α-Benzylation of Ketones by Reaction with Benzylamine. Regioselective Reduction of C–C Double Bonds in Conjugated Enones

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Prolonged reaction of some ketones with benzylamine at reflux converts them into α-benzyl derivatives by a route involving Aldol condensation of the related ketimine with benzaldimine followed by exclusive reduction of the resultant C–C double bond. Reduction does not occur when pure benzylamine is used under oxygen-free nitrogen, however the inclusion of a trace of benzaldehyde restores the efficiency of the reaction. Treatment of several ketones in this manner established the scope of the process. When the reaction was extended to the reduction of α,β-unsaturated enones again using benzylamine, reaction times were shorter and the product yield greater. The possibility that the reductive step was an intramolecular 1,5-hydrogen transfer was studied.

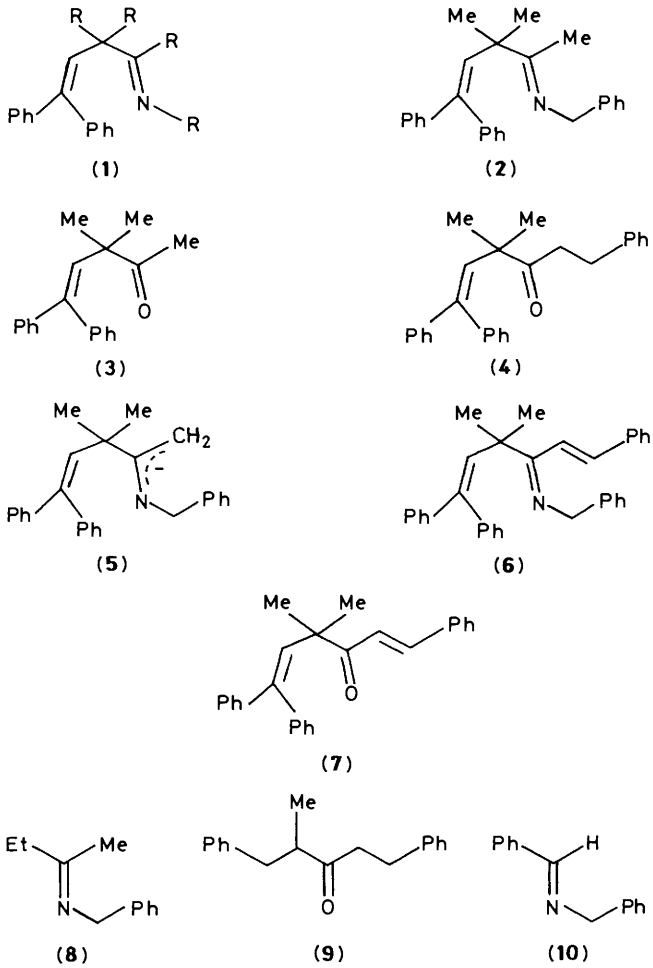
During a study of the novel aza-di-π-methane reaction[1] of the imine (**1**) the synthesis of a variety of these compounds was carried out. Benzylamine was used for the synthesis of benzylimines from ketones and normally, with short reaction times, the reaction was completely successful. However with longer reaction times α-benzylation of the ketone took place without affecting the β,γ-unsaturation. The process appeared to be specific. The results have been published in a preliminary form[2] and the present paper gives details of the reaction and also of experiments designed to establish the scope of the process.

Results and Discussion

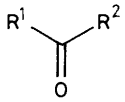
A typical reaction of the above type is the synthesis in high yield of the imine (**2**) by reaction of the enone (**3**) with benzylamine for 3 h. With a longer reaction time (≥40 h) and chromatographic separation a new ketone (47% yield) was isolated. The spectroscopic details of this new product suggested that the enone (**3**) had unexpectedly undergone α-benzylation to yield the substituted hex-5-en-3-one (**4**). Final proof of structure was achieved by independent synthesis involving benzylation of the enone (**3**) with benzyl chloride.[3]

Clearly, the formation of the enone (**4**) by reaction of the enone (**3**) with benzylamine cannot arise by attack of the anion (**5**) on benzylamine. A possible route involves condensation of the imine (**2**) with benzaldimine, formed by aerial oxidation of benzylamine, to yield the azadiene (**6**), the carbon–carbon double bond in conjugation with the imine entity of this then undergoes *in situ* regioselective reduction. There is no evidence for reduction of the other C–C double bond. The feasibility of this step was substantiated by conversion of the enone (**7**), preformed by condensation of the enone (**3**) with benzaldehyde,[4] in refluxing benzylamine into (**4**).

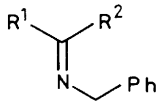
It seemed likely that the purity of the benzylamine could be critical to the success of the reaction. In order to verify this point the reactivity of the imine (**8**) towards benzylamine was examined. Normally this was converted into the doubly benzylated ketone (**9**) in low (10%) yield. Although the imine (**8**) when heated under reflux with pure redistilled benzylamine for 20 h under nitrogen gave no products of α-benzylation, addition of a little benzaldehyde gave rise to the ketone (**9**) (34%). Since the species involved in the Aldol-like condensation will be the imine (**10**) formed by reaction of benzaldehyde with benzylamine, it seems clear that benzaldimine is involved in the α-benzylation of the imines (**2**) and (**8**) and that aerial oxidation of benzylamine to give this is a key step in the process. Condensation of the imine (**2**) with benzaldimine would yield the imine (**6**), which upon reduction (see later) would then give benzylated product (**4**).



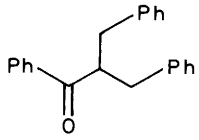
Since the process described above appears to have some generality, the reactivity of some simple ketones (**11**) as their benzylimines (**12**), has also been studied. Both single and double benzylation occurs to give the ketones (**13**)—(**16**) in variable yields. Steric factors appear to influence the reactivity observed with the Aldol condensation reaction.[5]



(**11**)

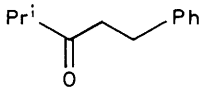


(**12**)

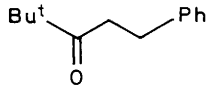


(**13**)
(69%)

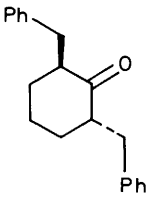
(**11a**), (**12a**) R^1 = Ph, R^2 = Me
(**11b**), (**12b**) R^1 = Pr^i, R^2 = Me
(**11c**), (**12c**) R^1 = Bu^t, R^2 = Me
(**11d**), (**12d**) $R^1 = R^2 = (CH_2)_5$



(**14**)
(42%)

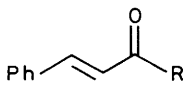


(**15**)
(63%)

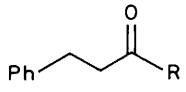


(**16**)
(58%)

The described reaction should be applicable to the reduction of conjugated enones since these, or their corresponding imines, are intermediates in the reductive sequence. Although there are literature precedents for the reduction of such compounds using benzylamine in the presence of t-butoxide as base,[6,7] we believe that the conditions used in the present work are novel. Reduction of the enone (**17a**) with benzylamine under these conditions gave after conventional work-up, the ketone (**18a**) (5%) and the α-benzylated/reduced product (**19**) (16%). The poor yields of products were attributed to the prolonged period under reflux and the vigorous isolation procedure. A shorter reflux time (3 h) and an improved method of hydrolysis and isolation gives a higher yield (36%) of the sole product (**18a**). Similarly the enones (**17b**), (**17c**), and (**17d**) gave the ketones (**18b**), (**14**), and (**15**) in improved yields (16.5 ⟶ 27.5%), (14 ⟶ 45%), and (49 ⟶ 59%) respectively.

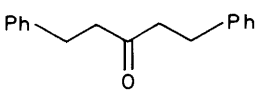


(**17**)



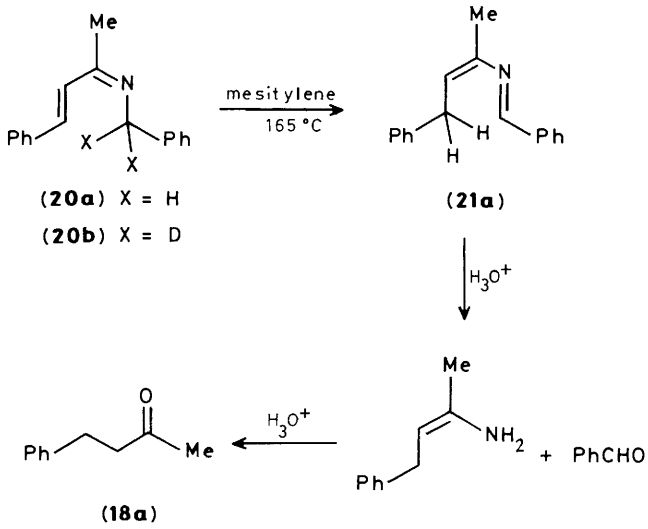
(**18**)

(**17a**), (**18a**) R = Me
(**17b**), (**18b**) R = Et
(**17c**), (**14**) R = Pr^i
(**17d**), (**15**) R = Bu^t



(**19**)

Of several possible mechanisms one involving intramolecular 1,5-hydrogen migration was considered seriously. Such a migration is supported by the work of Aue and Thomas,[8] who demonstrated that 2-azadienes obtained from the vacuum thermolysis of 1-azetines isomerized cleanly by 1,5-hydrogen migration into 1- or 2-azadienes. To test the feasibility of the 1,5-hydrogen migration the imine (**20a**), prepared independently by the reaction of enone (**17a**) with benzylamine, was heated under reflux in mesitylene under nitrogen for 3 h, in the absence of benzylamine. The n.m.r. spectrum of the crude material showed only the presence of (**17a**) and (**18a**) in a ratio of 3:7 in a total yield of 90%. Interestingly the dideuterio analogue (**20b**) failed to isomerise under the same conditions giving instead, a complex mixture of products in which none of the expected isomeric ketones could be detected. The failure of this reaction could be due to a high deuterium isotope effect * inhibiting the 1,5-migration and permitting the operation of other reaction paths. It is clear from the experiment with (**20a**) that the intramolecular 1,5-H migration can be operative. This will involve the transfer of a hydrogen from the benzyl imine group to the terminal carbon of the 1-azadiene system. This results in the formation of the isomeric 2-azadiene (**21**) which as a result of hydrolysis during work-up yields the reduced ketone (**18a**) (see Scheme). This path is preferred to the alternative base-induced isomerisation described by others.[7] Although it seems likely



Scheme.

that the base induced process can account for the formation of the reduced mono-benzylated products, it is difficult to explain how this reductive path can lead to the bis-benzylated products. Thus, in cases where bis-benzylation occurs an alternative mechanism such as a Sommelet reaction[9] could be operative in which reduction occurs by intermolecular hydride transfer from an amine such as benzylamine to the imine system such as (**20a**).

Experimental

M.p.s were determined on a Buchi 510D apparatus in open capillaries and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 257 spectrophotometer and band positions are reported in wavenumbers. ^{1}H N.m.r. spectra were recorded on a Varian T-60A and ^{13}C n.m.r. spectra on a Varian FT 80A spectrometer. Chemical shifts (δ) are reported in p.p.m. downfield from Me_4Si as internal standard. Mass spectra were determined on a Varian MAT-711 spectrometer. Elemental analyses were performed by the Consejo Superior de Investigaciones Cientificas, Madrid.

* In sigmatropic 1,5-hydrogen migrations there is a large primary isotope effect k_H/k_D = 12.2 at 25 °C. T. H. Lowry and K. S. Richardson, 'Mechanism and Theory in Organic Chemistry,' Harper and Row, N.Y., 1976, p. 664.

General Procedure for the Synthesis of Imines (**2**), (**8**), *and* (**12**).—3,4,4-Trimethyl-1,6,6-triphenyl-2-azahexa-2,5-diene (**2**) was synthesized by the method previously described.[10] The others (**8**) and (**12**) were synthesized by the following procedure. Equimolar proportions of benzylamine and the corresponding ketone together with zinc chloride (*ca.* 50 mg) were refluxed in benzene or toluene with azeotropic removal of water *via* a Dean and Stark trap. The mixture was then cooled, the catalyst was filtered off, and the solution evaporated under reduced pressure to yield the imine. This was purified by distillation *in vacuo*; isolated yields after purification are indicated.

The imines (**8**) and (**12**) are moisture sensitive and were synthesized and used without further purification. The imines (**12a**) and (**12d**) have been recorded in the literature and the imines (**8**), (**12b**), and (**12c**) were characterized on the basis of spectroscopic properties. The n.m.r. of the crude mixtures showed that the conversion into imine was quantitative in each case.

3-*Methyl*-1-*phenyl*-2-*azapent*-2-*ene* (**8**). Butanone (10.1 g, 140 mmol), and benzylamine (15 g, 140 mmol) in benzene (120 ml) were refluxed for 1 h to yield imine (**8**) (21.4 g, 96%); b.p. 52—53 °C/0.5 mmHg; $\delta_H(CCl_4)$ 1.10 (3 H, t, CH_3), 1.75 (3 H, s, CH_3), 2.30 (2 H, q, CH_2), 4.40 (2 H, s, CH_2), and 7.10—7.35 (5 H, m, ArH); $\nu_{max.}$(film) 1 665 cm^{-1}.

1,3-*Diphenyl*-2-*azabut*-2-*ene* (**12a**). Acetophenone (**11a**) (10 g, 83 mmol), and benzylamine (8.9 g, 83 mmol) in toluene (100 ml) were refluxed for 7 h to yield (**12a**) (15.3 g, 88%); b.p. 118—119 °C/0.05 mmHg (lit.,[11] m.p. 43—44 °C); $\delta_H(CCl_4)$ 2.15 (3 H, s, CH_3), 4.60 (2 H, s, CH_2), 7.0—7.4 (8 H, s, ArH), and 7.60—7.90 (2 H, m, *o*-ArH); $\nu_{max.}$(film) 1 635 cm^{-1}.

3,4-*Dimethyl*-1-*phenyl*-2-*azapent*-2-*ene* (**12b**). 3-Methylbutan-2-one (**11b**) (12.04 g, 140 mmol) and benzylamine (14.98 g, 140 mmol) in benzene (30 ml) were refluxed for 6 h to yield (**12b**) (10.7 g, 44%); b.p. 55— 56 °C/0.5 mmHg; $\delta_H(CCl_4)$ 1.30 (6 H, d, 2 × CH_3), 1.90 (3 H, s, CH_3), 2.60 (1 H, m, CH), 4.50 (2 H, s, CH_2), and 7.3 (5 H, m, ArH); $\nu_{max.}$(film) 1 660 cm^{-1}.

3,4,4-*Trimethyl*-1-*phenyl*-2-*azapent*-2-*ene* (**12c**). 3,3-Dimethylbutan-2-one (**11c**) (5 g, 50 mmol) and benzylamine (5.35 g, 50 mmol) in benzene (50 ml) were refluxed for 2 h to yield (**12c**) (2.0 g, 22%); b.p. 65 °C/0.04 mmHg; $\delta_H(CCl_4)$ 1.15 (9 H, s, 3 × CH_3), 4.40 (2 H, s, CH_2N), and 7.10—7.30 (5 H, m, ArH); $\nu_{max.}$(film) 1 655 cm^{-1}.

N-*Benzylcyclohexanimine* (**12d**). Cyclohexanone (**11d**) (14.25 g, 142 mmol), and benzylamine (15.25 g, 142 mmol) in toluene (25 ml) were refluxed for 5 h to yield (**12d**) (22 g, 81%); b.p. 102—103 °C/0.03 mmHg (lit.,[12] b.p. 125—128 °C/1 mmHg); $\delta_H(CDCl_3)$ 1.50—1.80 (6 H, m, 3 × CH_2), 2.15—2.50 (4 H, m, 2 × CH_2), 4.55 (2 H, br s, CH_2N), and 7.15—7.30 (5 H, m, aryl-H); $\nu_{max.}$(film) 1 665 cm^{-1}.

Reaction of 3,3-*Dimethyl*-5,5-*diphenylpent*-4-*en*-2-*one* (**3**) *with Benzylamine.*—A mixture of (**3**) (4.0 g, 15.1 mmol) and benzylamine (16.1 ml, 151 mmol) was refluxed for 43 h. The benzylamine was distilled off under reduced pressure and the residual colourless oil was chromatographed on silica gel with hexane–ethyl acetate (99.5:0.5) as eluant yielding 4,4-*dimethyl*-1,6,6-*triphenylhex*-4-*en*-3-*one* (**4**) (2.7 g, 47%) as a white crystalline solid that was identified by independent synthesis (see below) and from spectroscopic data; m.p. 75—76 °C (from ethanol–water); $\delta_H(CDCl_3)$ 1.15 (6 H, s, 2 × CH_3), 2.65 (4 H, s, 2 × CH_2), 6.00 (1 H, s, vinyl-H), and 7.00—7.35 (15 H, m, ArH); δ_C 25.8 (CH_3), 26.51 (CH_3), 50.28 (CH_2), 127.19, 127.52, 127.67, 127.92, 128.07, 129.97, 133.91, 139.35, 142.94, 143.30, and 209.77 (C=O); $\nu_{max.}$(KBr) 1 695 C=O cm^{-1}; *m/z* 354 (M^+, 1%), 307 (2), 221 (100), 191 (4), 165 (4), 143 (43), 128 (8), 105 (34), 93 (31), and 77 (5) (Found: C, 88.3; H, 7.5. $C_{26}H_{26}O$ requires C, 88.10; H, 7.35%).

Independent synthesis of (**4**). This was carried out by the method described by Hill *et al.*[3] for similar compounds. 3,3-Dimethyl-5,5-diphenylpent-4-en-2-one (**3**) (5.3 g, 20 mmol) in ethanol (20 ml) was added dropwise over 1 h to finely ground sodamide (0.8 g, 20 mmol) with stirring. The mixture was then refluxed for 3.5 h and benzyl chloride (2.5 g, 19.7 mmol) was added. After the mixture had been refluxed for an additional 17 h, diethyl ether (50 ml) and water (10 ml) were added. The organic layer was separated, washed with dilute hydrochloric acid, dried ($CaCl_2$), and evaporated under reduced pressure. The residual oil was distilled *in vacuo* to yield the ketone compound (**4**) (1.99 g, 28%); b.p. 158—160 °C °C/0.1 mmHg. The physical data were identical to those reported above.

Synthesis of 4,4-*Dimethyl*-1,6,6-*triphenylhexa*-1,5-*dien*-3-*one* (**7**).—This compound was synthesized following a general method described for similar compounds.[4] A solution of 3,3-dimethyl-5,5-diphenylpent-4-en-2-one (**3**) (300 mg, 0.9 mmol) and sodium hydroxide (0.75 g) in a mixture of water (6 ml) and ethanol (2 ml, 95%) was cooled in ice, benzaldehyde (105 mg, 0.3 mmol) was added and the reaction mixture was stirred for 24 h. After work-up the crude product was chromatographed on silica gel and with benzene as eluant yielded (**7**) (280 mg, 70%) as a colourless oil; b.p. 148—151 °C/0.08 mmHg; $\delta_H(CCl_4)$ 1.3 (6 H, s, 2 × CH_3), 6.2 (1 H, s, 5-H), and 6.9—7.5 (17 H, m, ArH and 2- and 3-H); $\nu_{max.}$(KBr) 1 665 cm^{-1} (Found: C, 88.4; H, 6.6. $C_{26}H_{24}O$ requires C, 88.64; H, 6.82%).

Reaction of 4,4-*Dimethyl*-1,6,6-*triphenylhexa*-1,5-*dien*-3-*one* (**7**) *with Benzylamine.*—A mixture of (**7**) (0.1 g, 0.3 mmol) and benzylamine (4.5 ml, 41 mmol) was refluxed for 24 h. The benzylamine was distilled off under reduced pressure and the residual colourless oil was chromatographed on silica gel with hexane–ethyl acetate (99.5:0.5) as eluant to yield the ketone (**4**) (71 mg, 70%) as a white crystalline solid. The physical data were identical to those detailed above.

Reaction of 3-*Methyl*-1-*phenyl*-2-*azapent*-2-*ene* (**8**) *in Benzylamine.*—A mixture of (**8**) (3.3 g, 20.5 mmol) and benzylamine (22 ml, 20.1 mmol) was refluxed for 20 h. The excess amine was distilled off under reduced pressure and the oily residue was chromatographed on silica gel with benzene as eluant yielding 2-methyl-1,5-diphenylpentan-3-one (**9**) (520 mg, 10%); b.p. 145 °C/0.5 mmHg (lit.,[13] m.p. 47—48 °C); $\delta_H(CDCl_3)$ 0.9—1.2 (3 H, m, CH_3), 2.4—3.0 (7 H, m, aliphatic H), and 7.0—7.3 (10 H, m, ArH); $\nu_{max.}$(KBr) 1 710 cm^{-1}.

Reaction of 3-*methyl*-1-*phenyl*-2-*azapent*-2-*ene* (**8**) *with benzylamine at reflux under nitrogen.* The reaction was carried out using the same quantities and conditions as above but under an atmosphere of nitrogen. After work-up butanone was recovered in 100% yield.

Reaction of 3-*methyl*-1-*phenyl*-2-*azapent*-2-*ene* (**8**) *with benzylamine at reflux under nitrogen in the presence of benzaldehyde.* The reaction was carried out under the same conditions as above but with the addition of benzaldehyde (1.06 mg). After work-up 2-methyl-1,5-diphenylpentan-3-one (**9**) was isolated (1.76 g, 34%).

General Procedure for Benzylation of Imines (**12**).—A solution of the imine (24 mmol) in benzylamine (26 ml, 240 mmol) was refluxed for 20 h. The benzylamine was distilled off under reduced pressure, the crude reaction product was hydrolysed using 5% sulphuric acid (10 ml) in tetrahydrofuran (THF) (40 ml) with stirring for 30 min at room temperature. The reaction mixture was extracted with ether (50 ml), and the extract washed with 10% aqueous sodium hydrogen carbonate (20 ml), dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residual colourless oil was chromatographed on silica gel to yield the corresponding benzylated product.

Benzylation of the imine (**12a**). Chromatography with benzene as eluant gave a colourless oil which crystallized from ethanol to give the benzylated product (**13**) (2 g, 69%) as a white solid; this was identified by independent synthesis and from spectroscopic data; m.p. 75—76 °C (lit.,[14] 75—76 °C); $\delta_H(CCl_4)$ 2.55—3.30 (4 H, m, 2 × CH_2), 3.80 (1 H, m, CH), 6.95—7.30 (13 H, m, ArH), and 7.50—7.70 (2 H, m, ArH); $\nu_{max.}$(KBr) 1 655 cm^{-1}.

Benzylation of the imine (**12b**). Chromatography with hexane–ethyl acetate (99.5:0.5) as eluant gave the benzylated product (**14**) (1.53 g, 42.4%) as a colourless oil, which was identified by independent synthesis and from spectroscopic data; b.p. 90—100 °C/0.5 mmHg (lit.,[15] b.p. 142—144 °C/20 mmHg); $\delta_H(CCl_4)$ 1.10 (6 H, d, 2 × CH_3), 2.60 (1 H, m, CH), 2.90 (4 H, 2 t, 2 × CH_2), and 7.20 (5 H, s, ArH); $\nu_{max.}$(film) 1 660 cm^{-1}.

Benzylation of the imine (**12c**). Chromatography with hexane–ethyl acetate (99.5:0.5) as eluant gave the benzylated product (**15**) (0.9 g, 63%) as a colourless oil, b.p. 65 °C/0.04 mmHg (lit.,[3] b.p. 153 °C/40 mmHg); $\delta_H(CCl_4)$ 1.05 (9 H, s, 3 × CH_3), 2.80 (4 H, t, 2 × CH_2), and 7.10—7.25 (5 H, m, ArH); $\nu_{max.}$(film) 1 700 cm^{-1}.

Benzylation of the imine (**12d**). Chromatography with hexane–ethyl acetate (99.5:0.5) as eluant gave a colourless oil that crystallized from ethanol to give the benzylated product (**16**) (5.1 g, 58%) as a pale yellow solid; this was identified from spectroscopic data; m.p. 113—114 °C (lit.,[4] m.p. 114 °C); $\delta_H(CDCl_3)$ 1.3—3.5 (12 H, m, 6 × CH_2), and 7.1—7.4 (10 H, m, ArH); $\nu_{max.}$(KBr) 1 680 cm^{-1}.

General Reaction Conditions for Reduction of the α,β-Unsaturated Ketones (**17a—d**).—The enone (10 mmol) in benzylamine (10.9 ml, 100 mmol) was refluxed for 3 h. The benzylamine was removed by extraction with 10% hydrochloric acid and the reaction mixture was extracted with ether (50 ml). The extract was washed with 10% aqueous sodium hydrogencarbonate (20 ml), dried ($MgSO_4$), and evaporated under reduced pressure and the residual colourless oil was flash-chromatographed on silica gel to yield the corresponding reduced product. In all cases the reduced compound was identified by its spectroscopic data and by comparison with authentic samples obtained by catalytic reduction of the corresponding α,β-unsaturated enone.

Reduction of the enone (**17a**). Chromatography with hexane–ethyl acetate (95:5) as eluant gave a colourless oil (0.53 g, 36%) which was identified as the reduced product (**18a**) from spectroscopic data; b.p. 80—82 °C/0.5 mmHg (lit.,[16] b.p. 117—118 °C/8 mmHg); $\delta_H(CCl_4)$ 2.0 (3 H, s, CH_3), 2.7 (4 H, m, 2 × CH_2), and 7.3 (5 H, s, ArH); $\nu_{max.}$(film) 1 700 cm^{-1}.

Reduction of the ketone (**17b**). Chromatography with hexane–ethyl acetate (95:5) as eluant gave a colourless oil (0.45 g, 28%) which was identified as the reduced product (**18b**) from spectroscopic data; b.p. 90—100 °C/0.5 mmHg (lit.,[17] b.p. 128 °C/17 mmHg); $\delta_H(CCl_4)$ 0.8 (3 H, t, CH_3), 2.2 (2 H, q, CH_2), 2.60 (4 H, m, 2 × CH_2), and 7.0 (5 H, s, ArH); $\nu_{max.}$(film) 1 690 cm^{-1}.

Reduction of the ketone (**17c**). Chromatography with hexane–ethyl acetate (95:5) as eluant gave a colourless oil (0.79 g, 45%) which was identified as the reduced product (**14**) from spectroscopic data; b.p. 90—100 °C/0.5 mmHg (lit.,[15] b.p. 142—144 °C/20 mmHg); $\delta_H(CCl_4)$ 1.10 (6 H, d, 2 × CH_3), 2.60 (1 H, m, CH), 2.90 (4 H, 2 t, 2 × CH_2), and 7.20 (5 H, s, ArH); $\nu_{max.}$(film) 1 660 cm^{-1}.

Reduction of the ketone (**17d**). Chromatography with hexane–ethyl acetate (95:5) as eluant gave a colourless oil (0.93 g, 59%) which was identified as the reduced product (**15**) from spectroscopic data; b.p. 80—90 °C/0.5 mmHg (lit.,[3] b.p. 153 °C/40 mmHg); $\delta_H(CCl_4)$ 1.05 (9 H, s, 3 × CH_3), 2.80 (4 H, t, 2 × CH_2), and 7.10 (5 H, m, ArH); $\nu_{max.}$(film) 1 700 cm^{-1}.

Synthesis of 3-Methyl-1,5-diphenyl-2-azapenta-2,4-diene (**20a**).—A mixture of benzylamine (840 mg, 7.8 mmol), benzylideneacetone (**17a**) (1.14 g, 7.8 mmol), and zinc chloride (*ca.* 50 mg) as catalyst in benzene (25 ml) was refluxed for 4 h with azeotropic removal of water *via* a Dean and Stark trap. The mixture was then cooled and the catalyst filtered off. The solution was concentrated under reduced pressure to yield a pale yellow crystalline solid which recrystallized from hexane to give *imine* (**20a**) (1.8 g, 98%); m.p. 60—61 °C; $\delta_H(CDCl_3)$ 2.2 and 2.4 (3 H, 2 s, CH_3), 4.7 (2 H, s, CH_2), and 7.0—7.5 (12 H, m, vinyl H and ArH); $\nu_{max.}$(film) 1 655 cm^{-1} (Found: C, 86.7: H, 7.6; N, 5.7. $C_{16}H_{19}N$ requires C, 86.81; H, 7.23; N, 5.95%).

Thermal Isomerization of 3-Methyl-1,5-diphenyl-2-azapenta-2,4-diene (**20a**).—3-Methyl-1,5-diphenyl-2-azapenta-2,4-diene (**20a**) (0.80 g, 3.4 mmol) in mesitylene (5 ml) was refluxed under nitrogen for 3 h. The reaction mixture was then cooled and concentrated under reduced pressure. The crude reaction product was hydrolysed using 5% sulphuric acid (15 ml) in THF (40 ml) with stirring for 30 min at room temperature. The reaction mixture was extracted with ether (50 ml), and the extract washed with a 10% aqueous sodium hydrogencarbonate (20 ml), dried ($MgSO_4$), and evaporated at reduced pressure. The ^1H n.m.r. spectrum of the residual colourless oil (0.41 g, 90%) showed the presence of the ketones (**17a**) and (**18a**) in a ratio of 3:7.

Synthesis of the Imine (**20b**).—Benzonitrile (0.52 g, 5 mmol) was treated with $LiAlD_4$ (0.50 g, 5 mmol) in dry ether (50 ml) at reflux for 4 h.[18] Conventional work-up gave 1,1-dideuteriobenzylamine (0.33 g, 63%) as a colourless oil; $\delta_H(CDCl_3)$ 1.55 (2 H, s, NH_2) and 7.25 (5 H, s, ArH). The dideuteriobenzylamine (0.30 g, 2.7 mmol) was treated with benzylideneacetone (0.40 g, 2.7 mmol) in the presence of zinc chloride (50 mg) in benzene at reflux for 4 h. Work-up similar to that described above for the imine (**20a**) gave the imine (**20b**) (0.56 g, 86%); $\delta_H(CDCl_3)$ 2.1 and 2.3 (3 H, s, CH_3), and 6.60—7.40 (12 H, m, vinyl H and ArH); $\nu_{max.}$(film) 1 670 cm^{-1}.

Thermal Reaction of the Imine (**20b**).—The thermal reaction was carried out in a fashion identical with that for the imine (**20a**) using the imine (**20b**) (0.50 g) in mesitylene (3.5 ml) for 3 h at reflux under nitrogen. Work-up gave a complex mixture of products which was neither separated nor identified.

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References

1 D. Armesto, J. A. F. Martin, R. Perez-Ossorio, and W. M. Horspool, *Tetrahedron Lett.*, 1982, **23**, 2149; D. Armesto, W. M. Horspool, J. A. F. Martin, and R. Perez-Ossorio, *J. Chem. Res.*, 1986, (*S*) 46.
2 D. Armesto, W. M. Horspool, J. A. F. Martin, and R. Perez-Ossorio, *Tetrahedron Lett.*, 1985, **26**, 5217.
3 G. A. Hill, C. S. Spear, and J. S. Lachowicz, *J. Am. Chem. Soc.*, 1923, **45**, 1557.
4 R. Cornubert, M. de Demo, and M. Andre, *Bull. Soc. Chim. Fr.*, 1939, 113.
5 A. T. Nielsen and W. J. Houlihan, *Org. Reactions*, 1968, **16**, 1.
6 P. A. Wender and M. A. Eissenstat, *J. Am. Chem. Soc.*, 1978, **100**, 292.
7 S. K. Malhotra, D. F. Moakley, and F. Johnson, *J. Am. Chem. Soc.*, 1967, **89**, 2794.
8 D. H. Aue and D. Thomas, *J. Org. Chem.*, 1975, **440**, 1349.
9 S. J. Angyal, *Organic Reactions*, 1954, **8**, 197.
10 D. Armesto, F. Langa, J. A. F. Martin, R. Perez-Ossorio, and W. M. Horspool, *J. Chem. Soc., Perkin Trans. 1*, 1987, 743.

11 E. Melendez, R. Perez-Ossorio, and S. del Olmo, *Anal. Quim.*, 1962, **58B**, 713.
12 R. Baltzly and O. Kauder, *J. Org. Chem.*, 1951, **16**, 173.
13 G. Massara and A. di Leo, *Gazz. Chim. Ital.*, 1933, **63**, 199.
14 R. C. Fuson, W. E. Ross, and C. H. McKeever, *J. Am. Chem. Soc.*, 1938, **60**, 2935.
15 R. Jacquier and H. Mousseron, *Bull. Soc. Chim. Fr.*, 1956, 1653.
16 J. W. Kern, R. L. Shriner, and R. L. Adams, *J. Am. Chem. Soc.*, 1925, **47**, 1147.
17 C. Harrier and G. H. Müller, *Ber.*, 1902, **35**, 966.
18 R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, 1948, **70**, 3738.

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