

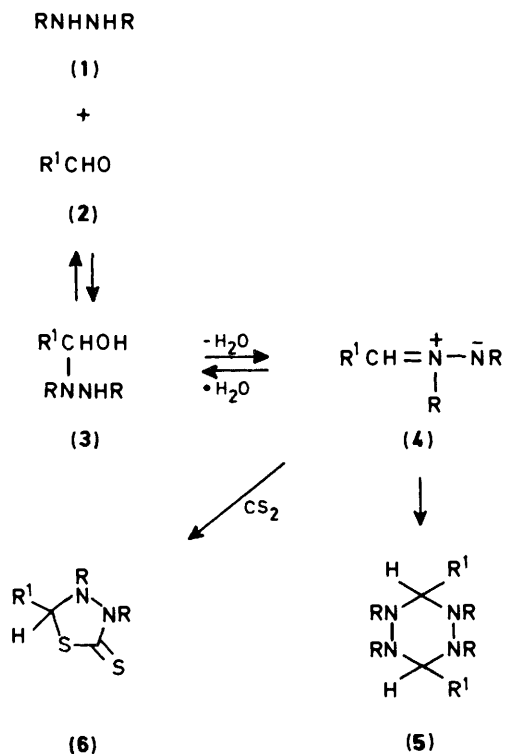
## Reaction of Aromatic Aldehydes with 1,2-Dibenzylhydrazine

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The reactions of 1,2-dibenzylhydrazine with several aromatic aldehydes in refluxing toluene gave the benzaldehyde dibenzylhydrazones (9) and (13) in high yield. It is suggested from labelling studies and from the failure to trap an azomethine imine in the reaction between dibenzylhydrazine and benzaldehyde that such intermediates are not involved in the formation of the hydrazones. These products may be formed directly *via* hydride transfer in the hydrazinocarbinal (18) or the hydrazone ion (19).

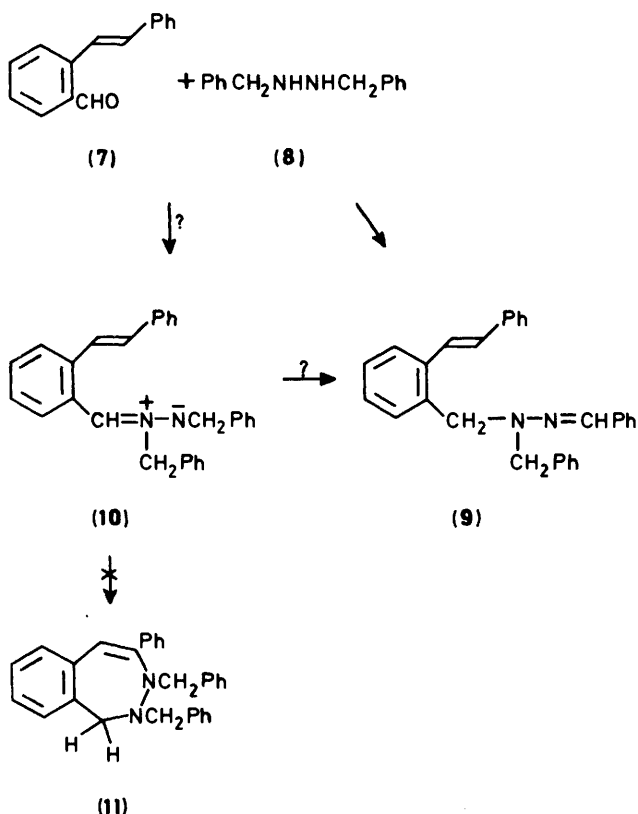
Reactions between 1,2-disubstituted hydrazines (1) and aldehydes (2) have been investigated by several groups, mainly with the objective of generating azomethine imines (4) (Scheme 1). The earliest reports on the use of 1,2-diarylhydrazines were by Rassow<sup>1</sup> who obtained the hexahydrotetrazines (5).



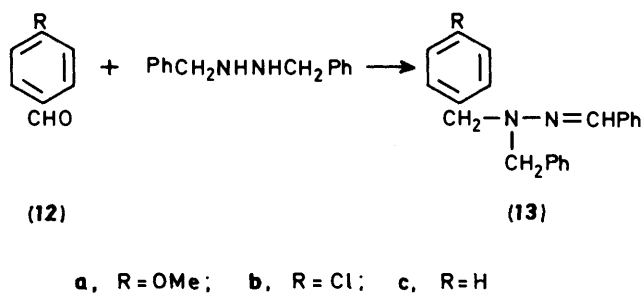
Huisgen later showed that dialkylhydrazines react in the same way and, more interestingly, that the reaction path could be diverted by the presence of carbon disulphide<sup>2</sup> or other dipolarophiles<sup>3</sup> to give cycloadducts, *e.g.* the 1,3,4-thiadiazolidine system (6). These results were rationalised on the basis of the mechanism shown in Scheme 1 in which the primary product, the hydrazinocarbinal (3), loses water to give the azomethine imine (4) which either dimerises to give the tetrazine (5) or can be trapped by added dipolarophiles such as carbon disulphide. It was, however, pointed out that alternative mechanisms, for example one in which the hydrazine reacts first with carbon disulphide, could not be excluded.<sup>2</sup> More recently Oppolzer has made extensive use of the reactions of *N*-acyl-*N'*-alkylhydrazines with aldehydes in the generation of azomethine

imines for both inter- and intra-molecular cycloaddition reactions with alkenes.<sup>4</sup>

Our initial objective was to utilise this route to azomethine imines in pursuance of our study of the electrocycloaddition reactions of diene-conjugated 1,3-dipolar intermediates.<sup>5</sup> This note records the results of reactions of 1,2-dibenzylhydrazine (8) with *E*-2-formylstilbene (7) and with other substituted benzaldehydes.



The reaction between dibenzylhydrazine (8) and the aldehyde (7) was first attempted at temperatures of 60–70 °C, similar to the highest temperatures used previously<sup>2</sup> in the reaction of dimethyl- and dibenzyl-hydrazines, but no reaction occurred. However, at 110 °C in refluxing toluene, the conditions used by Oppolzer in the reactions of *N*-acyl-*N'*-alkylhydrazines, the reaction was complete in *ca.* 1 h and gave benzaldehyde benzyl(2-styrylbenzyl)hydrazone (9) in 73% yield, rather than the expected cyclisation product (11). Since this was an unexpected reaction path several other aromatic aldehydes (12)

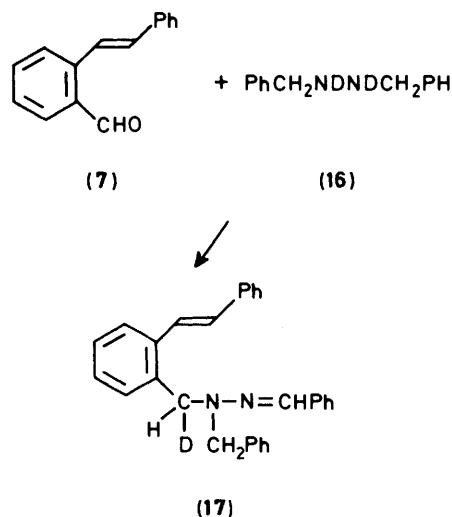
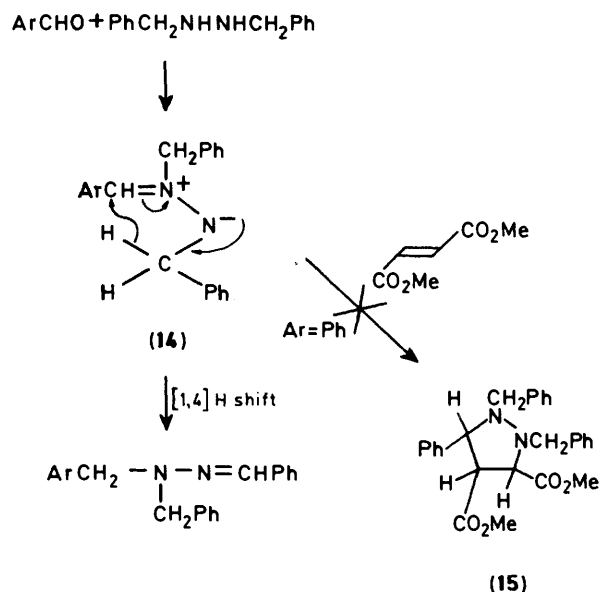


Scheme 2.

were also treated with dibenzylhydrazine under the same conditions. All gave similar reactions (Scheme 2). The structure of the unsubstituted hydrazone (13c) was confirmed by comparison with a sample prepared by the reaction of 1,1-dibenzylhydrazine with benzaldehyde and the other hydrazones were identified by analogy and by their n.m.r. and i.r. spectra.

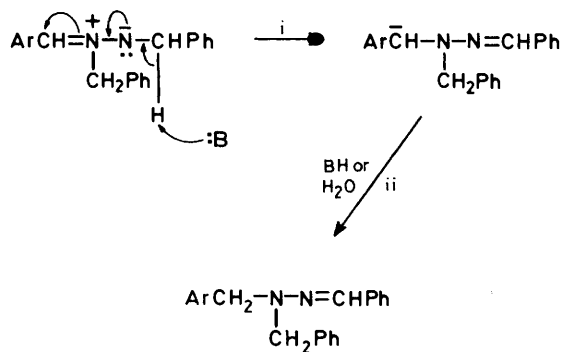
The reaction conditions were slightly different from those used previously in that in most cases the free 1,2-dibenzylhydrazine was liberated from its more stable hydrochloride *in situ* by an added base which was either pyridine or anhydrous sodium carbonate. However, in one case, the hydrochloride was treated with benzaldehyde without any added base and the same product (13c) was obtained but in lower yield (50% rather than 77% in the presence of sodium carbonate). The hydrazine itself rather than the hydrochloride/base combination was also used in one case, when its reaction with *p*-chlorobenzaldehyde gave a product which contained predominantly (87%) the expected hydrazone (13b) but also small amounts of products formulated from the mass spectrum of the mixture as benzaldehyde dibenzylhydrazone (13c) (8%) (confirmed by h.p.l.c.), and *p*-chlorobenzaldehyde benzyl(*p*-chlorobenzyl)hydrazone (5%). A control experiment in which benzaldehyde dibenzylhydrazone (13c) and *p*-chlorobenzaldehyde were boiled under reflux for 5 h showed that *ca.* 0.5% of *p*-chlorobenzaldehyde dibenzylhydrazone was formed by hydrazine transfer. The minor products may result from transfer reactions involving (13b) and/or intermediates in the reaction (see later).

Several reasonable reaction mechanisms can be written for the formation of the hydrazones (9) and (13). In view of previous work their formation *via* a sigmatropic [1,4]hydrogen migration in the putative azomethine imine intermediates (14) (Scheme 3) seemed very likely. It was of particular interest to us to find out if such intermediates were being generated because if so then apparently the [1,4]hydrogen shift in (10), giving (9), is preferred to the expected 1,7-electrocyclisation reaction leading to (11). Two experimental tests were carried out. In the first an attempt was made to detect the presence of an azomethine imine intermediate (14; Ar = Ph) in the reaction of 1,2-dibenzylhydrazine with benzaldehyde by carrying out the reaction in the presence of dimethyl fumarate as a dipolarophile. No adduct (15) was obtained and the reaction followed its usual path to give benzaldehyde dibenzylhydrazone (13c) in 93% yield. A second experiment was devised to find out whether the postulated [1,4]hydrogen shift converting (10) into (9) was, in fact, an intramolecular process. To this end partially deuterated dibenzylhydrazine (16) was prepared and allowed to react with the aldehyde (7). Operation of the mechanism in Scheme 3 would result in formation of the intermediate azomethine imine (10) containing no deuterium and its subsequent conversion into the deuterium free hydrazone (9). In the event, the reaction gave the hydrazone (17) with *ca.* 27% deuterium incorporation as shown. Control experiments showed no deuterium/protium exchange when the hydrazone (17) was crystallised from ethanol or when a sample of the non-

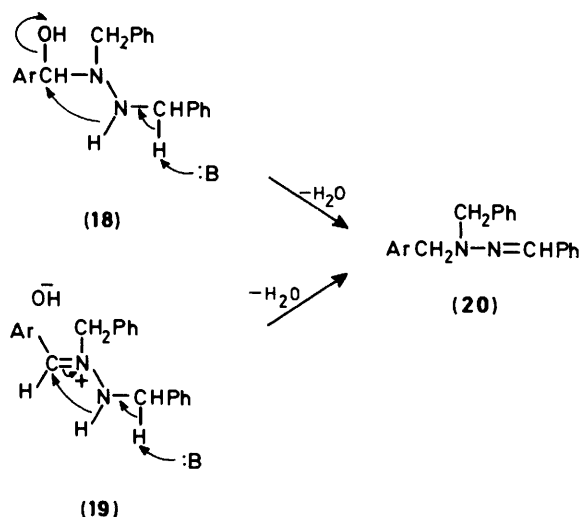


deuterated hydrazone (9) was boiled under reflux in toluene in the presence of the deuterated 1,2-dibenzylhydrazine hydrochloride, sodium carbonate, and a trace of deuterium oxide in a simulation of the reaction conditions. These experiments thus rule out the mechanism shown in Scheme 3. This and the failure to trap any of the postulated azomethine imine (14; Ar = Ph) with dimethyl fumarate throw much doubt on the formation of azomethine imines in this system. However their participation cannot be totally excluded since it remains possible that they could undergo a very fast intermolecular base-catalysed proton migration as shown in Scheme 4. However, if that is so then the results show that step (i) cannot be reversible since there was no deuterium incorporation into the imine position of the hydrazone (17).

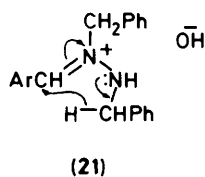
There are several plausible reaction mechanisms leading to the hydrazones (9) and (13) which do not involve azomethine imines and which are consistent with the deuteration result; two are shown in Schemes 5 and 6. That in Scheme 5 involves hydride transfer from nitrogen either in the hydrazinocarbinal (18) or its ionised form the hydrazone ion (19), and leads



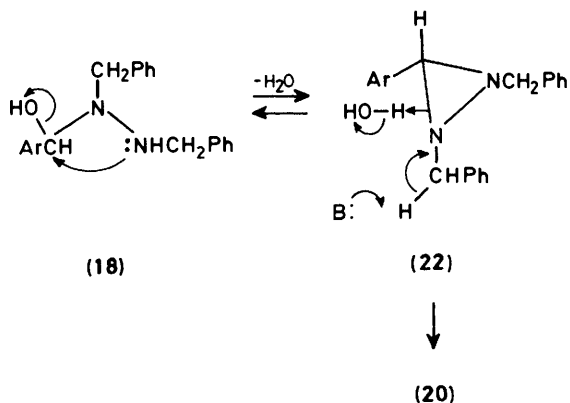
Scheme 4.



Scheme 5.



(21)



Scheme 6.

directly to the hydrazone (20). The alternative, Sommelet type hydride transfer from carbon, shown in (21), involves a less strained transition state but is not consistent with the deuteration result. Alternatively it is possible that ring closure to give a diaziridine (22) occurs (Scheme 6) which subsequently undergoes cleavage as shown.\* This route would, however, require the operation of a previously unobserved mode of hydrolytic cleavage of diaziridines<sup>6</sup> and requires further work, possibly *via* the independent synthesis of (22), to determine its feasibility. Whatever the mechanism, however, it is clear that the presence of benzyl substituents on the hydrazine much favours the hydrazone-forming reaction path so that it dominates under these reaction conditions over the equilibrium 1,3-dehydration leading to azomethine imines (Scheme 1) observed with other hydrazines.

### Experimental

N.m.r. spectra were obtained on Varian EM360 (<sup>1</sup>H, 60 MHz), HA100 (<sup>1</sup>H, 100 MHz), and CFT20 (<sup>13</sup>C, 20 MHz) spectrometers. Samples were run as solutions in deuteriochloroform and chemical shifts are reported as  $\delta$  values. Mass spectra were obtained on an AEI MS902 using electron ionisation (70 eV). Column chromatography was carried out on alumina (100/200 mesh) deactivated to Grade III.

1,2-Dibenzylhydrazine hydrochloride was prepared by the method of Curtius.<sup>7</sup> *N*-Deuteriated 1,2-dibenzylhydrazine hydrochloride was prepared by two recrystallisations of a sample (0.302 g) from deuterium oxide (10 ml). The mass spectrum showed 72% <sup>2</sup>H<sub>3</sub>, 18% <sup>2</sup>H<sub>2</sub>, and 10% <sup>2</sup>H<sub>1</sub>.

*Reactions of Aromatic Aldehydes with 1,2-Dibenzylhydrazine.*—*trans*-2-Formylstilbene (7). (i) A mixture of 1,2-dibenzylhydrazine hydrochloride (1.79 g, 7.20 mmol), pyridine (0.571 g, 7.22 mmol), and *E*-2-formylstilbene (1.0 g, 4.81 mmol) in dry toluene (25 ml) was boiled under reflux under nitrogen for 1 h. The solution was washed with water (2 × 50 ml), dried, and filtered. Evaporation of the solvent under reduced pressure gave a yellow solid (1.85 g) which was crystallised from ethanol to give benzaldehyde benzyl(2-styrylbenzyl)hydrazone (9) (1.41 g, 73%), m.p. 98.5–99 °C (Found: C, 86.5; H, 6.5; N, 7.0. C<sub>29</sub>H<sub>26</sub>N<sub>2</sub> requires C, 86.2; H, 6.5; N, 7.0%);  $\delta_{\text{H}}$  (100 MHz) 4.50 (2 H, s, CH<sub>2</sub>), 4.68 (2 H, s, CH<sub>2</sub>), 7.0–8.7 (22 H, m, aromatic, olefinic, and CH = N); *m/z* 57 (28), 71 (20), 91 (98), 115 (83), 178 (35), 181 (15), 192 (18), 193 (100), 194 (25), 208 (13), 210 (25), 298 (23), 311 (65), 312 (19), and 402 (30%). (ii) In a similar experiment *N*-deuteriated 1,2-dibenzylhydrazine hydrochloride (0.127 g, 0.505 mmol), *trans*-2-formylstilbene (0.072 g, 0.346 mmol), and sodium carbonate (0.059 g, 0.555 mmol) in toluene (10 ml) were boiled under reflux for 1 h. Filtration, evaporation of the solvent under reduced pressure, and recrystallisation of the residue from ethanol gave benzaldehyde benzyl(2-styrylbenzyl)hydrazone (0.076 g, 55%), shown by <sup>1</sup>H n.m.r. spectroscopy to be 26% deuteriated in the benzyl group of the 2-styrylbenzyl moiety. A second experiment gave 28% deuteration.

*Control experiments.* (a) The deuteriated hydrazone was recrystallised twice from ethanol. Its <sup>1</sup>H n.m.r. spectrum showed no loss of deuterium. (b) A mixture of the non-deuteriated hydrazone (0.053 g, 0.132 mmol), *N*-deuteriated 1,2-dibenzylhydrazine hydrochloride (0.034 g, 0.135 mmol), and sodium carbonate (0.016 g, 0.151 mmol) and deuterium oxide (2.6  $\mu$ l) in toluene (10 ml) was boiled under reflux for 1 h. Filtration, evaporation of the solvent under reduced pressure, and

\* We are obliged to a referee for this suggestion.

recrystallisation of the residue from ethanol gave recovered hydrazine (0.026 g, 50%) shown by  $^1\text{H}$  n.m.r. to contain no deuterium.

*p*-Methoxybenzaldehyde. A mixture of the hydrazine hydrochloride (0.733 g, 2.95 mmol), sodium carbonate (0.333 g, 3.14 mmol), and *p*-methoxybenzaldehyde (0.284 g, 2.09 mmol) in toluene (15 ml) was boiled under reflux for 3 h. The mixture was filtered and the solvent evaporated off under reduced pressure to give an oil (0.896 g) which was crystallised from ethanol to give benzaldehyde benzyl(*p*-methoxybenzyl)hydrazone (**13a**) (0.497 g, 72%), m.p. 89.5–90.5 °C (Found: C, 79.8; H, 6.7; N, 8.4.  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}$  requires C, 80.0; H, 6.7; N, 8.5%);  $\delta_{\text{H}}$  (100 MHz) 3.70 (3 H, s, OMe), 4.45 (4 H, s,  $2 \times \text{CH}_2$ ), 6.5–7.5 (15 H, m, aromatic and  $\text{CH} = \text{N}$ );  $m/z$  90 (7), 91 (31), 121 (100), 220 (10), 300 (11), and 330 (33%).

*Benzaldehyde*. (i) A similar reaction using benzaldehyde (0.132 g, 1.24 mmol), the hydrazine hydrochloride (0.466 g, 1.87 mmol), and sodium carbonate (0.233 g, 2.20 mmol) in toluene (10 ml) for 1 h gave benzaldehyde dibenzylhydrazone (**13c**) (0.288 g, 77%), m.p. 80–81 °C (from ethanol);  $\delta_{\text{H}}$  (100 MHz) 4.50 (4 H, s,  $2 \times \text{CH}_2$ ), and 7.1–7.5 (16 H, m, aromatic and  $\text{CH} = \text{N}$ );  $m/z$  90 (10), 91 (100), 92 (12), 103 (10), 165 (5), 166 (8), 181 (20), and 300 (80%). This sample was identical (m.p., mixed m.p., and spectra) with an authentic sample, m.p. 80–81 °C (lit., 78.5–80 °C<sup>8</sup> and 85 °C<sup>9</sup>), prepared by the reaction of benzaldehyde, 1,1-dibenzylhydrazine<sup>10</sup> hydrochloride and sodium acetate in toluene at room temperature. (ii) A similar reaction carried out in the absence of sodium carbonate gave the same product in 50% yield. (iii) A reaction in which hydrazine hydrochloride (0.933 g, 3.75 mmol), pyridine (0.327 g, 4.14 mmol), benzaldehyde (0.266 g, 2.51 mmol), and dimethyl fumarate (0.434 g, 2.52 mmol) in toluene (15 ml) were refluxed for 1 h gave benzaldehyde dibenzylhydrazone (0.701 g, 93%) as the only isolable product.

*p*-Chlorobenzaldehyde. (i) A mixture of the hydrazine hydrochloride (0.683 g, 2.75 mmol), *p*-chlorobenzaldehyde (0.258 g, 1.84 mmol), and sodium carbonate (0.319 g, 3.01 mmol) in toluene was boiled under reflux for 2 h. Work up gave benzaldehyde benzyl(*p*-chlorobenzyl)hydrazone (**13b**) (0.488 g, 80%), m.p. 67–67.5 °C (from ethanol) (Found: C, 75.1; H, 5.7; N, 8.3.  $\text{C}_{21}\text{H}_{19}\text{ClN}_2$  requires C, 75.3; H, 5.7; N, 8.4%);  $\delta_{\text{H}}$  (100 MHz) 4.41 (2 H, s,  $\text{CH}_2$ ), 4.45 (2 H, s,  $\text{CH}_2$ ), and 7.0–7.5 (15 H, m, aromatic and  $\text{CH} = \text{N}$ );  $m/z$  91 (100), 125 (56), 127 (20), 181

(16), 334 (64), and 336 (24%). (ii) A similar reaction using pyridine instead of sodium carbonate and a 2 h reflux period gave the same product in 38% yield. (iii) A solution of free 1,2-dibenzylhydrazine (0.610 g, 2.87 mmol) and *p*-chlorobenzaldehyde (0.392 g, 2.80 mmol) in toluene (15 ml) was boiled under reflux for 3 h. Evaporation under reduced pressure and chromatography of the residue (alumina, 10 vol % ether in light petroleum) gave a solid (0.405 g) shown by h.p.l.c. and mass spectrometry to contain 87% of benzaldehyde benzyl(*p*-chlorobenzyl)hydrazone and ca. 8% of benzaldehyde dibenzylhydrazone and ca. 5% of a compound thought to be *p*-chlorobenzaldehyde benzyl(*p*-chlorobenzyl)hydrazone;  $m/z$  of mixture 91 (100), 125 (37), 127 (13), 181 (12), 300 (20), 334 (50), 336 (16), 368 (1), 370 (1), and 372 (1%). As a control experiment benzaldehyde dibenzylhydrazone (0.250 g, 0.833 mmol) and *p*-chlorobenzaldehyde (0.587 g, 4.18 mmol) in toluene (15 ml) were boiled under reflux for 5 h. Chromatography (alumina, benzene) gave a solid m.p. 75–76 °C (from ethanol) shown by  $^1\text{H}$  n.m.r. and mass spectrometry to be the recovered hydrazone containing ca. 0.5% of *p*-chlorobenzaldehyde dibenzylhydrazone.

#### Acknowledgements

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#### References

- 1 B. Rassow, *J. Prakt. Chem.*, 1901, **64**, 129 and 136.
- 2 R. Grashey, R. Huisgen, Kwok Kun Sun, and R. M. Moriarty, *J. Org. Chem.*, 1965, **30**, 74.
- 3 R. Huisgen, R. Grashey, and J. Sauer, in 'The Chemistry of Alkenes,' ed. S. Patai, Wiley Interscience, New York, 1964, p. 739.
- 4 W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 10.
- 5 I. R. Robertson and J. T. Sharp, *J. Chem. Soc., Chem. Commun.*, 1983, 1003; and D. P. Munro and J. T. Sharp, *J. Chem. Soc., Perkin Trans. I*, 1980, 1718 and references cited therein.
- 6 E. Schmitz, *Adv. Heterocycl. Chem.*, 1963, **2**, 83.
- 7 T. Curtius, *J. Prakt. Chem.*, 1900, **62**, 83.
- 8 E. M. Kaiser, F. E. Hensch, and C. R. Hauser, *J. Am. Chem. Soc.*, 1968, **90**, 7287.
- 9 T. Curtius and H. Franzen, *Chem. Ber.*, 1901, **34**, 552.
- 10 M. Busch and B. Weiss, *Chem. Ber.*, 1900, **33**, 2701.

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