

## Heterocycles by Cycloaddition. Part II.<sup>1</sup> Cycloaddition–Extrusion Reactions of Five-Membered mesoionic Compounds with Benzyne: Preparation of Benz[c]azole and Benzo[c]thiophen Derivatives<sup>2</sup>

By Hiroshi Kato,\* Department of Chemistry, Faculty of Science, Shinshu University, Asahi, Matsumoto 390, Japan  
Sho Nakazawa, Takako Kiyosawa, and Kiyochi Hirakawa, Faculty of Textile Science and Technology,  
Shinshu University, Ueda, Nagano 386, Japan

Several five-membered mesoionic compounds react with benzyne to give benzo-fused five-membered heterocycles [(2) and (5)] with a formal quinonoid structure. A bridged intermediate adduct (4c) was isolated from the reaction of benzyne with a mesoionic thiazol-4-one (3c). Pyrolysis of the adduct gave an isobenzothiophen (5a), whereas its photolysis led to an isoquinolone (7). The corresponding adduct *S*-oxide (4e) gave the isoquinolone (7) by both pyrolysis and photolysis.

ALTHOUGH the cycloaddition reactions of mesoionic compounds with various dipolarophiles have been studied in detail,<sup>3</sup> the reaction of five-membered mesoionic compounds with an aryne has been reported only for 3-phenylsydnone.<sup>4,5</sup> It thus appeared worthwhile to study the applicability of the cycloaddition–extrusion reactions of five-membered mesoionic compounds with benzyne as a general synthetic route to benzo-fused heterocycles with a formal *o*-quinonoid structure.

Among various benzyne precursors,<sup>6</sup> 1-aminobenzotriazole appeared the most attractive provided that the

† The earlier workers used benzenediazonium-2-carboxylate as the benzyne precursor and isolated (2a) in moderate yields by chromatography.<sup>4</sup>

<sup>1</sup> Part I, H. Matsukubo and H. Kato, *J.C.S. Perkin I*, 1975, 632.

<sup>2</sup> Preliminary report, S. Nakazawa, T. Kiyosawa, K. Hirakawa, and H. Kato, *J.C.S. Chem. Comm.*, 1974, 621.

<sup>3</sup> M. Ohta and H. Kato, 'Nonbenzenoid Aromatics,' vol. 1, ed. J. P. Snyder, Academic Press, New York, 1969, p. 117.

heterocycle could survive the oxidative conditions necessary for benzyne generation.<sup>7</sup>

In agreement with the earlier findings,<sup>4</sup> treatment of 3-phenylsydnone (1a) with benzyne, generated by treatment of 1-aminobenzotriazole with lead tetra-acetate, gave a 73% yield of 2-phenylindazole (2a), isolated by simple extraction and recrystallisation.† A similar treatment of 3-benzyl-4-phenyl- and 4-methyl-3-phenylsydnone (1b and c) with benzyne from the same source afforded the corresponding indazoles (2b and c) in 68 and 64% yields, respectively.

Treatment of the mesoionic 2,5-diphenyl-1,3-dithiol-4-one (3a) with benzyne gave 1,3-diphenylisobenzo-

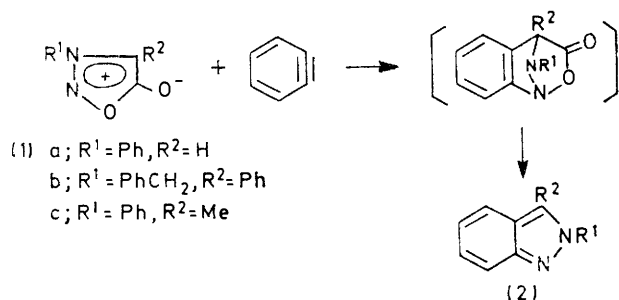
<sup>4</sup> A. Y. Lazaris, *Zhur. org. Khim.*, 1966, 2, 1322 (*Chem. Abs.*, 1967, **66**, 65,426); H. Gotthardt, R. Huisgen, and R. Knorr, *Chem. Ber.*, 1968, **101**, 1056.

<sup>5</sup> T. Sasaki, K. Kanematsu, and M. Uchide, *Bull. Chem. Soc. Japan*, 1971, **44**, 858.

<sup>6</sup> R. W. Hoffman, 'Dehydrobenzene and Cycloalkynes,' Academic Press, New York, 1967.

<sup>7</sup> C. D. Campbell and C. W. Rees, *J. Chem. Soc. (C)*, 1969, 742.

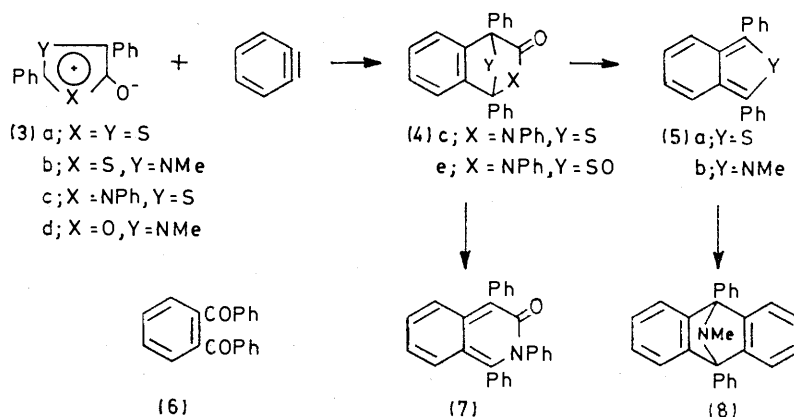
thiophen (5a) (36%), along with two by-products. The minor by-product was *o*-dibenzoylbenzene (6). The major by-product had an acetoxy-group, and elemental and mass spectral analyses showed that a molecule of



SCHEME 1

acetic acid was incorporated into the intermediate adduct (4; X = Y = S). Its structure was not pursued further.

From the synthetic point of view, the value of this procedure depends on the relative reactivity of mesoionic compounds and the reaction products towards benzyne.



SCHEME 2

For example, the reaction between benzyne and the mesoionic 3-methyl-2,4-diphenylthiazol-5-one (3b) gave the expected 2-methyl-1,3-diphenylisoindole (5b) only in a 4% yield, and the major product was 9,10-dihydro-11-methyl-9,10-diphenyl-9,10-iminoanthracene (8) (11%), the adduct of benzyne with the initially formed isoindole (5b) which is also a reactive diene.<sup>8</sup> Dibenzoylbenzene (6) (6%) was again isolated. The formation of dibenzoylbenzene in the two reactions described above may be due to a photo-oxidation, an auto-oxidation, or oxidation by lead tetra-acetate of the isobenzothiophen (5a) and the

isoindole (5b).<sup>9</sup> Treatment of the isobenzothiophen (5a) with lead tetra-acetate gave dibenzoylbenzene (6) in low yield.

In the case of the mesoionic 2,3,5-triphenylthiazol-4-one (3c), the primary adduct, 1,4-epithio-1,4-dihydro-1,2,4-triphenyl-3-isoquinolone (4c) could be isolated in 78% yield. The i.r. spectrum of (4c) ( $\nu_{\text{CO}}$  1720 cm<sup>-1</sup>) supports the presence of a strained amide group. Although such bridged intermediates are often isolable in the reactions of five-membered mesoionic compounds with olefins and hetero-cumulenes, they are rarely isolated from the reactions with alkynes.<sup>10</sup> Thermal fragmentation of the adduct (4c) in refluxing xylene gave, as expected, 1,3-diphenylisobenzothiophen (5a) (67%) and phenyl isocyanate, the latter identified by conversion into diphenylurea by treatment with aniline. In contrast to the thermal fragmentation, photolysis of the adduct (4c) through a Pyrex filter resulted in extrusion of sulphur to give 1,2,4-triphenyl-3-isoquinolone (7) (60%). It appeared that the sulphur was eliminated in an active form because the reaction mixture had a strong odour characteristic of a thiol. In neither case were products of the alternative route formed in amounts

detectable by t.l.c. These selective fragmentation reactions, though not without precedent,<sup>11</sup> are worthy of both theoretical and synthetic attention.

The adduct (4c) gave the S-oxide (4e) on treatment with an equimolar amount of *m*-chloroperbenzoic acid. Considerable deshielding of the benzene ring protons showed that the oxygen atom is *syn* to the benzene ring. The S-oxide (4e) gave the isoquinolone (7) both by pyrolysis and by photolysis.

With regard to the benzyne source, 1-aminobenzotriazole can be employed only when the mesoionic compounds are sufficiently stable in the oxidative environment, and do not react with the amine employed. Thus,

<sup>8</sup> R. Harrison, H. Heaney, and P. Lees, *Tetrahedron*, 1968, **24**, 4589.

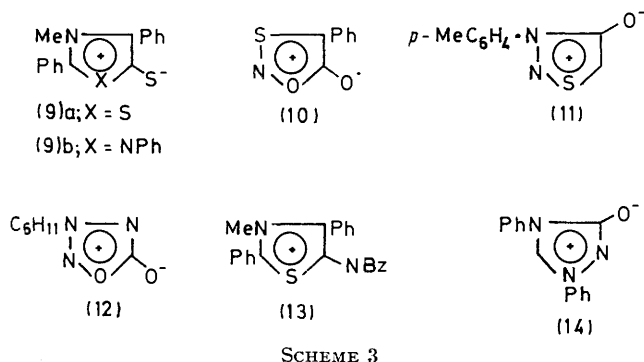
<sup>9</sup> F. Nahavandi, F. Razmara, and M. P. Stevens, *Tetrahedron Letters*, 1973, 301; E. D. Bergmann, S. Blumberg, P. Bracha, and A. Mitra, *Tetrahedron*, 1964, **20**, 195; M. P. Cava, M. Behrorouz, G. E. M. Husbands, and M. Srinivasan, *J. Amer. Chem. Soc.*, 1973, **95**, 2561; K. T. Potts and D. McKeough, *ibid.*, 1974, **96**, 4268, 4276; M. Ahmed, L. J. Kricka, and J. M. Vernon, *J.C.S. Perkin I*, 1975, 71; M. P. Cava and M. V. Lakshmikantham, *Accounts Chem. Res.*, 1975, **8**, 139; and references cited therein.

<sup>10</sup> W. E. McEwen, I. C. Mineo, and Y. H. Shen, *J. Amer. Chem. Soc.*, 1971, **93**, 4479; T. Iyata, M. Hamaguchi, and H. Kiyohara, *Chem. Letters*, 1975, 21.

<sup>11</sup> D. H. R. Barton, E. H. Smith, and B. J. Willis, *Chem. Comm.*, 1970, 1226; D. H. R. Barton and B. J. Willis, *J.C.S. Perkin I*, 1972, 305; R. M. Kellogg and S. Wassenaar, *Tetrahedron Letters*, 1970, 1987.

the mesoionic 3-methyl-2,4-diphenyloxazol-5-one (3d) gave only very low yields of the isoindole (5b) (2%) and the iminoanthracene (8) (4%) together with unidentified minor products, and a complex product mixture resulted from the reaction of benzyne from 1-aminobenzotriazole with the mesoionic 3-methyl-2,4-diphenylthiazole-5-thione (9a), 1-methyl-2,3,5-triphenylimidazole-4-thione (9b), 4-phenyl-1,3,2-oxathiazol-5-one (10), and 3-*p*-tolyl-1,2,3-thiadiazol-4-one (11).

The mesoionic 3-cyclohexyl-1,2,3,4-oxatriazol-5-one (12) and 5-benzoylimino-3-methyl-2,4-diphenylthiazole (13) did not react with benzyne. The mesoionic 1,4-diphenyl-1,2,4-triazol-3-one (14) was also unchanged after treatment with benzyne generated from 1-aminobenzotriazole. However, it did react with benzyne formed by pyrolysis of diphenyliodonium-2-carboxylate<sup>12</sup> to give 2-phenylindazole (2a), albeit only in 34% yield. Hence, this benzyne source may serve as an alternative when the mesoionic compounds are of relatively low reactivity, but can survive the pyrolytic conditions.



SCHEME 3

However, it is less attractive than 1-aminobenzotriazole: the reaction between 3-phenylsydnone (1a) and the thermally generated benzyne gave 2-phenylindazole (2a) in only 16% yield.

#### EXPERIMENTAL

M.p.s were determined on a Yanagimoto hot-stage apparatus. U.v. and i.r. (KBr) spectra were recorded on Hitachi EPS-3T and EPI-SII spectrophotometers, and n.m.r. spectra on a JEOL JNM-4H-100 (100 MHz) spectrometer for solutions in deuteriochloroform (tetramethylsilane as internal standard). All known compounds were adequately identified by elemental and spectral analyses. The yields reported are based on amounts of isolated products of adequate purity and on amounts of starting material consumed.

*Reactions of Mesoionic Compounds with Benzyne generated from 1-Aminobenzotriazole.—General procedures.* (a) To a stirred suspension of equimolar amounts of a mesoionic compound (0.5–1 g) and lead tetra-acetate in benzene (15–30 ml), an equimolar amount of 1-aminobenzotriazole

was added in small portions at room temperature. After 30 min, the suspension was filtered, the precipitate was washed with a suitable solvent, the washings and the filtrate were concentrated under reduced pressure, and the residue was worked up by an appropriate method. Procedure (b) was identical with procedure (a) except that 1-aminobenzotriazole and lead tetra-acetate were added alternately in small portions to a solution of a mesoionic compound in dichloromethane.

(i) 3-Phenylsydnone (1a). The product mixture from the reaction with (1a) (0.82 g, 5 mmol) by procedure (a) was extracted with petroleum and the product from the extract was recrystallised (petroleum) to give 2-phenylindazole (2a) as needles (0.71 g, 73%), m.p. 81–82° (lit.,<sup>4</sup> 82.2–82.4°).

(ii) 3-Benzyl-4-phenylsydnone (1b). Extraction (n-hexane) and recrystallisation (ethanol) of the product from (1b) (0.5 g, 2.1 mmol) by procedure (a) afforded 2-benzyl-3-phenylindazole (2b) as prisms (405 mg, 68%), m.p. 105.2–107° (Found: C, 84.6; H, 5.75; N, 10.0. C<sub>20</sub>H<sub>16</sub>N<sub>2</sub> requires C, 84.5; H, 5.65; N, 9.85%),  $\delta$  7.87–6.90 and 7.38 (14 H, m + s, ArH and Ph), and 5.59 (2 H, s, CH<sub>2</sub>).

(iii) 4-Methyl-3-phenylsydnone (1c). The product from (1c) (0.5 g, 2.8 mmol) by procedure (a) was chromatographed on silica with dichloromethane to give biphenylene (18 mg) and then 3-methyl-2-phenylindazole (2c) as plates (from petroleum) (376 mg, 64%), m.p. 88.5–89.8° (Found: C, 80.6; H, 5.8; N, 13.5. C<sub>14</sub>H<sub>12</sub>N<sub>2</sub> requires C, 80.75; H, 5.8; N, 13.45%),  $\delta$  7.87–6.92, 7.46 (9 H, m + s, ArH and Ph), and 2.60 (3 H, s, Me).

(iv) 2,5-Diphenyl-1,3-dithiolium-4-olate (3a). The product from (3a) (0.5 g, 1.9 mmol) by procedure (a) was extracted (n-hexane), the extract was concentrated, and the residue was washed with methanol. Compound (3a) (102 mg, 20%) was recovered from the washings. Recrystallisation (ethanol) of the residue gave 1,3-diphenylisobenzothiophen (5a) as yellow needles (0.15 g, 36%), m.p. 120–121° (lit.,<sup>13</sup> 119–120°). The residue remaining after the hexane extraction was recrystallised (n-hexane) to give an unidentified compound as needles (131 mg, 21%), m.p. 129–130° (Found: C, 67.7; H, 4.5%; rel. int. *M*:*M* + 1:*M* + 2, 100:26:11. Calc. for C<sub>23</sub>H<sub>18</sub>O<sub>3</sub>S<sub>2</sub>: C, 67.95; H, 4.45%; *M*:*M* + 1:*M* + 2, 100:27:10),  $\nu_{\max}$ . 1745 cm<sup>-1</sup> (C=O),  $\delta$  7.90–6.90 (15 H, m) and 1.76 (3 H, s, Me), *m/e* 406 (*M*, 6%), 300 (25), 258 (100), 257 (17), 134 (16), 121 (61), and 77 (18). The mother liquor was chromatographed on silica with carbon tetrachloride to give *o*-dibenzoylbenzene (6) as pale yellow prisms (from n-hexane) (18 mg, 4%), m.p. 146.5–148.5° (lit.,<sup>14</sup> 146–147°). The reaction of (3a) by procedure (b) gave essentially the same results.

(v) 3-Methyl-2,4-diphenylthiazolium-5-olate (3b). The product from (3b) (0.53 g, 2 mmol) by procedure (b) was chromatographed on silica with benzene and then with dichloromethane. The first eluate (benzene) contained 2-methyl-1,3-diphenylisoindole (5b) (30 mg, 4%), pale yellow leaflets (from ethanol), m.p. 147–149.5° (lit.,<sup>15</sup> 149.5–150°). The second fraction (dichloromethane) consisted of *o*-dibenzoylbenzene (6) (33 mg, 6%), m.p. 148–149.4°, and the third (dichloromethane) afforded 9,10-dihydro-11-methyl-9,10-diphenyl-9,10-iminoanthracene (8) (82 mg, 11%),

<sup>14</sup> C. J. Pouchert, 'The Aldrich Library of Infrared Spectra,' Milwaukee, Wisconsin, 1970, p. 653.

<sup>15</sup> J. C. Emmett, D. F. Veber, and W. Lwowski, *Chem. Comm.*, 1965, 272; J. D. White, M. E. Mann, H. D. Kirchenbaum, and A. Mitra, *J. Org. Chem.*, 1971, **36**, 1048.

<sup>12</sup> L. F. Fieser and M. J. Haddadin, *Org. Synth. Coll. Vol. V*, 1973, p. 1037.

<sup>13</sup> M. P. Cava, M. J. Mitchell, and A. A. Deana, *J. Org. Chem.*, 1960, **25**, 1481.

prisms (from ethanol), m.p. 176.5—177.5° (lit.,<sup>8</sup> 167—168°) (Found: C, 90.0; H, 5.9. Calc. for C<sub>27</sub>H<sub>21</sub>N: C, 90.2; H, 5.9%), i.r. and n.m.r. spectra as reported.

(vi) *2,3,5-Triphenylthiazolium-4-olate* (3c). The product from (3c) (0.66 g, 2 mmol) by procedure (b) was recrystallised (benzene–n-hexane) to give *1,4-epithio-1,4-dihydro-1,2,4-triphenyl-3-isoquinolone* (4c) (635 mg, 78%) as prisms, m.p. 140.2—140.6° (decomp.) (Found: C, 79.7; H, 4.7; N, 3.4. C<sub>27</sub>H<sub>19</sub>NOS requires C, 79.95; H, 4.7; N, 3.45%), λ<sub>max</sub> (MeCN) 242sh nm (log ε 4.103), ν<sub>max</sub> 1 720 cm<sup>-1</sup> (C=O), δ 7.75—6.88 (m, ArH and Ph).

(vii) *3-Methyl-2,4-diphenyloxazolium-5-olate* (3d). The product from (3d) (0.5 g, 2 mmol) by procedure (b) was chromatographed on silica with dichloromethane to give, besides unidentified minor products, biphenylene (20 mg), 2-methyl-1,3-diphenylisoindole (5b) (10 mg, 2%), and 9,10-dihydro-11-methyl-9,10-diphenyl-9,10-iminoanthracene (8) (25 mg, 4%), identical with authentic specimens.

*Oxidation of Diphenylisobenzothiophen* (5a).—A suspension of the isobenzothiophen (5a) (100 mg, 0.35 mmol) and lead tetra-acetate (155 mg, 0.35 mmol) in benzene (20 ml) was stirred for 2 h at room temperature. After addition of water, the organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated, and the residue was chromatographed on silica with benzene to give *o*-dibenzoylbenzene (6) (8 mg, 8%), m.p. 148.5—151° and unchanged isobenzothiophen (5a), identical with authentic specimens.

*Pyrolysis of the Adduct* (4c).—A solution of the adduct (4c) (100 mg, 0.25 mmol) in xylene (15 ml) was heated under reflux for 1 h. Aniline (23 μl, 0.25 mmol) was then added to the cooled solution, which was concentrated to one-third of its original volume, and the crystals which separated were collected to give diphenylurea (32 mg, 60%), m.p. and mixed m.p. 238.5—240.5°. The filtrate was concentrated further and the residue was recrystallised (from ethanol) to give 1,3-diphenylisobenzothiophen (5a) (47 mg, 67%), m.p. and mixed m.p. 121.8—122.6°. The formation of the isoquinolone (7) in the pyrolysate was not detected on t.l.c.

*Photolysis of the Adduct* (4c).—A solution of (4c) (100 mg, 0.25 mmol) in deaerated benzene (200 ml) was irradiated with a 100 W high-pressure mercury lamp through a Pyrex filter for 2 h below 20 °C. The solution was concentrated, and the residue was washed (n-hexane) and recrystallised (benzene) to give orange needles of 1,2,4-triphenyl-3-isoquinolone (7) (50 mg, 60%), m.p. 279—281° (lit.,<sup>16</sup> 274—275°).

A similar photolysis in benzene (180 ml) and methanol (20 ml) gave comparable results, and t.l.c. of the crude photolysate showed the absence of both the isoindole (5a) and methyl phenylcarbamate.

*1,4-Epithio-1,4-dihydro-1,2,4-triphenyl-3-isoquinolone* 9-

*Oxide* (4e).—A solution of *m*-chloroperbenzoic acid (0.2 mmol) in dichloromethane (5 ml) was added dropwise to a solution of the adduct (4c) (80 mg, 0.2 mmol) in dichloromethane (10 ml). The resulting solution was stirred for 15 min, then washed with aqueous sodium hydrogen carbonate and water, and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was distilled off, and the residue was recrystallised (benzene–cyclohexane) to give prisms of the *S-oxide* (4e) (72 mg, 83%), m.p. 145—147° (decomp.) (Found: C, 76.75; H, 4.35; N, 3.3. C<sub>27</sub>H<sub>19</sub>NO<sub>2</sub>S requires C, 76.95; H, 4.55; N, 3.3%), u.v. (MeOH) end absorption, ν<sub>max</sub> 1 705 (C=O) and 1 117 cm<sup>-1</sup> (SO), δ 8.05—7.85 (2 H, m, ArH) and 7.70—7.10 (17 H, m, ArH and Ph).

*Pyrolysis of the S-Oxide* (4e).—The *S-oxide* (4e) (10.7 mg, 0.025 mmol) was sealed under vacuum and kept at 150 °C for 75 min. The product was washed with methanol to give 1,2,4-triphenyl-3-isoquinolone (7) (9.3 mg, 98%), m.p. and mixed m.p. 277—278°. T.l.c. of the methanol washings did not show any spot corresponding to methyl phenylcarbamate.

*Photolysis of the S-Oxide* (4e).—A solution of the *S-oxide* (4e) (10.2 mg, 0.02 mmol) in deaerated benzene (200 ml) was irradiated through a Pyrex filter with a 100 W high-pressure mercury lamp for 75 min at 15 °C. The solution was concentrated and the residue was recrystallised (benzene–n-hexane) to give the isoquinolone (7) (9 mg, 100%), m.p. 280.5—282.5°, identical with an authentic specimen. T.l.c. of the reaction mixture showed only one spot, corresponding to the isoquinolone (7).

*Reactions of Benzynes (from Diphenyliodonium-2-carboxylate) with Mesoionic Compounds.*—(i) *1,4-Diphenyl-1,2,4-triazolium-3-olate* (14). A suspension of compound (14) (0.50 g, 2.1 mmol) and diphenyliodonium-2-carboxylate (0.68 g, 2.1 mmol) in *o*-diethylbenzene (15 ml) was heated under reflux for 2 h. After cooling, the crystals which had separated were collected to give unchanged (14) (0.18 g, 35%). The filtrate was concentrated and chromatographed on silica with dichloromethane to give 2-phenylindazole (2a) (87 mg, 34%), m.p. and mixed m.p. 82.2—83.4°. The formation of some biphenylene was suggested by t.l.c. of the crude product, but no attempt was made to isolate it.

(ii) *3-Phenylsydnone* (1a). Similar treatment of the sydnone (1a) (0.41 g, 2.5 mmol) with diphenyliodonium-2-carboxylate (0.81 g, 2.5 mmol) and chromatography of the product gave 3-phenylsydnone (1a) (21 mg, 5%) and 2-phenylindazole (2a) (73 mg, 16%), m.p. 80—83.2°, identical with authentic specimens.

[5/1611 Received, 15th August, 1975]

<sup>16</sup> J. M. Holland and D. W. Jones, *J. Chem. Soc. (C)*, 1970, 530.