the mixture set aside for 5 days. Morpholine hydrobromide was filtered from the ethereal solution, and the base extracted with hydrochloric acid and regenerated. The base distilled at 150°/0·05 mm. as a pale yellow viscous oil (Found : C, 81·5; H, 8·7; N, 5·0. $C_{20}H_{25}ON$ requires C, 81·4; H, 8·5; N, 4·8%). The *hydrochloride* separated from alcohol with a molecule of alcohol of crystallisation, m. p. 236—237° (decomp.) (Found : C, 69·8; H, 7·9; N, 3·7. $C_{20}H_{25}ON,HCl,C_2H_6O$ requires C, 69·9; H, 8·4; N, 3·7%). The *picrate* formed yellow plates, m. p. 145° from alcohol (Found : C, 59·2; H, 5·35; N, 10·9. $C_{20}H_{25}ON,C_6H_3O_7N_3$ requires C, 59·5; H, 5·35; N, 10·7%).

Reaction of Phenylacetylene and Piperidine.—Piperidine (4 g.) was warmed with cuprous chloride (0·5 g.), and phenylacetylene (10 g.) added. The exothermic reaction which began on heating was controlled at 98—102°, and the mixture finally heated on the steam-bath for 2 hours. The product, diluted with ether and filtered, was separated into basic and neutral portions. The latter on distillation gave a little acetophenone and diphenyldiacetylene, m. p. and mixed m. p. with an authentic specimen, 88°. The basic portion was distilled giving a yellow oil, b. p. 156—160°/0·15 mm. This was treated with picric acid (2·5 g.) in alcohol (200 c.c.), and the product crystallised to constant m. p. 3-*Piperidine*-1 : 4-*diphenylbut*-1-*yne picrate* separated from alcohol as yellow needles (3·2 g.), m. p. 141° (Found : C, 62·6; H, 5·1; N, 11·0. $C_{21}H_{23}N,C_6H_3O_7N_3$ requires C, 62·6; H, 5·5; N, 10·8%). The *base*, regenerated from the picrate with sodium hydroxide, had b. p. 150—155°/0·13 mm. (Found : C, 86·8; H, 7·6; N, 4·9. $C_{21}H_{23}N$ requires C, 87·2; H, 7·9; N, 4·8%). The *methiodide* formed white prisms from acetone, m. p. 152° (Found : C, 60·9; H, 5·7; N, 3·5; I, 29·7. $C_{22}H_{26}NI$ requires C, 61·2; H, 6·0; N, 3·25; I, 29·5%).

By interaction of crude 3-bromo-1 : 4-diphenylbut-1-yne (prepared as described above from the alcohol and phosphorus tribromide) and piperidine, the same 3-piperidino-1 : 4-diphenylbut-1-yne was obtained, b. p. 150—160°/0·15 mm., identified by its picrate, m. p. and mixed m. p. 141°, and its methiodide, m. p. and mixed m. p. 152°.

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