

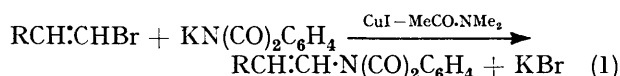
## Metal Ions and Complexes in Organic Reactions. Part XVI.<sup>1</sup> Extension of Copper-catalysed Gabriel Reactions to Vinylic Halides and to Analogues of Phthalimide Salts

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Catalysed conversions of vinylic bromides, RCH:CHBr (R = H, alkyl, or aryl) into the corresponding phthalimido-compounds were effected in a reaction system [KN(CO)<sub>2</sub>C<sub>6</sub>H<sub>4</sub> + CuI + MeCO·NMe<sub>2</sub> at 165°] previously found suitable for aryl halides; some mechanistic features are indicated. The response of aromatic-type heterocyclic bromides is also exemplified. Analogously, the sodium salts of succinimide, maleimide, dibenzamide, benzene-sulphonamide, and benzenesulphonanilide formed *N*-phenyl derivatives, but were less reactive than sodium phthalimide.

THE preceding paper<sup>1</sup> deals with copper-catalysed reactions between aryl halides and potassium phthalimide to produce *N*-arylphthalimides. Various analogues of such reactions may be envisaged and in this paper brief investigations of three types are reported: (a) substitutions of vinylic halides, in place of aryl halides; (b) substitutions by salts of other imides, and of sulphonamides, in place of the phthalimide; (c) examples of substitutions of aromatic-type heterocyclic bromides by potassium phthalimide.

*Catalysed Reactions between Vinylic Bromides and Potassium Phthalimide.*—*N*-Vinylphthalimides were obtained by substitutions of type (1), in which R in the halide is hydrogen, alkyl, or aryl, and the olefinic bond is *cis* or *trans*. Reactions of this type are not without



precedent; catalysis was used [copper(I) bromide and a trace of copper, without solvent, at 195°] for conversion of  $\omega$ -bromostyrene into the corresponding phthalimido-compound as a step in an isoquinoline synthesis.<sup>2</sup> The parent compound, *N*-vinylphthalimide, is of interest as a source of phthalimido-substituted polymers and copolymers, and thence of poly(vinylamine) by subsequent hydrazinolysis.<sup>3</sup> We suggest that the substitution process (1) provides a convenient

alternative to known routes to the monomer; these have customarily involved a pyrolytic elimination reaction,<sup>3,4</sup> *e.g.*, with *N*-2-acetoxyethylphthalimide.

Preparations of type (1) are exemplified in Table I. The conditions employed are those found suitable for aryl bromides<sup>1</sup> except that the volatile (aliphatic) members of the vinylic series were partly in an enclosed gaseous phase. The influence of the copper:phthalimide ratio on reaction rates<sup>1</sup> was not explored. The results demonstrate the process to be of practical value; also, there are features of theoretical interest which would merit further investigation. (a) *trans*-Vinylic bromides appear to be more reactive than the corresponding *cis*-isomers. This could be a steric effect, analogous to that observed with some aryl compounds.<sup>1</sup> (b) Stereochemical assignments are needed in the cases of the six products of type RCH=CH·N(CO)<sub>2</sub>C<sub>6</sub>H<sub>4</sub>. Three of these (R = Me, Ph, or *p*-NO<sub>2</sub>·C<sub>6</sub>H<sub>4</sub>) correspond with compounds which have previously been briefly described as products of elimination reactions [one is also known (R = Ph) from an earlier example of copper catalysis<sup>2</sup>], but the literature does not suggest whether structures are *cis* or *trans*. The tentative assignments given in Table I are based on consideration of available m.p., chromatographic, spectral, and preparative data. If correct, they signify retention of configuration in the

<sup>3</sup> D. D. Reynolds and W. O. Kenyon, *J. Amer. Chem. Soc.*, 1947, **69**, 911; M. L. Wolfrom and A. Chaney, *J. Org. Chem.*, 1961, **26**, 1319.

<sup>4</sup> W. E. Hanford and H. B. Stevenson, U.S.P. 2,276,840/1942; H. Hopff and P. Mühlethaler, *Chimia*, 1957, **11**, 336; J. Furukawa, A. Onishi, and T. Tsuruta, *J. Org. Chem.*, 1958, **23**, 672.

<sup>1</sup> Part XV, R. G. R. Bacon and Amna Karim, preceding paper.

<sup>2</sup> K. W. Rosenmund, M. Nothnagel, and H. Riesenfeldt, *Ber.*, 1927, **60**, 392.

copper-catalysed halide substitution process. (c) The effect of aromatic nuclear substituents, at least in the *para*-position, appears to be small. (d) Unlike the aryl substitutions,<sup>1</sup> those of  $\omega$ -styryl derivatives were accompanied by significant amounts of by-products; coupling reactions are suspected.

*Catalysed Reactions between Aryl Halides and Salts of Imides or Sulphonamides.*—It is known<sup>5</sup> that substitutions analogous to the Gabriel reaction may be performed with nucleophiles containing  $>NH$  centres of sufficient acidity, *i.e.*, amides, sulphonamides, or

phile under the conditions employed, and there was also response from analogous aliphatic imides, from an *NN*-diacylamine (but not from monoacylamines), and from sulphonamides,  $ArSO_2 \cdot NH_2$  or  $ArSO_2 \cdot NHAr$ . Effects of an *o*-nitro-substituent in the halide (*cf.* ref. 1) are indicated in the footnotes; in these cases partial hydrolysis of the *N*-phthaloyl or *N*-succinoyl group occurred during reaction or isolation of products.

*Reactions of Aromatic-type Heterocyclic Halides.*—In cases tested, preparations under the standard conditions<sup>1</sup> gave phthalimido-compounds, comparable in yield to

TABLE 1

Potassium phthalimide (0.01 mol) + copper(I) iodide (0.01 mol) + alkenyl bromides (*ca.* 0.02 mol) or arylalkenyl bromides (0.01 mol) in dimethylacetamide (100 ml) under nitrogen, 24 h at 165°

Halide	Product	Yield(%)
$CH_2:CHBr$	$CH_2:CH \cdot N(CO)_2C_6H_4$	73 <sup>a</sup>
$CH_2:CMeBr$	$CH_2:CMe \cdot N(CO)_2C_6H_4$	80
$CHMe:CHBr$	{(?) <i>cis</i> - $CHMe:CH \cdot N(CO)_2C_6H_4$	28
(70% <i>cis</i> + 30% <i>trans</i> )	{(?) <i>trans</i> - $CHMe:CH \cdot N(CO)_2C_6H_4$	35
<i>trans</i> -PhCH:CHBr	{(?) <i>trans</i> - $CHPh:CH \cdot N(CO)_2C_6H_4$	72 <sup>b</sup>
<i>trans</i> - <i>p</i> -MeO·C <sub>6</sub> H <sub>4</sub> ·CH:CHBr	{(?) <i>trans</i> - <i>p</i> -MeO·C <sub>6</sub> H <sub>4</sub> ·CH:CH·N(CO) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	93
<i>cis</i> - <i>p</i> -NO <sub>2</sub> ·C <sub>6</sub> H <sub>4</sub> ·CH:CHBr	{(?) <i>cis</i> - <i>p</i> -NO <sub>2</sub> ·C <sub>6</sub> H <sub>4</sub> ·CH:CH·N(CO) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	22 <sup>b</sup>
<i>trans</i> - <i>p</i> -NO <sub>2</sub> ·C <sub>6</sub> H <sub>4</sub> ·CH:CHBr	{(?) <i>trans</i> - <i>p</i> -NO <sub>2</sub> ·C <sub>6</sub> H <sub>4</sub> ·CH:CH·N(CO) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	82 <sup>b</sup>

<sup>a</sup> 22% Yield after 2 h, 64% after 12 h; a small amount of polymer was also observed. <sup>b</sup> Plus small amounts of unidentified by-products.

saccharin, in place of phthalimide. Among these reactions, with toluene-*p*-sulphonamide as nucleophile, there are examples of copper-assisted aryl substitutions, carried out in nitrobenzene, and involving as substrates *o*-halogenoaldehydes (with  $CuBr-Cu$ )<sup>6</sup> or 1-halogenoanthraquinones [with  $Cu(OAc)_2-Cu$ ].<sup>7</sup>

Table 2 shows results of catalysed reactions of bromobenzene, carried out in dimethylacetamide under standard conditions, with the salts generated by prior treatment of an imide, amide, or sulphonamide with sodium hydride. No reaction was observed with salts of

TABLE 2

Sodium salt of nucleophile (0.01 mol) + copper(I) iodide (0.01 mol) + bromobenzene (0.01 mol) in dimethylacetamide (100 ml) under nitrogen, 24 h at 165°

Nucleophile	Product	Yield (%)
Phthalimide <sup>a</sup>	<i>N</i> -Phenylphthalimide	62
Succinimide <sup>b</sup>	<i>N</i> -Phenylsuccinimide	31
Maleimide	<i>N</i> -Phenylmaleimide	17
Dibenzamide <sup>c</sup>	<i>N</i> -Phenyldibenzamide	17
Benzenesulphonamide	Benzenesulphonanilide	34
Benzenesulphonanilide	<i>NN</i> -Diphenylbenzenesulphonamide	12

<sup>a</sup> *o*-Bromonitrobenzene gave *N*-*o*-nitrophenylphthalimide (40%) and *o*-nitroaniline (7%). <sup>b</sup> *o*-Bromonitrobenzene gave *N*-*o*-nitrophenylsuccinimide (31%) and *o*-nitroaniline (24%); *o*-bromotoluene failed to react. <sup>c</sup> The reagent was partly converted into benzanilide (29%) during reaction or isolation of products.

acetanilide or benzanilide, or with saccharin. Summarising, phthalimide ion was the most reactive nucleo-

<sup>5</sup> G. Spielberger, in Houben-Weyl, 'Methoden der Organischen Chemie,' 4th edn., vol. 11/1, 1957, p. 96.

<sup>6</sup> P. Ruggli and F. Brandt, *Helv. Chim. Acta*, 1944, **27**, 274.

<sup>7</sup> F. Ullmann *et al.*, *Ber.*, 1910, **43**, 536; 1916, **49**, 732; *Annalen*, 1911, **381**, 1.

those resulting from aryl halides, from 2-bromopyridine (though the 3-isomer responded poorly), 3-bromopyridine, and 2-bromothiophen. Assuming copper complexes to be involved in transition states,<sup>1</sup> the difference in response of 2- and 3-bromopyridines could be connected with the position of halogen relative to the ligand-forming nitrogen atom; co-ordination through heteroatoms might emerge as a factor of general importance in further exploration of catalysed heterocyclic substitutions.

## EXPERIMENTAL

*Vinyl Bromides.*—Vinyl bromide, 1-bromopropene, 2-bromopropene, and (essentially *trans*-) $\omega$ -bromostyrene were commercial products. 1-Bromopropene<sup>8</sup> was known to be a mixture of isomers and was shown, by g.l.c. analysis on an Apiezon L-Celite column, to consist of 70% *cis*- and 30% *trans*-isomer.

Treatment of *erythro*-2,3-dibromo-3-*p*-methoxyphenylpropionic acid<sup>9</sup> with sodium hydrogen carbonate in a mixture of butan-2-one and diethylene glycol<sup>10</sup> afforded *trans*-*p*-methoxy- $\omega$ -bromostyrene, m.p. 54–55° (lit.,<sup>10</sup> 55–55.5°). Treatment of *erythro*-2,3-dibromo-3-*p*-nitrophenylpropionic acid<sup>10</sup> with sodium acetate in ethanol<sup>10,11</sup> gave *cis*-*p*-nitro- $\omega$ -bromostyrene, m.p. 43–46° (lit.,<sup>10</sup> 45–46°). *p*-Nitrobenzenediazonium bromide was treated with vinyl bromide in the presence of copper(II) bromide to yield 1,1-dibromo-2-*p*-nitrophenylethane,<sup>11</sup> which, on treatment with ethanolic sodium hydroxide<sup>11</sup> gave *trans*-*p*-nitro- $\omega$ -bromostyrene, m.p. 159–161° (lit.,<sup>11</sup> 156–157°).

<sup>8</sup> E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 1951, 2078; J. M. Birchall, T. Clarke, and R. N. Haszeldine, *ibid.*, 1962, 4977.

<sup>9</sup> W. Borsche and G. Walter, *Ber.*, 1927, **60**, 2112.

<sup>10</sup> E. R. Trumbull, R. T. Finn, K. M. Ibne-Rasa, and C. K. Sauers, *J. Org. Chem.*, 1962, **27**, 2339.

<sup>11</sup> S. J. Cristol and W. P. Norris, *J. Amer. Chem. Soc.*, 1954, **76**, 3005.

*N*-Vinylphthalimides (Table 1).—In the case of the aryl substituted vinyl bromides, the halide (0.01 mol) was treated with potassium phthalimide (0.01 mol) and copper(I) iodide (0.01 mol) in refluxing dimethylacetamide (100 ml) in an atmosphere of nitrogen for 24 h as previously described.<sup>1</sup> In the case of the volatile aliphatic vinylic bromides, the same system was used except that the reaction vessel was connected to a gas burette and the solution was magnetically stirred. An excess of the halide (*ca.* 0.02 mol) was injected into the vessel with a syringe, and was then partly in solution and partly in the gaseous phase, where a contraction was observed as reaction proceeded. Products were isolated by chromatography, as previously described.<sup>1</sup>

Vinyl bromide gave *N*-vinylphthalimide, m.p. 85–86° (from light petroleum) (lit.,<sup>3</sup> 85.5–86.5°), eluted with benzene–ether (9 : 1), followed by unchanged phthalimide, eluted with benzene–ether (4 : 1). 2-Bromopropene gave *N*-prop-2-enylphthalimide, m.p. 105° (from ethanol) (lit.,<sup>12</sup> 105–106°), eluted by light petroleum–ether (7 : 3), followed by unchanged phthalimide. 1-Bromopropene (mixed stereoisomers) gave *N*-(?)*trans*-prop-1-enylphthalimide, m.p. 149–150° (from ethanol) (lit.,<sup>13</sup> 151°),  $\tau$  2.1–2.35 (4H, m, ArH), 3.3–3.5 (2H, m, olefinic), and 8.15 (3H, q, Me), eluted by light petroleum–ether (7 : 3). This was followed by the (?)*cis*-isomer, m.p. 86–87° (from ethanol),  $\tau$  2.1–2.3 (4H, m, ArH), 3.8–4.3 (2H, m, olefinic), and 8.3 (3H, q, Me), eluted by light petroleum–ether (1 : 1) (Found: C, 70.8; H, 4.8; N, 7.5. C<sub>11</sub>H<sub>9</sub>NO<sub>2</sub> requires C, 70.6; H, 4.8; N, 7.5%), and then unchanged phthalimide, eluted by light petroleum–ether (1 : 4).

$\omega$ -Bromostyrene gave unidentified solid fractions (*ca.* 0.4 g), eluted with light petroleum, followed by (?)*trans*-1-phenyl-2-phthalimidoethylene, m.p. 190° (from ethanol) (lit.,<sup>2</sup> 188–189°; lit.,<sup>14</sup> 187.5–188.5°), eluted by benzene–ether (9 : 1), and then unchanged phthalimide, eluted by benzene–ether (7 : 3). *trans*-*p*-Nitro- $\omega$ -bromostyrene gave unidentified solid fractions (0.2 g), eluted by light petroleum–ether (1 : 1) and (?)*trans*-1-*p*-nitrophenyl-2-phthalimidoethylene, m.p. 282–283° (from acetic acid) (lit.,<sup>15</sup> 283°), eluted by dichloromethane–ether (1 : 1). *cis*-*p*-Nitro- $\omega$ -bromostyrene gave solid unidentified fractions (0.55 g), eluted by light petroleum–ether (1 : 1) and (?)*cis*-1-*p*-nitrophenyl-2-phthalimidoethylene, m.p. 220–222° (from acetic acid), eluted by dichloromethane–ether (1 : 4) (Found: C, 65.7; H, 3.6; N, 9.6. C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>O<sub>4</sub> requires C, 65.3; H, 3.4; N, 9.5%), *m/e* 294 (*M*<sup>+</sup>). *trans*-*p*-Methoxy- $\omega$ -bromostyrene gave (?)*trans*-1-*p*-methoxyphenyl-2-phthalimidoethylene, m.p. 164° (from ethanol),  $\tau$  2.1–2.8 (8H, m, ArH), 3.1–3.2 (2H, d, olefinic), and 6.25 (3H, s, Me), eluted by light petroleum–ether (3 : 2) (Found: C, 73.5; H, 4.9; N, 5.3. C<sub>17</sub>H<sub>13</sub>NO<sub>3</sub> requires C, 73.1; H, 4.7; N, 5.0%), *m/e* 279 (*M*<sup>+</sup>).

<sup>12</sup> S. Gabriel, *Ber.*, 1911, **44**, 3084.

<sup>13</sup> S. Gabriel and H. Ohle, *Ber.*, 1917, **50**, 804.

<sup>14</sup> A. Terada, *Nippon Kagaku Zasshi*, 1956, **77**, 1265 (*Chem. Abs.*, 1959, **53**, 5185).

<sup>15</sup> A. Terada, *Nippon Kagaku Zasshi*, 1960, **81**, 606 (*Chem. Abs.*, 1962, **56**, 1441).

<sup>16</sup> H. Meerwein, P. Laasch, R. Mersch, and J. Spille, *Ber.*, 1956, **89**, 209.

*Reactions of Bromobenzene with Salts of Imides or Sulphonamides* (Table 2).—The imides, amides, or sulphonamides were from commercial sources except dibenzamide, which was prepared from benzonitrile.<sup>16</sup> Prior to reaction with the halide, these reagents (0.01 mol) were treated with a slight excess of sodium hydride (50% dispersion in mineral oil) in dry dimethylacetamide (50 ml). The mixture was kept at reflux temperature under nitrogen for 12 h, cooled, and copper(I) iodide (0.01 mol) and bromobenzene (0.01 mol) were added. Refluxing was renewed for 24 h, during which time the mixtures remained turbid. After isolation and chromatography,<sup>1</sup> products were recrystallised (from ethanol unless otherwise stated); unchanged halide and (usually) nucleophile fractions were also obtained.

Sodium phthalimide thus gave *N*-phenylphthalimide,<sup>1</sup> m.p. 205°, eluted by light petroleum; with *o*-bromonitrobenzene in place of bromobenzene, the products were *o*-nitroaniline, followed by *N*-*o*-nitrophenylphthalimide,<sup>1</sup> m.p. 203°, eluted by ether–dichloromethane (4 : 1). Sodium succinimide and bromobenzene gave *N*-phenylsuccinimide, m.p. 155° (lit.,<sup>17</sup> 156°), whilst with *o*-bromonitrobenzene the products were *o*-nitroaniline and *N*-*o*-nitrophenylsuccinimide, m.p. 154–155° (lit.,<sup>18</sup> 155.5–156°), eluted by dichloromethane. Sodium maleimide gave *N*-phenylmaleimide, m.p. 90° (lit.,<sup>19</sup> 90–91°). Sodium dibenzamide gave *N*-phenyldibenzamide, m.p. 162–163° (lit.,<sup>20</sup> 160–161°), eluted by light petroleum–ether (1 : 1) followed by benzanilide, m.p. 161°, eluted by ether. Sodium benzenesulphonamide gave benzenesulphonanilide, m.p. 109–110°, eluted by light petroleum–ether (1 : 1). Sodium benzenesulphonanilide gave *NN*-diphenylbenzenesulphonamide, m.p. 123° (lit.,<sup>21</sup> 122–123°), eluted by light petroleum–ether (3 : 7).

*Heterocyclic Phthalimido-derivatives*.—Reactions were carried out for 24 h, as described for aryl halides,<sup>1</sup> with the heterocyclic bromide, potassium phthalimide, and copper(I) iodide (0.01 mol each) in refluxing dimethylacetamide (100 ml). The crude products from the heterocyclic bases were precipitated by adding the solutions to water instead of acid. 2-Bromopyridine thus gave *N*-2-pyridylphthalimide (70%), m.p. 227° (from ethanol) (lit.,<sup>22</sup> 226°), eluted by benzene–ether (9 : 1), whilst 3-bromopyridine gave the impure 3-pyridyl isomer (*ca.* 5%), m.p. 170–175°, eluted by benzene–ether (7 : 3). 3-Bromoquinoline gave *N*-3-quinolyphthalimide (31%), m.p. 215° (from ethanol), eluted by benzene–ether (4 : 1) (Found: C, 74.5; H, 3.6; N, 10.4. C<sub>17</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub> requires C, 74.5; H, 3.6; N, 10.2%), *m/e* 274 (*M*<sup>+</sup>). 2-Bromothiophen gave *N*-2-thienylphthalimide (50%), m.p. 197–198° (from ethanol) (lit.,<sup>23</sup> 198°).

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<sup>17</sup> W. H. Warren and R. A. Briggs, *Ber.*, 1931, **64**, 26.

<sup>18</sup> K. Auwers, *Annalen*, 1896, **292**, 132.

<sup>19</sup> von R. Anschütz and Q. Wirtz, *Annalen*, 1887, **239**, 137.

<sup>20</sup> P. Kay, *Ber.*, 1893, **26**, 2853.

<sup>21</sup> A. Ginzberg, *Ber.*, 1903, **36**, 2703.

<sup>22</sup> G. Vanags (Wanag), *Acta Univ. Lactviensis, Kim. Fakultat.*, 1939, Ser. 4, No. 8, 405 (*Chem. Abs.*, 1940, **34**, 1982).

<sup>23</sup> J. C. Craig and D. Willis, *J. Chem. Soc.*, 1955, 1071.