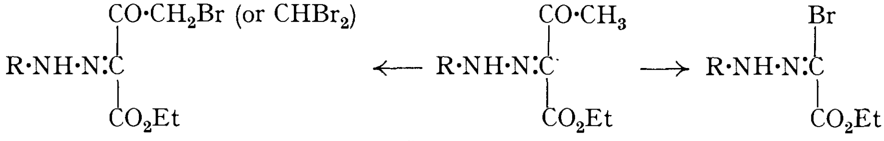
25. *The 3-Carbethoxy-4-hydroxy-1-nitrotolylpyrazoles.*

F. D. CHATTAWAY, D. R. ASHWORTH, and M. GRIMWADE.

THE nitrotolyldiazonium salts couple readily with ethyl acetoacetate to give the nitrotolylazoacetoacetates.

Bromine acts upon these compounds in the same way as upon other arylazoacetoacetates (cf. J., 1933, 475), and either replaces the acetyl group as a whole, when action takes place in acetic acid containing sodium acetate, or substitutes in the acetyl group when boiling acetic acid or chloroform is the solvent, ethyl α-bromoglyoxylate-nitrotolylhydrazones or ethyl nitrotolylazo-γ-bromo- or -γγ-dibromo-acetoacetates respectively being formed :



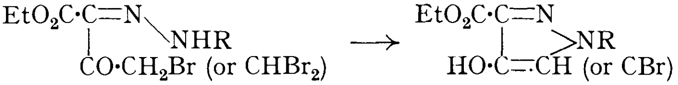
$$\begin{array}{c}\mathrm{CO{\cdot}CH_2Br\ (or\ CHBr_2)}\\ |\\ \mathrm{R{\cdot}NH{\cdot}N{:}C}\\ |\\ \mathrm{CO_2Et}\end{array} \longleftarrow \begin{array}{c}\mathrm{CO{\cdot}CH_3}\\ |\\ \mathrm{R{\cdot}NH{\cdot}N{:}C}\\ |\\ \mathrm{CO_2Et}\end{array} \longrightarrow \begin{array}{c}\mathrm{Br}\\ |\\ \mathrm{R{\cdot}NH{\cdot}N{:}C}\\ |\\ \mathrm{CO_2Et}\end{array}$$

$(R = C_6H_3Me{\cdot}NO_2)$

Only with ethyl 6-nitro-*o*-tolylazoacetoacetate dissolved in acetic acid containing sodium acetate does bromine, even when excess is used, substitute in the nucleus, the halogen, when this occurs, entering the para-position, ethyl α-bromoglyoxylate-4-bromo-6-nitro-*o*-tolylhydrazone being formed.

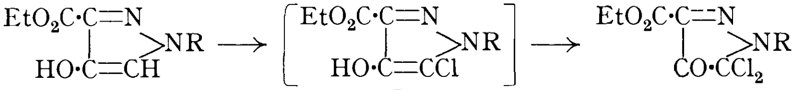
Compounds containing bromine in the nucleus can readily be obtained by coupling the appropriate brominated nitrotolyldiazonium salt with ethyl acetoacetate, and subsequent action of bromine upon these coupled products.

The bromine atoms which have either replaced or substituted the acetyl group are very reactive. For instance, on treatment with alcoholic ammonia, the ethyl α-bromoglyoxylate-nitrotolylhydrazones yield the corresponding α-amino-compounds. Also, on heating with alcoholic potassium acetate, the γ-bromoacetoacetates lose hydrogen bromide, with ring closure and formation of the corresponding 4-hydroxypyrazoles, whilst the γγ-dibromoacetoacetates similarly yield 5-bromo-4-hydroxypyrazoles, identical with those obtained by the action of bromine upon the corresponding 4-hydroxypyrazoles obtained as above :



$$\begin{array}{l}\mathrm{EtO_2C{\cdot}C{=}N\diagdown}\\ \quad |\qquad\quad \mathrm{\diagdown NHR}\\ \mathrm{CO{\cdot}CH_2Br\ (or\ CHBr_2)}\end{array} \longrightarrow \begin{array}{l}\mathrm{EtO_2C{\cdot}C{=}N}\\ \qquad\quad | \quad \mathrm{>NR}\\ \mathrm{HO{\cdot}C{=}CH\ (or\ CBr)}\end{array}$$

When chlorine is passed into a chloroform solution of any one of the 3-carbethoxy-4-hydroxy-1-nitrotolylpyrazoles, two atoms of chlorine substitute in the 5-position of the pyrazole ring, and 5 : 5-dichloro-3-carbethoxy-1-nitrotolyl-4-pyrazolones are formed (cf. J., 1933, 1389) :



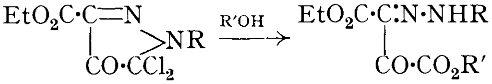
$$\begin{array}{l}\mathrm{EtO_2C{\cdot}C{=}N}\\ \qquad | \quad \mathrm{>NR}\\ \mathrm{HO{\cdot}C{=}CH}\end{array} \longrightarrow \left[\begin{array}{l}\mathrm{EtO_2C{\cdot}C{=}N}\\ \qquad | \quad \mathrm{>NR}\\ \mathrm{HO{\cdot}C{=}CCl}\end{array}\right] \longrightarrow \begin{array}{l}\mathrm{EtO_2C{\cdot}C{=}N}\\ \qquad | \quad \mathrm{>NR}\\ \quad\mathrm{CO{\cdot}CCl_2}\end{array}$$

(I.)

In the case of the 4-hydroxy-mono- and -di-brominated nitrotolylpyrazoles the presence of halogen in the tolyl nucleus checks the action, which does not proceed beyond the first stage, the corresponding 5-chloro-4-hydroxy-pyrazole (I) being the final product.

The 5 : 5-dichloro-1-nitrotolyl-4-pyrazolones are rather unstable, viscous solids of so low a melting point that in some cases they could not be obtained crystalline. They are all reduced by hydriodic acid to the corresponding 5-chloro-pyrazoles (I).

When the 5 : 5-dichloro-4-pyrazolones are heated with alcohols, the pyrazole ring is opened and esters of diketosuccinic acid nitrotolylhydrazone are formed :



$$\begin{array}{l}\mathrm{EtO_2C{\cdot}C{=}N}\\ \quad | \quad \mathrm{>NR}\\ \mathrm{CO{\cdot}CCl_2}\end{array} \xrightarrow{\mathrm{R'OH}} \begin{array}{l}\mathrm{EtO_2C{\cdot}C{:}N{\cdot}NHR}\\ \qquad\quad |\\ \qquad\mathrm{CO{\cdot}CO_2R'}\end{array}$$

EXPERIMENTAL.

Ethyl 2-*Nitro*-p-*tolylazoacetoacetate*.—A solution of 20 g. of 2-nitro-*p*-toluidine in the minimum quantity of acetic acid was poured into 100 c.c. of concentrated hydrochloric acid, the suspension diazotised at 0° with 10 g. of sodium nitrite in 30 c.c. of water, and the resulting filtered diazonium solution added dropwise to a mixture of 140 g. of crystalline sodium acetate, 20 g. of ethyl acetoacetate, and 100 c.c. of 50% aqueous alcohol. The above *compound* separated at once and was collected after 12 hours. It crystallised from alcohol in yellow prisms, m. p. 142°. Yield, 90% of the theoretical (Found : N, 14·5. $C_{13}H_{15}O_5N_3$ requires N, 14·3%).

Similarly were prepared the following ethyl acetoacetates (all were crystallised from alcohol) : 3-*nitro*-p-*tolylazo*, pale yellow needles, m. p. 104° (Found : N, 14·5%); 5-*nitro*-o-*tolylazo*, pale yellow prisms, m. p. 128° (Found : N, 14·4%); 4-*nitro*-o-*tolylazo*, yellow prisms, m. p. 131° (Found : N, 14·5%); 6-*bromo*-2-*nitro*-p-*tolylazo*, yellow prisms, m. p. 92° (Found : Br, 21·6. $C_{13}H_{14}O_5N_3Br$ requires Br, 21·5%); 6-*nitro*-o-*tolylazo*, yellow rhombic plates, m. p. 81° (Found : N, 14·3%); 6-*bromo*-3-*nitro*-p-*tolylazo*, pale yellow prisms, m. p. 126° (Found : Br, 21·6%); 4-*bromo*-5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 182° (Found : Br, 21·4%); 4-*bromo*-6-*nitro*-o-*tolylazo*, yellow rhombic plates, m. p. 84° (Found : Br, 21·5%); 6-*bromo*-4-*nitro*-o-*tolylazo*, yellow, long, slender prisms, m. p. 131° (Found : Br, 21·7%); 2 : 6-*dibromo*-3-*nitro*-p-*tolylazo*, pale yellow, rhombic plates, m. p. 102° (Found : Br, 35·4. $C_{13}H_{13}O_5N_3Br_2$ requires Br, 35·5%); 4 : 6-*dibromo*-5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 146° (Found : Br, 35·7%).

Ethyl α-*Bromoglyoxylate*-2-*nitro*-p-*tolylhydrazone*.—3 G. of bromine in 5 c.c. of acetic acid were added to a solution of 5 g. of ethyl 2-nitro-*p*-tolylazoacetoacetate and 2 g. of crystalline sodium acetate in 15 c.c. of cold acetic acid. The mixture became warm and, on cooling, the above *compound* separated. It crystallised from alcohol in yellow prisms, m. p. 160° (Found : Br, 24·1. $C_{11}H_{12}O_4N_3Br$ requires Br, 24·2%). In a similar manner the following ethyl α-bromoglyoxylate-hydrazones were obtained (all were crystallised from alcohol) : 3-*nitro*-p-*tolyl*, pale yellow needles, m. p. 142° (Found : Br, 24·0%); 5-*nitro*-o-*tolyl*, pale yellow prisms, m. p. 150° (Found : Br, 24·4%); 6-*nitro*-o-*tolyl*, orange-yellow prisms, m. p. 132° (Found : Br, 24·4%); 6-*bromo*-2-*nitro*-p-*tolyl*, orange-yellow flattened prisms, m. p. 99° (Found : Br, 38·9. $C_{11}H_{11}O_4N_3Br_2$ requires Br, 39·1%); 6-*bromo*-3-*nitro*-p-*tolyl*, pale yellow prisms, m. p. 153° (Found : Br, 39·0%); 4-*bromo*-5-*nitro*-o-*tolyl*, yellow prisms, m. p. 164° (Found : Br, 39·3%); 4-*bromo*-6-*nitro*-o-*tolyl* (by the action of 1 mol. of bromine upon ethyl 4-bromo-6-nitro-*o*-tolylazoacetoacetate in cold acetic acid and by the action of an excess of bromine upon ethyl 6-nitro-*o*-tolylazoacetoacetate in hot acetic acid), orange prisms, m. p. 127° (Found : Br, 39·3%); 2 : 6-*dibromo*-3-*nitro*-p-*tolyl*, very pale yellow, rectangular plates, m. p. 99° (Found : Br, 50·1. $C_{11}H_{10}O_4N_3Br_3$ requires Br, 50·3%); 4 : 6-*dibromo*-5-*nitro*-o-*tolyl*, pale yellow prisms, m. p. 116° (Found : Br, 50·3%).

Ethyl α-*aminoglyoxylate*-5-*nitro*-o-*tolylhydrazone*, prepared by stirring the corresponding α-bromo-compound into alcohol saturated with ammonia gas, crystallised from alcohol in orange prisms, m. p. 152° (Found : N, 20·9. $C_{11}H_{14}O_4N_4$ requires N, 21·05%).

Similarly were obtained : *ethyl* α-*aminoglyoxylate*-4-*bromo*-5-*nitro*-o-*tolylhydrazone*, red prisms from alcohol, m. p. 174° (Found : Br, 23·4. $C_{11}H_{13}O_4N_4Br$ requires Br, 23·2%); *ethyl* α-*aminoglyoxylate*-4 : 6-*dibromo*-5-*nitro*-o-*tolylhydrazone*, yellow prisms from alcohol, m. p. 160° (Found : Br, 37·8. $C_{11}H_{12}O_4N_4Br_2$ requires Br, 37·7%).

Ethyl 2-*Nitro*-p-*tolylazo*-γ-*bromoacetoacetate*.—1·6 G. of bromine in 5 c.c. of acetic acid were added to 3 g. of ethyl 2-nitro-*p*-tolylazoacetoacetate in 10 c.c. of boiling glacial acetic acid. On cooling, the above *compound* separated as a yellow solid. It crystallised from alcohol in small yellow needles, m. p. 139° (Found : Br, 21·3. $C_{13}H_{14}O_5N_3Br$ requires Br, 21·5%).

Similarly were prepared the following ethyl γ-bromoacetoacetates, all of which were crystallised from alcohol : 3-*nitro*-p-*tolylazo*, yellow prisms, m. p. 113° (Found : Br, 21·7%); 5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 136° (Found : Br, 21·6%); 6-*nitro*-o-*tolylazo* (with chloroform instead of acetic acid as solvent), yellow rhombic plates, m. p. 117° (Found : Br, 21·4%); 4-*nitro*-o-*tolylazo*, which separated from solution in alcohol as a labile form in long, yellow, hair-like prisms which gradually redissolved while the stable form separated as yellow rectangular plates, m. p. 145° (Found : Br, 21·6%); 6-*bromo*-2-*nitro*-p-*tolylazo*, yellow prisms, m. p. 121° (Found : Br, 35·4. $C_{13}H_{13}O_5N_3Br_2$ requires Br, 35·5%); 6-*bromo*-3-*nitro*-p-*tolylazo*, small yellow prisms, m. p. 137° (Found : Br, 35·6%); 4-*bromo*-5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 144° (Found : Br, 35·3%); 4-*bromo*-6-*nitro*-o-*tolylazo*, yellow prisms, m. p. 122° (Found : Br, 35·5%); 6-*bromo*-4-*nitro*-o-*tolylazo*, long, slender, yellow prisms, m. p. 157° (Found : Br, 35·7%); 2 : 6-*dibromo*-3-*nitro*-p-*tolylazo*, pale yellow, rhombic plates, m. p. 133° (Found : Br, 45·4. $C_{13}H_{12}O_5N_3Br_3$ requires Br, 45·3%); 4 : 6-*dibromo*-5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 139° (Found : Br, 45·1%).

Ethyl 2-*Nitro*-p-*tolylazo*-γγ-*dibromoacetoacetate*.—3·2 G. of bromine in 5 c.c. of acetic acid were added to 3 g. of ethyl 2-nitro-*p*-tolylazoacetoacetate in 10 c.c. of boiling acetic acid. On cooling, the above *compound* separated; it crystallised from alcohol in yellow, long, slender prisms, m. p. 141° (Found : Br, 35·3. $C_{13}H_{13}O_5N_3Br_2$ requires Br, 35·5%).

In a similar manner the following ethyl γγ-dibromoacetoacetates were prepared (crystallised from alcohol) : 3-*nitro*-p-*tolylazo*, small yellow prisms, m. p. 143° (Found : Br, 35·6%); 5-*nitro*-o-*tolylazo*, pale yellow prisms, m. p. 170° (Found : Br, 35·4%); 6-*nitro*-o-*tolylazo* (with chloroform instead of acetic acid as solvent), yellow rhombic plates, m. p. 88° (Found : Br, 35·3%); 6-*bromo*-2-*nitro*-p-*tolylazo*, yellow prisms, m. p. 156° (Found : Br, 45·3. $C_{13}H_{12}O_5N_3Br_3$ requires Br, 45·3%); 6-*bromo*-3-*nitro*-p-*tolylazo*, yellow, long, slender prisms, m. p. 157° (Found : Br, 45·4%); 4-*bromo*-5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 161° (Found : Br, 45·1%); 4-*bromo*-6-*nitro*-o-*tolylazo*, yellow prisms, m. p. 104° (Found : Br, 45·3%); 2 : 6-*dibromo*-3-*nitro*-p-*tolylazo*, pale yellow prisms, m. p. 130° (Found : Br, 52·7. $C_{13}H_{11}O_5N_3Br_4$ requires Br, 52·5%); 4 : 6-*dibromo*-5-*nitro*-o-*tolylazo*, yellow prisms, m. p. 163° (Found : Br, 52·5%).

Formation of 3-*Carbethoxy*-4-*hydroxy*-1-(2′-*nitro*-p-*tolyl*)*pyrazole*.—3 G. of potassium acetate were added to a solution of 5 g. of ethyl 2-nitro-*p*-tolylazo-γ-bromoacetoacetate in 50 c.c. of boiling alcohol. A vigorous action took place and the solution darkened, potassium bromide separating. After cooling, on careful addition of water to the resulting solution, the above *compound* separated as a dark solid. It crystallised from alcohol in yellow, long, slender prisms, m. p. 119° (Found : N, 14·6. $C_{13}H_{13}O_5N_3$ requires N, 14·4%).

Similarly were obtained the following 3-carbethoxy-4-hydroxy-1-tolylpyrazoles, all of which were crystallised from alcohol : 3′-*nitro*-p-*tolyl*, colourless, short, flattened prisms, m. p. 182° (Found : N, 14·2%); 5′-*nitro*-o-*tolyl*, pale yellow prisms, m. p. 114° (Found : N, 14·5%); 6′-*nitro*-o-*tolyl*, pale yellow, short, flattened prisms, m. p. 99° (Found : N, 14·2%); 4′-*nitro*-o-*tolyl*, colourless hair-like needles, m. p. 177° (Found : N, 14·3%); 4′-*bromo*-6′-*nitro*-o-*tolyl*, colourless rhombic plates, m. p. 162° (Found : Br, 21·8. $C_{13}H_{12}O_5N_3Br$ requires Br, 21·6%); 6′-*bromo*-4′-*nitro*-o-*tolyl*, colourless, short, flattened prisms, m. p. 183° (Found : Br, 21·8%); 6′-*bromo*-2′-*nitro*-p-*tolyl*, very pale yellow, rhombic plates, m. p. 165° (Found : Br, 21·4%); 2′ : 6′-*dibromo*-3′-*nitro*-p-*tolyl*, colourless, short, flattened prisms, m. p. 184° (Found : Br, 35·7. $C_{13}H_{11}O_5N_3Br_2$ requires Br, 35·6%); 4′ : 6′-*dibromo*-5′-*nitro*-o-*tolyl*, colourless, long, slender prisms, m. p. 219° (Found : Br, 35·9%). The *acetyl* derivative of the last compound (warm acetic anhydride and a drop of sulphuric acid) crystallised from alcohol in colourless, long, slender prisms, m. p. 196° (Found : Br, 32·3. $C_{15}H_{13}O_6N_3Br_2$ requires Br, 32·6%).

5-*Bromo*-3-*carbethoxy*-4-*hydroxy*-1-(5′-*nitro*-o-*tolyl*)*pyrazole*.—(I) 1·5 G. of potassium acetate were added to a solution of 3 g. of ethyl 5-nitro-*o*-tolylazo-γγ-dibromoacetoacetate in 25 c.c. of boiling alcohol. A vigorous action took place and the solution darkened. On cooling and careful addition of water the above *compound* separated as a yellow solid. It crystallised from alcohol in colourless compact prisms, m. p. 133° (Found : Br, 21·8. $C_{13}H_{12}O_5N_3Br$ requires Br, 21·6%).

(II) 2 G. of bromine in 2 c.c. of acetic acid were added to a solution of 3 g. of 3-carbethoxy-4-hydroxy-1-(5′-nitro-*o*-tolyl)pyrazole in 10 c.c. of boiling acetic acid. On careful addition of water to the resulting solution a yellow solid was obtained which on crystallisation was found to be identical with the above 5-bromo-pyrazole.

Similarly have been prepared : 5-*bromo*-3-*carbethoxy*-4-*hydroxy*-1-(3′-*nitro*-p-*tolyl*)*pyrazole*, colourless, long, slender prisms from alcohol, m. p. 143° (Found : Br, 21·5%); 5-*bromo*-3-*carbethoxy*-4-*hydroxy*-1-(6′-*nitro*-o-*tolyl*)*pyrazole*, colourless, short, flattened prisms from alcohol, m. p. 146° (Found : Br, 21·7%).

Formation of 5 : 5-*Dichloro*-3-*carbethoxy*-1-(4′-*nitro*-o-*tolyl*)-4-*pyrazolone*.—1·5 G. of 3-carbethoxy-4-hydroxy-1-(4′-nitro-*o*-tolyl)pyrazole were dissolved in 10 c.c. of chloroform, and chlorine passed for 10 minutes. On removal of the chloroform on a water-bath the above *compound* remained as a viscous oil, which solidified on standing and scratching with ether. It crystallised from chloroform and light petroleum in yellow, long, slender prisms, m. p. 124° (Found : Cl, 20·0. $C_{13}H_{11}O_5N_3Cl_2$ requires Cl, 19·7%).

The 2′-nitro-*p*-tolyl, 5′-nitro-*o*-tolyl, 6′-nitro-*o*-tolyl, and 3′-nitro-*p*-tolyl analogues were similarly obtained as viscous oils, which could not be made to crystallise but yielded crystalline derivatives.

Formation of 5-*Chloro*-3-*carbethoxy*-4-*hydroxy*-1-(4′-*nitro*-o-*tolyl*)*pyrazole*.—2 G. of potassium iodide in 5 c.c. of water were added to 2 g. of 5 : 5-dichloro-3-carbethoxy-1-(4′-nitro-*o*-tolyl)-4-

pyrazolone dissolved in 25 c.c. of acetic acid at 60°. After 20 minutes, sodium sulphite solution was added dropwise until all the iodine was removed. Subsequent careful addition of water precipitated the above *compound*. It crystallised from alcohol in clusters of colourless, long, slender prisms, m. p. 181° (Found : Cl, 10·7. $C_{13}H_{12}O_5N_3Cl$ requires Cl, 10·9%).

The following analogues were similarly prepared : *5′-nitro-*o*-tolyl*, stellate clusters of colourless, long, slender prisms, m. p. 101° (Found : Cl, 10·8%) ; *6′-nitro-*o*-tolyl*, pale yellow, flattened, rectangular prisms, m. p. 135° (Found : Cl, 11·1%) ; *3′-nitro-*p*-tolyl*, colourless, irregular, compact plates, m. p. 128° (Found : Cl, 10·6%).

Formation of 1-*Ethyl* 2-*Methyl Diketosuccinate*-1-(4′-*nitro*-o-*tolyl*)*hydrazone*.—2 G. of 5 : 5-dichloro-3-carbethoxy-1-(4′-nitro-*o*-tolyl)-4-pyrazolone were heated for 2 minutes in 10 c.c. of methyl alcohol. On cooling, the above *compound* separated as a viscous solid. It crystallised from ethyl alcohol in yellow, long, slender prisms, m. p. 145° (Found : N, 12·6. $C_{14}H_{15}O_7N_3$ requires N, 12·5%).

Similarly, by using the appropriate alcohol, were obtained the *5′-nitro-*o*-tolyl* analogue, yellow hair-like needles from methyl alcohol, m. p. 139° (Found : N, 12·5%), and the *2′-nitro-*p*-tolyl* analogue, yellow slender prisms from alcohol, m. p. 132° (Found : N, 12·4%), and *diethyl diketosuccinate-2-nitro-*p*-tolylhydrazone*, yellow, long, slender needles from alcohol, m. p. 97° (Found : N, 11·9. $C_{15}H_{17}O_7N_3$ requires N, 12·0%).

Formation of 5-*Chloro*-3-*carbethoxy*-4-*hydroxy*-1-(6′-*bromo*-2′-*nitro*-p-*tolyl*)*pyrazole*.—2 G. of 3-carbethoxy-4-hydroxy-1-(6′-bromo-2′-nitro-*p*-tolyl)pyrazole were dissolved in 10 c.c. of chloroform, and chlorine passed for 10 minutes. On removal of the chloroform the above *compound* remained as a viscous solid. It crystallised from alcohol in colourless, irregular, flattened prisms, m. p. 168° (Found : Cl, 8·7; Br, 19·6. $C_{13}H_{11}O_5N_3ClBr$ requires Cl, 8·8; Br, 19·8%).

The following were similarly obtained, and crystallised from alcohol : *6′-bromo-4′-nitro-*o*-tolyl*, colourless compact prisms, m. p. 202° (Found : Cl, 8·9; Br, 19·9%) ; *4′-bromo-6′-nitro-*o*-tolyl*, yellow, short, compact prisms, m. p. 164° (Found : Cl, 8·8; Br, 19·9%) ; *2′ : 6′-dibromo-3′-nitro-*p*-tolyl*, colourless, short, rectangular prisms with domed ends, m. p. 169° (Found : Cl, 7·4; Br, 33·1. $C_{13}H_{10}O_5N_3ClBr_2$ requires Cl, 7·4; Br, 33·1%) ; *4′ : 6′-dibromo-5′-nitro-*o*-tolyl*, colourless, compact, flattened, rectangular prisms, m. p. 165° (Found : Cl, 7·3; Br, 32·9%).

THE QUEEN'S COLLEGE LABORATORY, OXFORD.

[*Received, October* 15*th*, 1934.]