A Stereospecific Synthesis of Azo Nitriles

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A series of α,α'-dicyanoazoalkanes **2** have been prepared in high isolated yield (96–98%) by treatment of the corresponding α,α'-dichloroazoalkanes **3** (generated from ketazines **1**) with trimethylsilyl cyanide and 50 mol % stannic chloride at low temperature. Use of 5 mol % stannic chloride resulted in the formation of α-chloro-α'-cyanoazoalkanes **4**. Single-crystal X-ray diffraction analysis of 2,2′-dichloro-3,3,3′,3′-tetramethyl-2,2′-azobutane (**3a**) and the 2-chloro-2′-cyano (**4a**) and the 2,2′-dicyano (**2a**) derivatives established that all three have the same relative configuration and thus the complete stereospecificity of the cyanation. The utility of the reaction was demonstrated by the successful synthesis of (2*S*,2′*R*,4*S*,4′*S*)-2,2′-dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile (**11**, X = CN).

α,α'-Dicyanoazoalkanes[1] have long been important synthetic targets due to their use as initiators for and the study of the mechanism of free radical chain reactions. The classical method of synthesis involves the preparation of an α,α'-dicyanohydrazine from a ketone, either by a one-pot Strecker-type synthesis[2-4] or by a two-step process involving addition of HCN to a ketazine **1**, followed by oxidation to **2**.[5-7] (Scheme I).

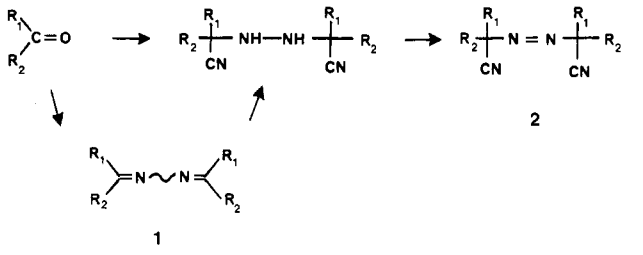
Alternatively, α-amino nitriles may be oxidized directly to **2** in the presence of hypochlorite.[8] These reactions commonly suffer from one or more of the following: low to moderate yields, long reaction times, excessive amounts of HCN, solvent sensitivity, and product instability under the reaction conditions. For systems in which $R_1 \neq R_2$, another serious drawback of these methods is their lack of stereochemical control.

In connection with our work on the mechanism of termination of free radical chain reactions,[9,10] we required a stereocontrolled synthesis of α,α'-dicyanoazoalkanes, since one of our target molecules, 2,2′-dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile (**11b**), has four chiral centers and the possibility of six diastereoisomers.

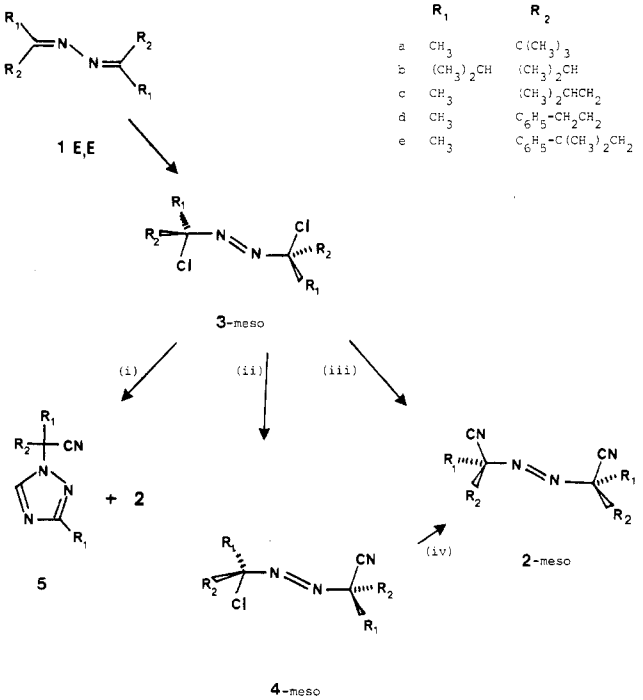
In 1970 Malament and McBride reported that 1,4-addition of chlorine to ketazines proceeds smoothly and stereospecifically at −60 °C such that symmetrical ketazines (*E,E*)-**1** or (*Z,Z*)-**1** give *meso*-α,α'-dichloroazoalkanes **3** (Scheme II) whereas unsymmetrical ketazines (*E,Z*)-**1** give the *dl* diastereomer.[11] Substitution of chlorine by a range of nucleophiles has been reported, including aqueous cyanide ion, albeit in low yield.[12,13] Since the α,α'-dichloroazoalkanes hydrolyze in aqueous media,[13,14] we sought alternative sources of nucleophilic cyanide in the hope that we might achieve a high-yielding reaction with stereochemical control over the sequence **1** → **3** → **2**.

We wish to report the successful stereospecific synthesis of **2** from **3** with the aid of trimethylsilyl cyanide in the

Scheme I



Scheme II[a]



[a] (i) 2.6 equiv of Me_3SiCN, 50 mol % $SnCl_4$, 0.5 h, −78 °C; (ii) 1.1 equiv of Me_3SiCN, 5 mol % $SnCl_4$, 0.5 h, −78 °C; (iii,iv) 2.6 equiv of Me_3SiCN, 50 mol % $SnCl_4$, 0.5 h, −78 °C; 1.5 h, room temperature.

(1) Timberlake, J. W.; Stowell, J. C. In *The Chemistry of the Hydrazo, Azo and Azoxy Groups*; Patai, S., Ed.; Wiley: New York, 1975; Part 1, Chapter 4, p 86. Hegarty, A. F. In *Chemistry of the Hydrazo, Azo and Azoxy Groups*; Patai, S., Ed.; Wiley: New York, 1975; Part 2, Chapter 16, p 701.
(2) Thiele, J.; Heuser, K. *Justus Liebigs Ann. Chem.* **1896**, *290*, 1.
(3) Overberger, C. G.; O'Shaughnessy, M. T.; Shalit, H. *J. Am. Chem. Soc.* **1949**, *71*, 2661.
(4) Overberger, C. G.; Huang, P.; Berenbaum, M. B. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. 4, p 274.
(5) Overberger, C. G.; Berenbaum, M. B. *J. Am. Chem. Soc.* **1951**, *73*, 2618.
(6) Robertson, J. A. U.S. Patent 2 586 995, 1952.
(7) Overberger, C. G.; Huang, P.; Berenbaum, M. B. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. 4, p 66.
(8) Fuchs, J. J. U.S. Patent 3 783 148, 1974.
(9) Serelis, A. K.; Solomon, D. H. *Polym. Bull.* **1982**, *7*, 39.
(10) Bizilj, S.; Kelly, D. P.; Serelis, A. K.; Solomon, D. H.; White, K. E. *Aust. J. Chem.* **1985**, *38*, 1657.
(11) Malament, D. S.; McBride, J. M. *J. Am. Chem. Soc.* **1970**, *92*, 4586.
(12) Benzing, E. *Justus Liebigs Ann. Chem.* **1960**, *631*, 1.
(13) Malament, D. S.; McBride, J. M. *J. Am. Chem. Soc.* **1970**, *92*, 4593.
(14) Benzing, E. *Justis Liebigs Ann. Chem.* **1960**, *631*, 10.

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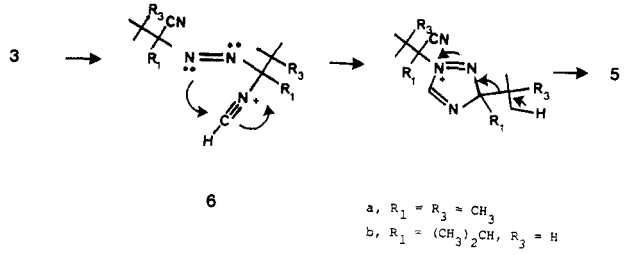
Scheme III



presence of stannic chloride at low temperature.

Results and Discussion

Ketazines 1a–e. The ketazines **1a–e** were prepared by the normal reaction of hydrazine hydrate with the appropriate ketone,[12–15] **1a** and **1b** being isolated as single isomers.[11] NMR spectroscopy[16,17] confirmed that **1a** was entirely the *E,E* isomer.[11] Ketazine **1c** was isolated as an equilibrium mixture of *E,E*, *E,Z*, and *Z,Z* isomers from which the *E,E* isomer was isolated by radial chromatography and chlorinated immediately in order to minimize reequilibration. Both **1d** and **1e** were isolated as mixtures of *E,E* and *E,Z* isomers, and in each case the *E,E* isomer was separated by fractional crystallization. Successive crystallizations of the reequilibrated ketazine mixture recovered from the filtrate allowed isolation of pure (*E,E*)-**1d** and (*E,E*)-**1e** in overall yields of 96% and 95%, respectively.

Chlorination of the *E,E* ketazines,[11,12,15,18] in dichloromethane at −78 °C proceeded cleanly and quantitatively to give single isomers *meso*-**3a–e** (Scheme II). The *meso* α,α'-dichloro derivative **3c** was also prepared by chlorination of the mixture of ketazines **1c**, followed by low-temperature crystallization of the resulting mixture (64:36 *meso*/*dl* by NMR) and seeding with pure *meso*-**3c**.

In order to overcome the problem of hydrolysis of **3** when treated with aqueous cyanide ion, we investigated the use of trimethylsilyl cyanide (Me_3SiCN) in the presence of stannic chloride, a procedure used successfully by Reetz et al. to prepare tertiary alkyl cyanides.[19] A modification of this method was developed which involved treatment of **3a** and **3b** with 2.6 equiv of Me_3SiCN and 50 mol % $SnCl_4$ at −78 °C for 30 min. This procedure yielded mixtures of the desired dinitriles **2a** and **2b**, together with additional compounds identified as the substituted 1,2,4-triazoles **5a** and **5b**, respectively (Scheme II (i)). The mechanism for substitution by cyanide as proposed by Reetz[19] involves an isonitrile intermediate. This suggested a mechanism for the reaction **3** → **5** whereby premature workup results in protonation of the second isonitrile (**6**) prior to rearrangement (Scheme III). Cyclization may then occur by attack of the γ-nitrogen lone pair, and subsequent loss of 2-methylpropene or propene then gives **5a** or **5b**, respectively.

Indeed, when the reaction mixture of **3a** was warmed to room temperature and stirred for a further 1.5 h, the ratio **2**/**5** increased from 70:30 to 88:12, while for **3b** it increased from 84:16 to 100:0. The remaining azo dichlorides **3c–e** were also converted to the desired dinitriles in excellent yields (96–98%) (Scheme II (iii)). Proton NMR showed that in every case, the *meso* diastereomer **3** gave rise to single isomers. In the case of the 64:36 mixture of *meso*- and *dl*-**3c**, the two stereoisomers of **2c** were produced in the same ratio.

Scheme IV

3		**4**[20]		**2**	
meso	inv.	dl	inv.	meso	(1)
meso	ret.	meso	ret.	meso	(2)
meso	inv.	dl	ret.	dl	(3)
meso	ret.	meso	inv.	dl	(4)

Other variations in the reaction conditions produced most interesting results. Treatment of **3a–e** with 1.1–2.6 equiv of Me_3SiCN and 5% stannic chloride (Scheme II (ii)) yielded the α-chloro-α'-cyanoazoalkanes **4a–e** in excellent yields (95–98%), and once again only single isomers were isolated. These could be converted cleanly into **2a–e** with additional Me_3SiCN and 50 mol % stannic chloride as in the original conditions (Scheme II (iv)).

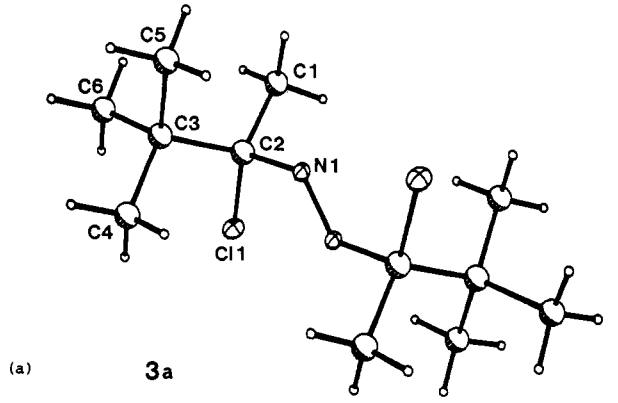
Since it had been previously established that observation of (*E,E*)-**1** ($R_1 = C_2H_5$, $R_2 = C_6H_5$) produced the corresponding *meso* azo dichloride **3** ($R_1 = C_2H_5$, $R_2 = C_6H_5$),[11] we had good reason to believe our chlorinations of (*E,E*)-**1a–e** proceeded similarly. Examination of proton spectra of **2a–e** showed that these too were all single diastereomers, thought likely to be *meso*, although this was by no means certain. Furthermore, the ease with which single diastereomers of **4a–e** could be isolated in high yield with no detectable **2a–e** raised the distinct possibility that the overall conversion of **3** → **2** might involve significant differences in the mechanism of the successive steps, perhaps even to the extent of different stereochemical outcomes. The four possible configurational sequences, based on *meso*-**3** are summarized in Scheme IV.

Determination of the configuration of both **2** and **4** would thus provide evidence for the mechanism of the reaction. X-ray crystallography was employed to provide the answer.

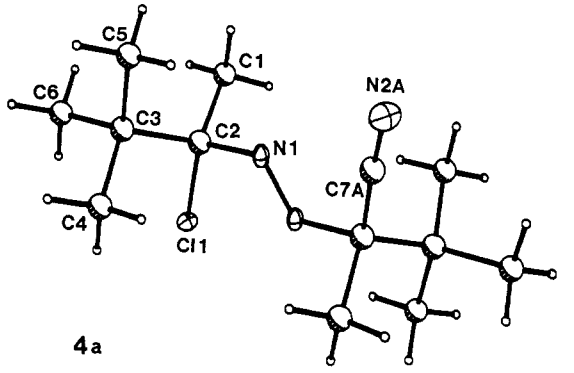
Single-crystal X-ray diffraction analysis of dichloroazoalkane **3a** first confirmed the *meso* stereochemistry of chlorination of *E,E* ketazine **1a** (Figure 1a). Similarly the crystal structure of **2a** showed that it too was *meso* (Figure 1c). Finally X-ray analysis of the intermediate **4a** again revealed that it was the *meso* diastereomer[20] (Figure 1b) and therefore that the two replacement steps must both proceed with retention of configuration at each center (Scheme IV).

The reaction sequence was also shown to be *stereospecific* by the following experiments. Chlorination of the mixture of *E,E*, *E,Z*, and *Z,Z* (60:36:4) ketazine isomers **1c** yielded a mixture of *meso* and *dl* (64:36) azo dichlorides **3c**, which was separated into pure *meso*-**3c** and *dl*-**3c** by exhaustive low-temperature recrystallization. Treatment of *meso*-**3c** with Me_3SiCN and 50 mol % $SnCl_4$ and with Me_3SiCN and 5 mol % $SnCl_4$ produced pure *meso*-**2c** and *meso*-**4c**, respectively. Likewise *dl*-**3c** gave *dl*-**2c** and *dl*-**4c**. Further confirmation of the stereospecificity was provided by the case of the phenyl-substituted compounds **1d** → **2d**. Photolysis of ketazine (*E,E*)-**1d** followed by chlorination and fractional recrystallization yielded both pure *meso*-**3d** and pure *dl*-**3d**. Treatment of each of these with $Me_3SiCN/SnCl_4$ (50 mol %) in the usual manner gave pure *meso*-**2d** and pure *dl*-**2d**, respectively. Alternative treat-

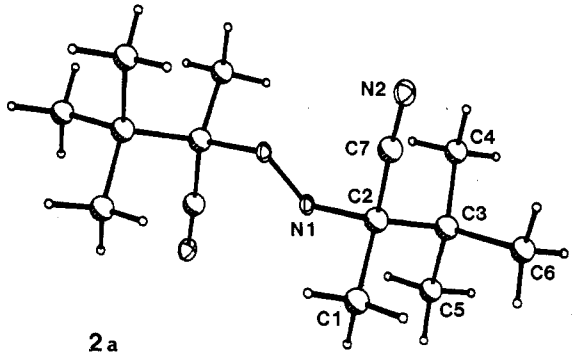
(15) Duismann, W.; Beckhaus, H.-D.; Ruchardt, C. *Justus Liebigs Ann. Chem.* **1974**, 1348.
(16) Elguero, J.; Jacquier, R.; Marzin, C. *Bull. Soc. Chim. Fr.* **1968**, 713.
(17) Arnal, E.; Elguero, J.; Jacquier, R.; Marzin, C.; Wylde, J. *Bull. Soc. Chim. Fr.* **1965**, 877.
(18) Goldschmidt, S.; Acksteiner, B. *Justus Liebigs Ann. Chem.* **1958**, *618*, 173.
(19) Reetz, M. T.; Chatziiosifidis, I.; Künzer, H.; Müller-Starke, H. *Tetrahedron* **1983**, *39*, 961.
(20) For purposes of comparison, these compounds (**4**) are called *dl* and *meso* rather than the more correct terms threo and erythro.



(a) 3a



(b) 4a



(c) 2a

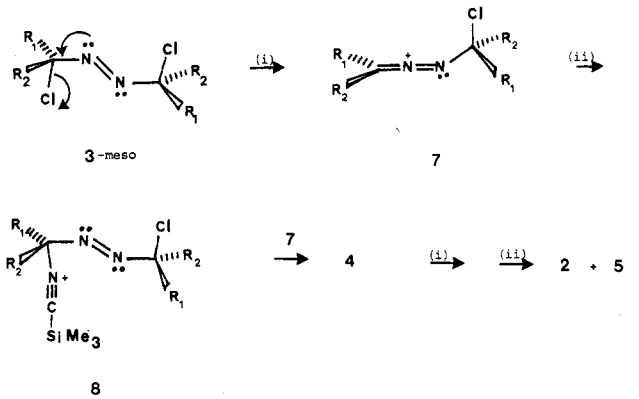
Figure 1.

ment with $Me_3SiCN/SnCl_4$ (5 mol %) provided the pure azo chloro nitriles *meso*-**4d** and *dl*-**4d**, respectively.

On the basis of the studies of Malament and McBride[11,13] and of Reetz et al.,[19] a mechanism of the cyanation may be proposed as first involving Lewis acid promoted heterolysis of the C–Cl bond in the conformation antiperiplanar to the β-nitrogen lone pair, to form an allene-like intermediate **7**, the same intermediate as generated during chlorination of the ketazine[13] (Scheme V). Attack by Me_3SiCN occurs such that the more anomerically favored trans (antiperiplanar) arrangement of the attacking substitutent and the lone pair is generated in the product **8**.[13] Rearrangement via another mole of the allene-like cation gives the isolable α-chloro-α′-cyano intermediate **4**. Repetition of this process at the other chiral center generates the final α,α′-dicyano compound **2** or in the case of **a** and **b** if workup is premature, both **2** and the triazole **5**.

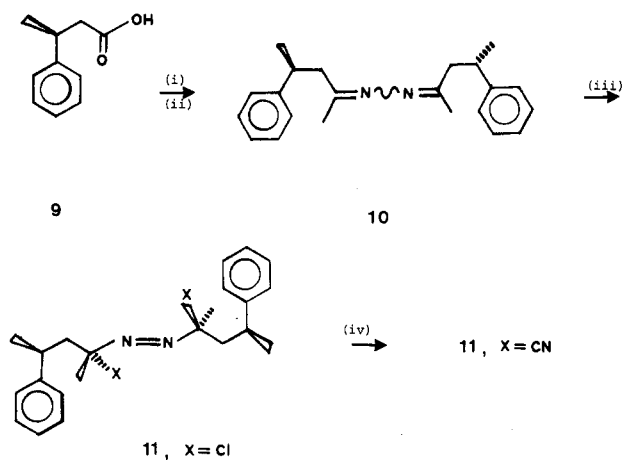
The similarities of the two steps of this mechanism for the transformation **3** → **4** → **2** is not entirely consistent with the dramatic difference in rates of the two steps, as

Scheme V[a]



[a] (i) $SnCl_4$; (ii) Me_3SiCN.

Scheme VI[a]



[a] (i) MeLi; (ii) $NH_2NH_2 \cdot H_2O$; (iii) Cl_2/CH_2Cl_2, −78 °C; (iv) $SnCl_4/Me_3SiCN$.

implied by the fact that **4** can be isolated in high yield free of traces of **2**. However, if the intermediate were in fact a cyclic chloronium ion[21] rather than the acyclic species **7**, substantial stabilization would result. Stabilization of the cationic intermediate in the second step **4** → **2** could only be provided by the newly introduced and much less effective cyano group. Such interactive stabilizations would also account for the retention of stereochemistry in both substitutions.

(2*S*,2′*R*,4*S*,4′*S*)-2,2′-Dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile (11, X = CN). The success of the above methodology encouraged us to develop a convenient route to a single diastereomer of our target compound 2,2′-dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile. Of the chiral centers present in the molecule, two arise from the ketone and the remaining two are introduced by the reaction sequence **1** → **3** → **2**. Application of our synthetic strategy to racemic ketone would reduce the number of possible diastereomers from six to three. However, use of optically pure ketone and isolation and chlorination of the *E*,*E* ketazine would furnish a single diastereomer of the α,α′-dichloroazoalkane, with the newly formed chiral centers bearing a *meso* relationship. Stereospecific substitution of chloride by cyanide should therefore give the azo dinitrile as a single diastereomer (Scheme VI).

In the event, racemic 3-phenylbutyric acid was resolved with (*S*)-(−)-1-phenylethylamine according to the literature

(21) Olah, G. A.; Bollinger, J. M. *J. Am. Chem. Soc.* **1968**, *90*, 947 and references therein.

procedure[22] to give the S-(+) enantiomer **9**. Treatment with methyllithium gave (S)-4-phenyl-2-pentanone in 97% yield after distillation.

Reaction of the optically active ketone with hydrazine hydrate gave the ketazine **10** as a mixture of *E,E*, *E,Z*, and *Z,Z* isomers (48:44:8 by NMR). Attempts to isolate the *E,E* isomer in the pure form by chromatography were unsuccessful due to rapid reequilibration. Chlorination of the isomeric ketazine mixture afforded a mixture of three diastereomers (~5:2:2 by NMR). Low-temperature fractional recrystallization gave the major isomer, (2*S*,2′*R*,4*S*,4′*S*)-2,2′-dichloro-4,4′-diphenyl-2,2′-azopentane (**11**, X = Cl), in 32% yield. The two minor isomers, presumably (2*S*,2′*S*,4*S*,4′*S*)-**11** (X = Cl) and (2*R*,2′*R*,4*S*,4′*S*)-**11** (X = Cl), were also isolated. Treatment of the major isomer with trimethylsilyl cyanide in the presence of 50 mol % $SnCl_4$ gave the required azo dinitrile (2*S*,2′*R*,4*S*,4′*S*)-2,2′-dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile (**11**, X = CN).

In conclusion, we have demonstrated that α,α′-dicyanoazoalkanes can be generated under very mild and stable conditions and can be isolated in high yields from the corresponding α,α′-dichloroazoalkanes. In this way we have been able to prepare **2e**, which was not possible by conventional methods. In addition, determination of the structures of **4a**, **3a**, and **2a** has shown conclusively that the reaction is stereospecific, a fact which allowed us to prepare the diastereomerically pure target compound, (2*S*,2′*R*,4*S*,4′*S*)-2,2′-dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile.

The decomposition studies of some of these azo dinitriles will be reported elsewhere.

Experimental Section

Crystallography. General. Intensity data were collected with a Nicolet R3m four-circle diffractometer by using monochromatized Mo Kα radiation (λ 0.7107 Å). The measured densities were determined by flotation in aqueous potassium iodide solution. Cell parameters were determined by least-squares refinement, the setting angles of 25 accurately centered reflections ($2\theta > 28°$) being used. Throughout data collections the intensities of three standard reflections were monitored at regular intervals, and this indicated no significant crystal decomposition. The intensities were corrected for Lorentz and polarization effects, but no correction for absorption was deemed necessary. Reflections with intensities $I > 3\sigma(I)$ were used for structure solution and refinement.

The structures were solved by direct methods and refined by blocked cascade least-squares procedures. All three compounds crystallize with only half a molecule in the asymmetric unit, the other half being related by a crystallographic center of inversion. Crystals of **3a** and **4a** are isostructural. The Cl and CN atoms in the asymmetric unit of **4a** therefore have site occupancies of one-half, their positions being disordered over the two sites within the whole molecule. No improvement was obtained by refinement of this structure in the lower symmetry space groups $P2_1$ and $P1$. Except for the nitrile carbon of **4a**, all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included in calculated positions with isotropic thermal parameters equal to the isotropic equivalent of their carrier atoms. The functions minimized were $w(|F_o| - |F_c|)^2$, with $w = [\sigma^2(F_o)]^{-1}$. The magnitude of residual electron density in final Fourier syntheses was <0.35 e·A^{-3}. All calculations (including diagrams) were performed on a Nova 4X computer using SHELXTL.[23]

Table I lists the atomic coordinates for the three structures, with standard deviations in parentheses. Tables of bond lengths, bond angles, hydrogen atom coordinates, anisotropic thermal parameters, and temperature factors are available as supplementary material. Comparable bonding geometry, including conformations, is similar within the three structures and is similar to that previously reported for related structures.[11,24,25]

Table I. Atom Coordinates (×10⁴) and Temperature Factors ($A^2 \times 10^3$)

atom	x	y	z	U_{eq}[a]
		3a		
Cl(1)	4832 (1)	2850 (1)	5171 (1)	25 (1)
N(1)	4705 (2)	59 (1)	4414 (1)	18 (1)
C(1)	2338 (2)	1569 (2)	3425 (2)	25 (1)
C(2)	4352 (2)	1504 (2)	3903 (1)	17 (1)
C(3)	5554 (2)	1750 (2)	2832 (2)	19 (1)
C(4)	7542 (2)	1684 (2)	3439 (2)	25 (1)
C(5)	5171 (2)	597 (2)	1774 (2)	30 (1)
C(6)	5154 (2)	3194 (2)	2178 (2)	28 (1)
		4a		
Cl(1)[b]	4785 (3)	2841 (2)	4482 (2)	27 (1)
N(1)	4724 (3)	−121 (2)	4428 (2)	26 (1)
C(1)	2275 (4)	1050 (3)	3079 (3)	36 (1)
C(2)	4301 (3)	1133 (2)	3594 (2)	23 (1)
C(3)	5511 (3)	1047 (3)	2522 (2)	23 (1)
C(4)	7505 (3)	1071 (3)	3149 (3)	33 (1)
C(5)	5130 (4)	−331 (3)	1771 (3)	38 (1)
C(6)	5116 (4)	2285 (3)	1589 (3)	34 (1)
N(2)[b]	4831 (12)	3344 (8)	4865 (8)	49 (3)
C(7)[b]	4596 (11)	2372 (8)	4342 (8)	22 (2)[c]
		2a		
N(1)	312 (1)	828 (2)	178 (1)	19 (1)
C(1)	869 (2)	2956 (3)	−1224 (2)	26 (1)
C(2)	1477 (2)	1299 (3)	−280 (2)	20 (1)
C(3)	2792 (2)	2058 (3)	749 (2)	21 (1)
C(4)	3300 (2)	261 (3)	1627 (2)	29 (1)
C(5)	2414 (2)	3970 (3)	1343 (2)	29 (1)
C(6)	3966 (2)	2686 (3)	290 (2)	30 (1)
N(2)	2191 (2)	−2036 (3)	−1223 (1)	28 (1)
C(7)	1858 (2)	−613 (3)	−809 (2)	21 (1)

[a] U_{eq} = 1/3(trace orthogonalized U_{ij} tensor). [b] Disordered. Site occupancy, 1/2. [c] Isotropic.

Crystal Data for 3a at 140 K: $C_{12}H_{24}N_2Cl_2$; M_r 267.3; monoclinic, space group $P2_1/n$; a = 7.564 (1) Å, b = 9.452 (1) Å, c = 10.347 (2) Å; β = 99.30 (2)°; U = 730.1 (2) Å^3; $F(000)$ = 288; D_m = 1.21 (2) g cm^{-3}, D_c (Z = 2) = 1.22 g cm^{-3}; μ = 4.3 cm^{-1}; colorless crystal with dimensions 0.77 × 0.40 × 0.33 mm, $\theta/2\theta$ scans, $2\theta_{max}$ = 50°, N = 1452, N_o = 1217 (four reflections suffered from low-angle extinction and were omitted from the final least-squares analysis), 73 parameters, R = 0.029, R_w = 0.034.

Crystal Data for 4a at 140 K: $C_{13}H_{24}N_3Cl$; M_r 257.8; monoclinic, space group $P2_1/n$; a = 7.526 (1) Å, b = 9.576 (1) Å, c = 10.507 (2) Å; β = 100.03 (1)°; U = 745.1 (2) Å^3; $F(000)$ 280; D_m = 1.14 (2) g cm^{-3}, D_c (Z = 2) = 1.15 g cm^{-3}; μ = 2.4 cm^{-1}; colorless crystal with dimensions 0.60 × 0.44 × 0.31 mm, $\theta/2\theta$ scans, $2\theta_{max}$ = 50°, N = 1482, N_o = 1272, 86 parameters, R = 0.058, R_w = 0.066.

Crystal Data for 2a at 140 K: $C_{14}H_{24}N_4$; M_r 248.4; monoclinic, space group $P2_1/c$; a = 10.107 (2) Å, b = 6.342 (2) Å, c = 12.333 (3) Å; β = 110.23 (1)°; U = 741.8 (3) Å^3; F(000) = 272; D_m = 1.08 (2) g cm^{-3}, D_c (Z = 2) 1.11 g cm^{-3}; μ = 0.6 cm^{-1}; colorless crystal with dimensions 0.41 × 0.38 × 0.11 mm, $\theta/2\theta$ scans, $2\theta_{max}$ = 50°, N = 1521, N_o = 1031, 82 parameters, R = 0.042, R_w = 0.038.

Synthesis. General. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Radial thin-layer chromatography was performed by a Harrison Research Chromatotron fitted with a 24 cm diameter glass rotor coated with silica gel 60 PF-254 containing gypsum (Merck). Infrared spectra were recorded on a Perkin-Elmer 983 G grating infrared spectrophotometer. The spectra of the liquid samples were recorded as films between sodium chloride plates and the solids as potassium bromide disks unless stated otherwise. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded as solutions

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in $CDCl_3$ on a JEOL FX-90Q, FX-100, or GX-400 instrument. Chemical shifts (δ) are reported as ppm relative to internal tetramethylsilane (Me_4Si). Carbon NMR (^{13}C NMR) spectra were recorded at 22.5, 25.0, or 100 MHz as solutions in $CDCl_3$. The ^{13}C NMR chemical shifts (δ) are reported as ppm relative to internal (Me_4Si). Optical rotation measurements were performed on a Perkin-Elmer 141 polarimeter. Mass spectra were recorded on a Micromass V.G. 70–70 F mass spectrometer operating at 70 eV in positive ion mode unless stated otherwise. Elemental analyses were determined by the Micro-analytical Service AMDEL, Port Melbourne. Dichloromethane was distilled over CaH_2 and stored over 4-Å molecular sieves. Petrol refers to petroleum ether of bp 40–60 °C.

(*E*,*E*)-3,3-Dimethyl-2-butanone (1,2,2-Trimethylpropylidene)hydrazone (1a). A solution of methyl *tert*-butyl ketone (30.0 g, 0.30 mol) and hydrazine hydrate (7.50 g, 0.15 mol) in ethanol (30 cm^3) was stirred at room temperature. After 66 h the ethanol was removed under vacuum, and the residue was diluted with 3:1 ether–dichloromethane (300 cm^3). The organic layer was washed with water (50 cm^3) and dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The residue was distilled [74–75 °C (5 Torr) (lit.[5] bp 87.5–88.0 °C (9 Torr))] to give the ketazine as an almost colorless liquid (24.6 g, 84%): IR ν_{max} (film) 2965, 2929, 2904, 2869, 1628, 1477, 1463, 1364, 1146 cm^{-1}; ^1H NMR (100 MHz) δ 1.68 (s, 6 H), 1.17 (s, 18 H); ^{13}C NMR (25 MHz) δ 164.5 (s), 38.4 (s), 27.8 (q), 12.3 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 197 (4), 196 (32), 155 (36), 139 (67), 100 (38), 98 (53), 57 (100), 42 (88).

2,4-Dimethyl-3-pentanone [2-Methyl-1-(1-methylethyl)propylidene]hydrazone (1b). Following the procedure outlined by Elguero et al.,[16] a solution of 2,4-dimethyl-3-pentanone (10.0 g, 0.088 mol) and hydrazine hydrate (2.19 g, 0.044 mol) in ethanol (35 cm^3) was heated at reflux for 9 h. The ethanol was evaporated under reduced pressure, and the residue was distilled [56–57 °C (0.20 Torr) (lit.[16] bp 117 °C (16 Torr))] to give the (60). as a pale yellow liquid (7.0 g, 71%): IR ν_{max} (film) 2963, 2931, 2870, 1624, 1468, 1379, 1363, 1013 cm^{-1}; ^1H NMR (100 MHz) δ 3.12 (sept, 2 H, *J* = 7.1 Hz), 2.61 (sept, 2 H, *J* = 6.8 Hz), 1.15 (d, 12 H, *J* = 6.8 Hz), 1.04 (d, 12 H, *J* = 7.1 Hz); ^{13}C NMR (22.5 MHz) δ 170.8 (s), 30.6 (d), 29.5 (d), 21.9 (q), 19.0 (q); MS (+EI, 70 eV), *m/z* (relative intensity) 225 (3), 224 (20), 181 (11), 112 (49), 111 (36), 96 (41), 70 (100), 43 (91), 41 (34), 28 (60).

4-Methyl-2-pentanone (1,3-Dimethylbutylidene)hydrazone (1c). A mixture of 4-methyl-2-pentanone (30.0 g, 0.30 mol) and hydrazine hydrate (7.50 g, 0.15 mol) in ethanol (24 cm^3) was stirred at room temperature. After 16 h the bulk of the ethanol was removed under reduced pressure. The residue was diluted with 3:1 ether–dichloromethane (200 cm^3), washed with water (70 cm^3), and dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The crude product was distilled [94–95 °C (9 Torr) (lit.[15] 178 °C (13 Torr); lit.[5] 101–103 °C (16 Torr))] to give the ketazine as an almost colorless liquid (27.9 g, 95%), which was seen by NMR to be a mixture of the *E,E*, *E,Z*, and *Z,Z* isomers (60:36:4): ^1H NMR (400 MHz) δ 2.25 (d, *J* = 7.6 Hz, CH_2, *Z,Z*), 2.22 (d, *J* = 7.6 Hz, CH_2, *E,Z*), 2.17 (d, *J* = 7.1 Hz, CH_2, *E,E*), 2.15 (d, *J* = 7.1 Hz, CH_2, *E,Z*), 2.05–1.95 (m, $(CH_3)_2CHCH_2$, *E,E* + *E,Z* + *Z,Z*), 1.99 (s, $C(CH_3)$=N, *E,Z*), 1.98 (s, $C(CH_3)$=N, *Z,Z*), 1.80 (s, $C(CH_3)$=N, *E,Z*), 1.76 (s, $C(CH_3)$=N, *E,E*), 0.95 (d, *J* = 6.6 Hz, $(CH_3)_2CH$, *E,E* + *E,Z*), 0.89 (d, *J* = 6.6 Hz, $(CH_3)_2CH$, *Z,Z*), 0.88 (d, *J* = 6.6 Hz, $(CH_3)_2CH$, *E,Z*).

Radial chromatography (2-mm plate; load 220 mg; eluent 2:1 petrol–ethyl acetate gave (*E,E*)-4-methyl-2-pentanone (1,3-dimethylbutylidene)hydrazone (*E,E*-**1c**) as a yellow oil in 59% yield: IR ν_{max} (film) 2956, 2870, 1640, 1465, 1363 cm^{-1}; ^{13}C NMR (22.5 MHz) δ 160.4 (s), 48.0 (t), 26.1 (d), 22.6 (q), 16.9 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 197 (1), 195 (1), 181 (25), 140 (61), 139 (74), 113 (100), 100 (32), 98 (52), 84 (22), 71 (23), 58 (37), 57 (50).

(*E*,*E*)-4-Phenyl-2-butanone (1-Methyl-3-phenylpropylidene)hydrazone (1d). A homogenous solution of 4-phenyl-2-butanone (10.0 g, 0.068 mol) and hydrazine hydrate (1.69 g, 0.034 mol) in ethanol (10 cm^3) was stirred at room temperature for 24 h. The solvent was removed under reduced pressure, and the residue was dried under vacuum to give the ketazine as a colorless lumpy solid (9.88 g, 100%; mp 38–43 °C), which was seen by NMR to be a mixture of the *E,E* and *E,Z* isomers (88:12): ^1H NMR (100 MHz) δ 7.36–7.10 (m, Ar H, *E,E* + *E,Z*), 3.01–2.50 (m, CH_2CH_2, *E,E* + *E,Z*), 1.98 (s, CH_3, *E,Z*), 1.73 (s, CH_3, *E,Z*), 1.67 (s, CH_3, *E,E*). The *E,E* isomer was selectively crystallized from methanol–pentane as colorless chunky crystals (6.61 g, 67%). The mother liquor was evaporated and the residue dissolved in methanol–pentane and seeded with a crystal of *E,E* ketazine. The product was filtered off and the process repeated until the *E,E* isomer was obtained in an overall yield of 96% (based on the starting ketone): mp 46.5–47.7 °C (lit.[26] mp 40 °C); IR ν_{max} (KBr) 3055, 3021, 2955, 2886, 1638, 1601, 1494, 1449, 1360, 1183, 754, 700, 518 cm^{-1}; ^1H NMR (100 MHz) δ 7.31–7.20 (m, 10 H), 3.01–2.50 (m, 8 H), 1.67 (s, 6 H); ^{13}C NMR (25 MHz) δ 160.4 (s), 141.4 (s), 128.4 (d), 125.9 (d), 40.2 (t), 32.5 (t), 16.7 (q); MS (+EI, 10 eV), *m/z* (relative intensity) 293 (1), 292 (1), 251 (100), 160 (83), 147 (41), 104 (43). Anal. Calcd for $C_{20}H_{24}N_2$: C, 82.2; H, 8.3; N, 9.6; Found: C, 82.3; H, 8.5; N, 9.6.

(*E*,*E*)-4-Methyl-4-phenyl-2-pentanone (1,3-Dimethyl-3-phenylbutylidene)hydrazone (1e). Reaction of 4-methyl-4-phenyl-2-pentanone (10.00 g, 0.057 mol), prepared from mesityl oxide,[27] with hydrazine hydrate (1.42 g, 0.028 mol) following the above procedure yielded the ketazine as a pale yellow solid (9.90 g, 100%), which was seen by NMR to be a mixture of the *E,E* and *E,Z* isomers (89:11). Slow crystallization from methanol–pentane and reequilibration of the mother liquors as for **1d** furnished the *E,E* ketazine **1e** as colorless needles (9.47 g, 95%): mp 69.1–70.2 °C; IR ν_{max} (KBr) 2965, 2937, 2905, 1617, 1496, 1442, 1359, 1239, 1030, 769, 700, 588 cm^{-1}; ^1H NMR (100 MHz) δ 7.42–7.15 (m, 10 H), 2.60 (s, 4 H), 1.38 (s, 12 H), 1.20 (s, 6 H); ^{13}C NMR (25 MHz) δ 159.0 (s), 148.7 (s), 128.1 (d), 125.8 (d), 53.4 (t), 38.0 (s), 29.2 (q), 18.7 (q); MS (+EI, 70 eV), *m/z* (relative intensity) 348 (2), 230 (42), 119 (100), 111 (44), 91 (53), 41 (32). Anal. Calcd for $C_{24}H_{32}N_2$: C, 82.7; H, 9.3; Found: C, 82.9; H, 9.2.

General Procedure for the Chlorination of Ketazines. Following the procedure outlined by Malament and McBride,[11] a 10% solution (w/v) of the ketazine in dichloromethane was cooled to ca. −78 °C. Chlorine gas was bubbled through the solution until an excess was observed as a permanent green color. The mixture was stirred at −78 °C for 5 min, after which the excess chlorine and solvent were removed by using a rotary evaporator.

***meso*-2,2′-Dichloro-3,3,3′,3′-tetramethyl-2,2′-azobutane (3a).** Chlorination of the ketazine **1a** following the general procedure gave **3a** as a pale yellow solid in quantitative yield. A small amount was recrystallized from ether to give pale yellow chunky crystals: mp 93.1–94.7 °C (lit.[11] mp 93 °C); IR ν_{max} (KBr) 2980, 2913, 2876, 1465, 1396, 1370, 1238, 1133, 1069, 839, 756, 625 cm^{-1}; ^1H NMR (90 MHz) δ 1.77 (s, 6 H), 1.15 (s, 18 H); ^{13}C NMR (25 MHz) δ 103.5 (s), 40.6 (s), 26.0 (q), 24.5 (q); MS (+EI, 70 eV), *m/z* (relative intensity) 233 (5), 231 (16), 175 (19), 121 (26), 119 (85), 83 (100), 69 (42), 57 (62), 55 (50), 43 (68), 41 (88), 29 (31).

3,3′-Dichloro-2,2′,4,4′-tetramethyl-3,3′-azopentane (3b). Chlorination of the ketazine **1b** following the general procedure gave **3b** as a yellow solid in quantitative yield. A small amount was recrystallized from ether–pentane to give the azo chloride as pale yellow chunky crystals: mp 60.9–62.3 °C (lit.[15] mp 60–61 °C); IR ν_{max} (KBr) 2978, 2939, 2880, 1466, 1389, 1307, 1092, 821, 806, 653, 560 cm^{-1}; ^1H NMR (100 MHz) δ 2.69 (sept, 4 H, *J* = 6.6 Hz), 1.05 (d, 24 H, *J* = 6.6 Hz); ^{13}C NMR (22.5 MHz) δ 108.1 (s), 35.9 (d), 17.8 (q), 17.6 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 261 (3), 259 (8), 223 (16), 222 (12), 133 (14), 127 (17), 112 (11), 97 (100), 77 (18), 57 (17), 43 (43).

***meso*-2,2′-Dichloro-4,4′-dimethyl-2,2′-azopentane (3c). Method A.** The *E,E* ketazine isomer (*E,E*)-**1c**, isolated above, was chlorinated before a significant amount of reequilibration had occurred. The azo dichloride **3c** was furnished in quantitative yield as a pale yellow solid being a single diastereomer (by NMR), mp 0–20 °C. Recrystallization from ether–petrol at −15 °C gave almost colorless chunky crystals: mp 23.6–24.9 °C (lit.[15] mp 0–10 °C); IR ν_{max} (film) 2958, 2934, 2871, 1469, 1450, 1374, 1138, 1046 cm^{-1}; ^1H NMR (400 MHz) δ 2.21 (dd, 2 H, *J* = 14.6, 6.1 Hz), 2.03 (dd, 2 H, *J* = 14.6, 5.5 Hz), 1.96–1.84 (m, 2 H), 1.82 (s, 6 H), 0.98 (d, 6 H, *J* = 6.8 Hz), 0.89 (d, 6 H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz)

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δ 95.85 (s), 50.89 (t), 29.18 (q), 24.67 (d), 24.18 (q), 23.89 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 231 (1), 181 (20), 155 (13), 140 (50), 139 (71), 113 (100), 100 (21), 98 (41), 84 (16), 83 (43), 71 (13), 58 (21), 57 (31), 43 (30).

Method B. The mixture of ketazine isomers (60:36:4) (14.0 g, 0.071 mol) was chlorinated following the general procedure to yield a yellow liquid as a mixture of diastereomers (19.1 g, 100%) (~64:36 *meso*/*dl* by NMR). The mixture of diastereomers was dissolved in petrol, seeded with the *meso* diastereomer obtained by method A, and left to crystallize at −15 °C. The supernatant liquor was removed, and the remaining crystals were washed with cold petrol and dried under vacuum to give almost colorless chunky crystals (8.6 g, 45%): mp between 0 and 20 °C. The NMR spectrum was identical with that of **3c** prepared by method A.

The solvent was evaporated from the supernatant liquor, and extensive low-temperature (<−20 °C) fractional recrystallization of the residue from petrol gave ***dl*-2,2′-dichloro-4,4′-dimethyl-2,2′-azopentane (3c)** as almost colorless crystals (2.8 g, 15%): mp <20 °C; IR ν_{max} (film) 2958, 2934, 2871, 1469, 1450, 1374, 1256, 1138, 1039 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.19 (dd, 2 H, *J* = 14.5, 6.0 Hz), 2.06 (dd, 2 H, *J* = 14.5, 5.4 Hz), 1.98–1.88 (m, 2 H), 1.77 (s, 6 H), 0.99 (d, 6 H, *J* = 6.8 Hz), 0.93 (d, 6 H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz) δ 95.75 (s), 50.98 (t), 28.99 (q), 24.77 (d), 24.24 (q), 24.01 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 233 (1), 231 (4), 140 (29), 139 (49), 119 (25), 113 (71), 100 (24), 84 (29), 83 (100), 58 (24), 57 (24), 43 (84). Anal. Calcd for $C_{12}H_{24}Cl_2N_2$: C, 53.9; H, 9.1; N, 10.5. Found: C, 54.3; H, 9.5; N, 10.7.

***meso*-2,2′-Dichloro-4,4′-diphenyl-2,2′-azobutane (3d).** The *E,E* ketazine isomer **1d** was chlorinated following the general procedure outlined above to give the azo dichloride in quantitative yield. Recrystallization from petrol–ether gave **3d** as colorless needles (96% yield): mp 114.5–116.0 °C; IR ν_{max} (KBr) 3064, 3029, 2987, 2941, 2913, 1497, 1195, 1178, 1058, 751, 700, 636, 506 cm^{-1}; ^{1}H NMR (100 MHz) δ 7.37–7.19 (m, 10 H), 3.00–2.26 (m, 8 H), 1.89 (s, 6 H); ^{13}C NMR (25.0 MHz) δ 140.8 (s), 128.5 (d), 128.4 (d), 126.1 (d), 95.5 (s), 44.2 (t), 30.4 (t), 28.9 (q); MS (+EI, 10 eV), *m/z* (relative intensity) 329 (1), 327 (2), 291 (6), 277 (7), 251 (40), 187 (18), 169 (13), 167 (40), 160 (30), 131 (100), 91 (100). Anal. Calcd for $C_{20}H_{24}Cl_2N_2$: C, 66.1; H, 6.7; N, 7.7. Found: C, 66.3; H, 6.9; N, 8.0.

***dl*-2,2′-Dichloro-4,4′-diphenyl-2,2′-azobutane (3d).** A 10% (w/v) solution of (*E,E*)-**1d** in dichloromethane was irradiated through Pyrex with light from a high-pressure Hg lamp. After 25 h a ^{1}H NMR spectrum (400 MHz) indicated the appearance of a pair of methyl singlets at δ 1.981 and 1.733 together with a small methyl singlet at δ 1.978. These peaks were assigned to the *E,Z* and *Z,Z* isomers, respectively (*E,E*/*E,Z*/*Z,Z* = 58:37:5 by NMR). The mixture was immediately chlorinated in the normal manner to give a mixture of two isomers (63:37 by NMR). Fractional recrystallization from petrol–ether gave the major isomer as white needles and was identified as *meso*-**3d** by comparison of spectral data with that prepared above. Protracted fractional recrystallization of the residue gave the minor isomer, *dl*-**3d**, as long white needles: mp 79.1–80.6 °C; IR ν_{max} (KBr) 3025, 2984, 2931, 1604, 1499, 1454, 1439, 1214, 1084, 1070, 775, 714, 699, 632 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.31–7.17 (m, 10 H), 2.82 (ddd, 2 H, *J* = 13.4, 12.0, 4.8 Hz), 2.66 (ddd, 2 H, *J* = 13.4, 12.3, 4.6 Hz), 2.56 (ddd, 2 H, *J* = 14.0, 12.0, 4.6 Hz), 2.41, (ddd, 2 H, *J* = 14.0, 12.3, 4.8 Hz), 1.86 (s, 6 H); ^{13}C NMR (22.5 MHz) δ 141.0 (s), 128.5 (d), 128.3 (d), 126.1 (d), 95.1 (s), 44.4 (t), 30.7 (t), 28.4 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 327 (1), 251 (68), 249 (19), 187 (32), 160 (100), 158 (13), 147 (36), 144 (13), 132 (16), 131 (20), 104 (40), 91 (30). Anal. Calcd for $C_{20}H_{24}Cl_2N_2$: C, 66.1; H, 6.7; N, 7.7. Found: C, 66.2; H, 7.0; N, 7.7.

***meso*-2,2′-Dichloro-4,4′-dimethyl-4,4′-diphenyl-2,2′-azopentane (3e).** The *E,E* ketazine isomer **1e** was chlorinated following the general procedure to give a single diastereomer of the azo dichloride **3e** as a pale yellow solid, mp 90.6–93.3 °C. A small amount was recrystallized from ether to give pale yellow chunky crystals: mp 91.2–93.3 °C; IR ν_{max} (KBr) 2972, 2931, 1600, 1497, 1446, 1379, 1367, 1234, 1119, 1080, 1058, 768, 701, 565 cm^{-1}; ^{1}H NMR (100 MHz) δ 7.48–7.17 (m, 10 H), 2.77 (d, 2 H, *J* = 15.0 Hz), 2.56 (d, 2 H, *J* = 15.0 Hz), 1.39 (s, 6 H), 1.36 (s, 6 H), 1.34 (s, 6 H); ^{13}C NMR (25 MHz) δ 148.7 (s), 128.1 (d), 126.0 (d), 125.8 (d), 96.2 (s), 56.0 (t), 38.3 (s), 31.4 (q), 30.4 (q), 29.0 (q); MS (+EI, 12 eV), *m/z* (relative intensity) 384 (2), 382 (5), 347 (17), 266 (18), 264 (51), 230 (55), 119 (100). Anal. Calcd for $C_{24}H_{32}Cl_2N_2$: C, 68.7; H, 7.7; N, 6.7. Found: C, 68.4; H, 7.6; N, 7.0.

General Procedure for the Synthesis of α-Chloro-α′-cyanoazoalkanes (4). A solution of α,α′-dichloroazoalkane **3** in anhydrous CH_2Cl_2 (ca. 5 cm^3 of CH_2Cl_2 per mmol of **3**) was stirred at −78 °C under a nitrogen atmosphere. Trimethylsilyl cyanide (1.1 mol equiv) was added followed by stannic chloride (5 mol %), and the mixture was stirred at −78 °C for 0.5 h. The mixture was poured into cold water and shaken vigorously. The organic layer was separated, the aqueous layer was extracted three times with CH_2Cl_2, and the combined organic phase was washed with 10% $NaHCO_3$. The organic phase was dried (Na_2SO_4), the solvent evaporated at ambient temperature under reduced pressure, and the residue dried in vacuo to give the crude monosubstituted product **4**.

***meso*-2-Chloro-2′-cyano-3,3,3′,3′-tetramethyl-2,2′-azobutane (4a).**[20] Treatment of the crude azo chloride **3a** (2.67 g, 10 mmol) under the general reaction conditions, using, however, 2.6 equiv of trimethylsilyl cyanide, cleanly gave the monosubstituted product **4a** as a pale yellow solid (2.44 g, 95%): mp 91–96 °C dec. A small amount was recrystallized from ether to give pale yellow chunky crystals: mp 102.1–102.9 °C dec; IR ν_{max} (KBr) 2969, 2915, 2877, 2231, 1481, 1466, 1400, 1371, 1234, 1132, 1079, 859, 642 cm^{-1}; ^{1}H NMR (90 MHz) δ 1.78 (s, 3 H), 1.59 (s, 3 H), 1.16 (s, 9 H), 1.15 (s, 9 H); ^{13}C NMR (22.5 MHz) δ 118.7 (s), 103.0 (s), 79.0 (s), 40.8 (s), 37.4 (s), 26.0 (q), 25.4 (q), 24.5 (q), 19.7 (q); MS (+EI, 70 eV), *m/z* (relative intensity) 231 (1), 214 (1), 119 (38), 83 (58), 57 (88), 55 (47), 43 (58), 41 (100), 29 (33). Anal. Calcd for $C_{13}H_{24}ClN_3$: C, 60.6; H, 9.4; N, 16.3. Found: C, 60.3; H, 9.1; N, 16.6.

3-Chloro-3′-cyano-2,2′,4,4′-tetramethyl-3,3′-azopentane (4b). Following the general procedure, a sample of crude azo chloride **3b** (1.00 g, 3.4 mmol) was transformed to give **4b** as a pale yellow solid (0.93 g, 96%); mp 65.5–70.1 °C. A small amount was recrystallized from petrol to give almost colorless chunky crystals: mp 75.8–77.0 °C; IR ν_{max} (KBr) 2978, 2942, 2881, 2237, 1467, 1391, 1372, 1302, 1019, 902, 880, 750 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.71 (sept, 2 H, *J* = 6.6 Hz), 2.59 (sept, 2 H, *J* = 6.8 Hz), 1.10 (d, 6 H, *J* = 6.8 Hz), 1.08 (d, 6 H, *J* = 6.8 Hz), 1.06 (d, 12 H, *J* = 6.6 Hz); ^{13}C NMR (25.0 MHz) δ 117.3 (s), 108.0 (s), 84.6 (s), 35.8 (d), 32.5 (d), 18.1 (q), 17.8 (q), 17.6 (q), 17.1 (q); MS (+E.I, 15 eV), *m/z* (relative intensity) 257 (1), 222 (16), 221 (9), 133 (12), 97 (100), 82 (36), 77 (20), 57 (15), 55 (18), 43 (67). Anal. Calcd for $C_{15}H_{28}ClN_3$: C, 63.0; H, 9.9; N, 14.7. Found: C, 63.1; H, 9.9; N, 15.0.

***meso*-2-Chloro-2′-cyano-4,4′-dimethyl-2,2′-azopentane (4c).**[20] Exposure of the *meso* azo chloride **3c** (1.00 g, 3.74 mmol) to the general reaction conditions furnished the monosubstituted product **4c** as a pale yellow solid and as a single isomer (0.94 g, 98%). A small amount was recrystallized from petrol at −15 °C to furnish almost colorless prisms: mp 33.5–34.8 °C; IR ν_{max} (KBr), 2960, 2939, 2915, 2874, 2236, 1466, 1448, 1392, 1137, 1046, 903, 655 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.23 (dd, 1 H, *J* = 14.6, 6.2 Hz), 2.11 (dd, 1 H, *J* = 14.2, 6.8 Hz), 2.04 (dd, 1 H, *J* = 14.6, 5.4 Hz), 1.91 (dd, 1 H, *J* = 14.2, 6.2 Hz), 1.94–1.78 (m, 2 H), 1.83 (s, 3 H), 1.67 (s, 3 H), 1.02 (d, 3 H, *J* = 6.8 Hz), 0.99 (d, 3 H, *J* = 6.8 Hz), 0.91 (d, 3 H, *J* = 6.8 Hz), 0.90 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz) δ 118.81 (s), 95.56 (s), 71.08 (s), 50.72 (t), 46.38 (t), 29.25 (q), 24.81 (d), 24.75 (q), 24.68 (d), 24.17 (q), 23.83 (q), 23.31 (q), 23.27 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 231 (1), 229 (3), 194 (8), 119 (16), 111 (14), 84 (13), 83 (100), 77 (9), 69 (13), 68 (24), 67 (10), 55 (16), 43 (86). Anal. Calcd for $C_{13}H_{24}ClN_3$: C, 60.6; H, 9.4; N, 16.3. Found: C, 60.7; H, 9.6; N, 16.7.

***dl*-2-Chloro-2′-cyano-4,4′-dimethyl-2,2′-azopentane (4c).**[20] Reaction of *dl*-**3c** (0.700 g, 2.62 mmol) in the usual manner yielded a pale yellow liquid (0.639 g, 95%). Low-temperature (−15 °C) recrystallization from petrol gave *dl*-**4c** as colorless cubes: mp 14–16 °C; IR ν_{max} (film) 2959, 2936, 2873, 2239, 1470, 1454, 1389, 1374, 1144 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.20 (dd, 1 H, *J* = 14.6, 6.0 Hz), 2.09 (dd, 1 H, *J* = 14.1, 6.6 Hz), 2.07 (dd, 1 H, *J* = 14.6, 5.6 Hz), 1.98–1.81 (m, 2 H), 1.93 (dd, 1 H, *J* = 14.1, 6.0 Hz), 1.77 (s, 3 H), 1.62 (s, 3 H), 1.04 (d, 3 H, *J* = 6.6 Hz), 1.01 (d, 3 H, *J* = 6.6 Hz), 0.96 (d, 3 H, *J* = 6.6 Hz), 0.95 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR (100 MHz) δ 119.45 (s), 95.96 (s), 71.27 (s), 51.07 (t), 46.57 (t), 29.00 (q), 24.96 (d), 24.90 (d), 24.86 (q), 24.33 (q), 24.13 (q), 23.53 (q), 23.48 (q); MS (+EI, 15 eV), *m/z* (relative intensity) 231 (1), 229 (3), 111 (49), 84 (42), 83 (100), 69 (56), 68 (36), 67

(38), 57 (20), 43 (77), 42 (23). Anal. Calcd for $C_{13}H_{24}ClN_3$: C, 60.6; H, 9.4; N, 16.3. Found: C, 60.4; H, 9.3; N, 16.5.

***meso*-2-Chloro-2′-cyano-4,4′-diphenyl-2,2′-azobutane (4d).**[20] Due to the poor solubility of *meso*-**3d** in CH_2Cl_2 at low temperatures, the procedure was modified for the synthesis of **4d**. After being stirred at −78 °C for 1 h, the reaction mixture was allowed to warm slowly. When the flocculent white precipitate dissolved to leave a clear yellow/orange solution, stirring was continued for a further 5 min, after which the reaction was worked up as before to give a pale yellow solid (0.92 g, 95%). A small amount was recrystallized from ether to furnish **4d** as fine white needles: mp 122.3–123.0 °C dec; IR ν_{max} (KBr) 3030, 2981, 2920, 2244, 1601, 1495, 1059, 758, 700 cm^{-1}; ^{1}H NMR (100 MHz) δ 7.38–7.11 (m, 10 H), 2.92–2.16 (m, 8 H), 1.90 (s, 3 H), 1.73 (s, 3 H); ^{13}C NMR (100 MHz) δ 139.88 (s), 139.14 (s), 128.04 (d), 127.96 (d), 127.78 (d), 127.72 (d), 125.88 (d), 125.64 (d), 118.03 (s), 94.81 (s), 71.58 (s), 43.84 (t), 39.86 (t), 30.50 (t), 30.29 (t), 28.81 (q), 24.05 (q); MS (+EI, 10 eV), m/z (relative intensity) 325 (2), 290 (5), 186 (4), 169 (2), 167 (8), 159 (3), 131 (24), 91 (100). Anal. Calcd for $C_{21}H_{24}ClN_3$: C, 71.3; H, 6.8; N, 11.9. Found: C, 71.5; H, 6.6; N, 12.2.

***dl*-2-Chloro-2′-cyano-4,4′-diphenyl-2,2′-azobutane (4d).**[20] Treatment of *dl*-2,2′-dichloro-4,4′-diphenyl-2,2′-azobutane (*dl*-**3d**) (0.500 g, 1.4 mmol) with trimethylsilyl cyanide, as in the preparation of *meso*-**4d** gave a white solid (0.473 g, 97%). Recrystallization from ether–petrol gave *dl*-**4d** as white needles: mp 78.5–79.7 °C; IR ν_{max} (KBr) 3025, 2935, 2241, 1604, 1499, 1454, 1440, 1216, 1086, 773, 711, 698 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.31–7.18 (m, 10 H), 2.88–2.77 (m, 2 H), 2.71–2.60 (m, 2 H), 2.60–2.52 (m, 1 H), 2.49–2.37 (m, 2 H), 2.34–2.26 (m, 1 H), 1.87 (s, 3 H), 1.71 (s, 3 H); ^{13}C NMR (22.5 MHz) δ 140.8 (s), 140.1 (s), 128.7 (d), 128.4 (d), 126.6 (d), 126.3 (d), 118.7 (s), 95.1 (s), 71.9 (s), 44.5 (t), 40.4 (t), 30.8 (t), 28.5 (q), 23.9 (q); MS (+EI, 10 eV), m/z (relative intensity) 327 (3), 325 (6), 317 (5), 291 (16), 290 (61), 251 (33), 187 (12), 160 (13), 131 (27), 91 (100). Anal. Calcd for $C_{21}H_{24}ClN_3$: C, 71.3; H, 6.8; N, 11.9. Found: C, 71.3; H, 7.1; N, 11.6.

***meso*-2-Chloro-2′-cyano-4,4′-dimethyl-4,4′-diphenyl-2,2′-azopentane (4e).**[20] Following the general procedure, the azo chloride **3e** gave **4e** (98%) as a pale yellow solid: mp 91.2–93.3 °C; IR ν_{max} (KBr) 2962, 2238, 1601, 1496, 1471, 1450, 1370, 1080, 1064, 772, 703, 572 cm^{-1}; ^{1}H NMR (100 MHz) δ 7.45–7.17 (m, 10 H), 2.74 (d, 1 H, J = 15.0 Hz), 2.53 (d, 1 H, J = 15.0 Hz), 2.53 (d, 1 H, J = 14.8 Hz), 2.42 (d, 1 H, J = 14.8 Hz), 1.45 (s, 3 H), 1.40 (s, 3 H), 1.37 (s, 6 H), 1.34 (s, 3 H), 1.28 (s, 3 H); ^{13}C NMR (100 MHz) δ 147.68 (s), 147.06 (s), 127.69 (d), 127.61 (d), 125.65 (d), 125.42 (d), 125.29 (d), 118.57 (s), 95.50 (s), 70.03 (s), 55.73 (t), 50.65 (t), 38.11 (s), 37.48 (s), 31.22 (q), 31.18 (q), 30.62 (q), 28.86 (q), 28.81 (q), 25.51 (q); MS (+EI, 10 eV), m/z (relative intensity) 381 (2), 346 (3), 345 (6), 265 (2), 264 (5), 263 (3), 262 (16), 227 (5), 226 (15), 120 (12), 119 (100). Anal. Calcd for $C_{25}H_{32}ClN_3$: C, 73.2; H, 7.9; N, 10.2. Found: C, 73.2; H, 7.9; N, 10.6.

General Procedure for the Synthesis of Azo Nitriles 2 from α,α′-Dichloroazoalkanes 3. Method A. The α,α′-dichloroazoalkane **3** was treated with trimethylsilyl cyanide (2.6 mol equiv) in the presence of stannic chloride (50 mol %) under the same reaction conditions outlined for the synthesis of α-chloro-α′-cyanoazoalkanes **4**. Similar workup gave the crude azo nitrile **2**.

Method B. The same reaction conditions as above were employed except, after the mixture was stirred at −78 °C for 0.5 h, the cooling bath was removed, and the solution was allowed to warm slowly to room temperature and stirred for a further 1.5 h.

***meso*-2,2′,3,3,3′,3′-Hexamethyl-2,2′-azobutanenitrile (2a). Method A.** Treatment of **3a** (1.00 g, 3.74 mmol) according to method A gave a pale yellow solid (0.82 g) as a mixture of two components (70:30 by ^{1}H NMR). Separation was achieved by radial chromatography with petrol–ethyl acetate (3:1) as eluant. The first component (631 mg) was found to be the desired azo nitrile and was recrystallized from ether–petrol as white plates (572 mg, 62%): mp 114.7–115.7 °C dec (lit.[5] "isomer I" platelike crystals mp 114–116 °C dec, "isomer II" needlelike crystals mp 116–118 °C dec); IR ν_{max} (KBr) 2994, 2970, 2874, 2236, 1492, 1463, 1401, 1377, 1369, 1153, 1131 cm^{-1}; ^{1}H NMR (90 MHz) δ 1.61 (s, 6 H), 1.16 (s, 18 H); ^{13}C NMR (25.0 MHz) δ 118.1 (s), 79.7 (s), 37.6 (s), 25.4 (q), 19.8 (q); MS (+EI, 15 eV), m/z (relative intensity) 220 (6), 111 (38), 110 (99), 96 (42), 95 (50), 68 (100), 57 (90), 43 (34).

The second component (209 mg) was recrystallized from petrol to give **2,3,3-trimethyl-2-(3-methyl-1,2,4-triazol-1-yl)butanenitrile (5a)** as colorless needles (186 mg, 26%): mp 68.1–69.0 °C; IR ν_{max} (KBr) 3135, 2969, 2240, 1697, 1517, 1374, 1321, 1198, 1004, 851 cm^{-1}; ^{1}H NMR (90 MHz) δ 8.24 (s, 1 H), 2.40 (s, 3 H), 2.00 (s, 3 H), 1.10 (s, 9 H); ^{13}C NMR (22.5 MHz) δ 161.1 (s), 143.4 (d, J_{CH} = 210 Hz), 118.4 (s), 66.3 (s), 39.3 (s), 25.7 (q), 21.2 (q), 14.0 (q); MS (+EI, 70 eV), m/z (relative intensity) 193 (2), 136 (51), 121 (17), 84 (10), 57 (100), 42 (25), 41 (32), 29 (18), 27 (10). Anal. Calcd for $C_{10}H_{16}N_4$: C, 62.5; H, 8.4; N, 29.1. Found: C, 62.3; H, 8.2; N, 29.3.

Method B. Treatment of **3a** (1.00 g, 3.74 mmol) according to method B gave a pale yellow solid (0.90 g) as a mixture of the azo nitrile **2a** and the 1,2,4-triazole **5a** (88:12 by ^{1}H NMR). Separation of the mixture was achieved by radial chromatography as above. The first component was recrystallized from ether–petrol to give the azo nitrile **2a** as white plates (0.74 g, 80%), the spectral data of which was identical with those of **2a** prepared by method A. The second component was collected and recrystallized from ether–petrol to give the 1,2,4-triazole **5a** as colorless needles (65 mg, 9%), which had spectra data identical with those of **5a** prepared by method A.

2,2′-Diisopropyl-3,3′-dimethyl-2,2′-azobutanenitrile (2b). Method A. Treatment of **3b** (2.95 g, 10 mmol) with trimethylsilyl cyanide according to method A gave a white solid (2.46 g) as a mixture of two components (84:16 by ^{1}H NMR). Separation of the mixture was achieved by radial chromatography with petrol–ethyl acetate (3:1) as eluant. The first component was recrystallized from ether to give the azo dinitrile **2b** as chunky crystals (1.86 g, 67%): mp 100.6–102.4 °C dec (lit.[28] mp 104–105 °C dec); IR ν_{max} (KBr) 2979, 2941, 2882, 2237, 1470, 1392, 1377, 1305, 1178, 1102, 1000, 939 cm^{-1}; ^{1}H NMR (90 Mz) δ 2.62 (sept, 4 H, J = 6.8 Hz), 1.11 (d, 12 H, J = 6.8 Hz), 1.10 (d, 12 H, J = 6.8 Hz); ^{13}C NMR (22.5 MHz) δ 116.7 (s), 85.4 (s), 32.6 (d), 18.1 (q), 17.2 (q); MS (+EI, 15 eV), m/z (relative intensity) 248 (1), 125 (9), 124 (4), 110 (8), 83 (8), 82 (100), 55 (14), 43 (20). The second component was purified by Kugelrohr distillation (0.01 Torr, oven temperature 60 °C) to give **3-methyl-2-(1-methylethyl)-2-[3-(1-methylethyl)-1,2,4-triazol-1-yl]butanenitrile (5b)** as a colorless liquid (335 mg, 14%): IR ν_{max} (film) 2973, 2937, 2246, 1509, 1471, 1392, 1335, 1203 cm^{-1}; ^{1}H NMR (100 MHz) δ 8.26 (s, 1 H), 3.07 (sept, 1 H, J = 6.8 Hz), 2.70 (sept, 2 H, J = 6.8 Hz), 1.31 (d, 6 H, J = 6.8 Hz), 1.05 (d, 6 H, J = 6.8 Hz), 0.97 (d, 6 H, J = 6.8 Hz); ^{13}C NMR (22.5 MHz) δ 170.4 (s), 143.9 (d), 116.9 (s), 72.2 (s), 33.9 (d), 28.3 (d), 21.6 (q) 17.9 (q), 16.9 (q); MS (+EI, 70 eV), m/z (relative intensity) 234 (5), 192 (51), 178 (14), 177 (100), 149 (10), 112 (20), 96 (18), 70 (34), 43 (64), 41 (34), 39 (13), 28 (16), 27 (23). Anal. Calcd for $C_{13}H_{22}N_4$: C, 66.6; H, 9.5; N, 23.9. Found: C, 66.6; H, 9.5; N, 23.9.

Method B. Treatment of **3a** (1.00 g, 3.4 mmol) with trimethylsilyl cyanide under the conditions of method B gave a white solid (0.93 g, 100%), mp 96.5–99.9 dec. Recrystallization from ether gave chunky crystals (0.79 g, 84%), mp 99.4–101.6 °C dec. Further recrystallization gave the pure product, mp 101.1–102.5 °C dec, the spectral data of which were identical with those of **2b** prepared by method A.

***meso*-2,2′,4,4′-Tetramethyl-2,2′-azopentanenitrile (2c).** Exposure of *meso*-**3c** (0.500 g, 1.87 mmol) to the conditions of method B yielded *meso*-**2c** as a pale yellow solid (0.454 g, 98%), mp 64.0–69.0 °C dec. Recrystallization from ether–petrol gave white plates (0.396 g, 85%, mp 73.2–75.4 °C dec. Further recrystallization afforded pure *meso*-**2c**: mp 74.9–75.9 °C dec (lit.[5] "isomer I" mp 75–76 °C dec, "isomer II" mp 56–57 °C dec); IR ν_{max} (KBr) 2977, 2955, 2940, 2916, 2237, 1469, 1459, 1449, 1371, 1268, 1188, 1172 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.13 (dd, 2 H, J = 14.3, 7.0 Hz), 1.93 (dd, 2 H, J = 14.3, 6.1 Hz), 1.87–1.77 (m, 2 H), 1.68 (s, 6 H), 1.03 (d, 6 H, J = 6.6 Hz), 0.92 (d, 6 H, J = 6.6 Hz); ^{13}C NMR (100 MHz) δ 118.21 (s), 71.60 (s), 46.21 (t), 24.81 (d), 24.78 (q), 23.25 (q), 23.21 (q); MS (+EI, 15 eV) m/z (relative

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intensity) 220 (1), 111 (22), 110 (25), 94 (12), 69 (18), 68 (100), 55 (16), 43 (36), 41 (47).

***dl*-2,2′,4,4′-Tetramethyl-2,2′-azopentanenitrile (2c).** Treatment of *dl*-**3c** (0.500 g, 1.87 mmol) under the conditions of method B gave a pale yellow solid (0.458 g, 98%). Recrystallization from ether–petrol gave *dl*-**2c** as white plates (0.328 g, 71%): mp 55.9–56.7 °C dec (lit.[5] "isomer I" mp 75–76 °C dec, "isomer II" mp 56–57 °C (dec); IR ν_{max} (KBr) 2957, 2872, 2240, 1469, 1447, 1388, 1367, 1268, 1189, 1162 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.10 (dd, 2 H, J = 14.3, 6.6 Hz), 1.95 (dd, 2 H, J = 14.3, 6.2 Hz), 1.91–1.81 (m, 2 H), 1.63 (s, 6 H), 1.05 (d, 6 H, J = 6.6 Hz), 0.98 (d, 6 H, J = 6.6 Hz); ^{13}C NMR (100 MHz) δ 118.34 (s), 71.43 (s), 46.21 (t), 24.84 (d), 24.70 (q), 23.37 (q), 23.34 (q); MS (+EI, 15 eV), m/z (relative intensity) 220 (4), 111 (30), 110 (42), 94 (8), 69 (21), 68 (100), 67 (15), 55 (13), 43 (25), 41 (18).

***meso*-2,2′-Dimethyl-4,4′-diphenyl-2,2′-azobutanenitrile (2d).** Treatment of *meso*-**3d** (1.00 g, 2.7 mmol) under the conditions of method B gave a yellow solid (0.94 g, 99%). Recrystallization from chloroform–methanol gave colorless needles (0.76 g, 80%), mp 109.9–112.0 °C dec. Further recrystallization raised the melting point to 111.4–112.6 °C dec (lit.[26] mp 110 °C): IR ν_{max} (KBr) 2980, 2949, 2921, 2857, 2246, 1602, 1490, 1455, 1228, 1072, 762, 722, 700, 504 cm^{-1}; ^{1}H NMR (90 MHz) δ 7.51–7.00 (m, 10 H) 2.88–1.99 (m, 8 H), 1.73 (s, 6 H); ^{13}C NMR (25 MHz) δ 139.5 (s), 128.6 (d), 128.3 (d), 126.5 (d), 118.0 (s), 72.5 (s), 39.8 (t), 30.6 (t), 24.2 (q); MS (+EI, 15 eV), m/z (relative intensity) 316 (3), 213 (15), 212 (73), 197 (29), 159 (32), 158 (15), 157 (37), 105 (15), 92 (39), 91 (100). Anal. Calcd for $C_{22}H_{24}N_4$: C, 76.7; H, 7.0. Found: C, 76.6; H, 7.3.

***dl*-2,2′-Dimethyl-4,4′-diphenyl-2,2′-azobutanenitrile (2d).** Exposure of *dl*-**3d** (0.500 g, 1.38 mmol) to the reaction conditions of method B gave *dl*-**2d** as a yellow solid (0.462 g, 97%). The crude product was recrystallized from methanol–petrol to give white needles (0.382 g, 81%), mp 99.6–101.5 °C dec. Further recrystallization raised the melting point to 101.6–102.9 °C dec: IR ν_{max} (KBr) 3025, 2991, 2940, 2907, 2242, 1605, 1499, 1454, 1444, 1240, 770, 748, 710, 696 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.32–7.18 (m, 10 H), 2.82 (ddd, 2 H, J = 13.3, 12.2, 4.9 Hz), 2.65 (ddd, 2 H, J = 13.3, 12.4, 5.1 Hz), 2.46 (ddd, 2 H, J = 13.9, 12.2, 5.1 Hz), 2.32 (ddd, 2 H, J = 13.9, 12.4, 4.9 Hz), 1.73 (s, 6 H); ^{13}C NMR (22.5 MHz) δ 139.8 (s), 128.8 (d), 128.4 (d), 126.6 (d), 118.1 (s), 72.4 (s), 40.1 (t), 30.8 (t), 23.8 (q); MS (+EI, 12 eV), m/z (relative intensity) 316 (7), 225 (17), 213 (16), 212 (100), 159 (44), 158 (14), 157 (48), 92 (19), 91 (79). Anal. Calcd for $C_{22}H_{24}N_4$: C, 76.7; H, 7.0. Found: C, 76.7; H, 7.2.

***meso*-4,4′-Diphenyl-2,2′,4,4′-tetramethyl-2,2′-azopentanenitrile (2e).** Exposure of crude **3e** (2.42 g, 5.77 mmol) to the conditions of method A gave **2e** as a pale yellow solid (2.20 g, 96%). Recrystallization from chloroform–petrol (−20 °C) gave white chunky crystals: mp ~99 °C dec (lit.[6] mp 75–76 °C, lit.[29] mp 96 °C dec); IR ν_{max} (KBr) 3062, 2969, 2957, 2243, 1600, 1497, 1450, 1441, 1390, 1238, 1031, 765, 699, 558 cm^{-1}; ^{1}H NMR (100 MHz) δ 7.40–7.17 (m, 10 H), 2.53 (d, 2 H, J = 14.9 Hz), 2.40 (d, 2 H, J = 14.9 Hz), 1.43 (s, 6 H), 1.38 (s, 6 H), 1.25 (s, 6 H); ^{13}C NMR (25 MHz) δ 147.3 (s), 128.3 (d), 126.2 (d), 125.9 (d), 118.4 (s), 70.8 (s), 50.5 (t), 37.6 (s), 31.1 (q), 29.5 (q), 25.5 (q); MS (+EI, 15 eV), m/z (relative intensity) 372 (2), 187 (8), 186 (3), 120 (12), 119 (100), 118 (6), 67 (2).

General Procedure for the Conversion of α-Chloro-α′-cyanoazoalkanes 4 to Azo Nitriles 2. Method B, described for the synthesis of azo nitriles **2** directly from α-chloro-α′-cyanoazoalkanes, was followed with the exception that only 1.1 equiv of Me_3SiCN was used.

***meso*-2,2′,4,4′-Tetramethyl-2,2′-azopentanenitrile (2c).** Treatment of *meso*-2-chloro-2′-cyano-4,4′-dimethyl-2,2′-azopentane (**4c**) (0.500 g, 1.94 mmol) under the above conditions yielded a single isomer as a pale yellow solid (0.458 g, 95%), the proton NMR spectrum of which was identical with that of *meso*-**2c** prepared above.

***dl*-2,2′,4,4′-Tetramethyl-2,2′-azopentanenitrile (2c).** Treatment of *dl*-2-chloro-2′-cyano-4,4′-dimethyl-2,2′-azopentane (**4c**) (0.500 g, 1.94 mmol) under the general reaction conditions gave a pale yellow solid as a single isomer (0.462 g, 96%), the proton NMR spectrum of which was identical with that of *dl*-**2c** prepared above.

(*S*)-(+)-3-Phenylbutyric Acid (9). Resolution of the commercially available racemic acid was accomplished by using (*S*)-(−)-1-phenylethylamine, $[\alpha]^{20}_D$ −39° (neat). Six recrystallizations from ethanol/water gave a pure salt (33%): mp 146.7–147.7 °C (lit.[22] mp 144.5–146 °C). The acid was liberated[30] and purified by Kugelrohr distillation [120 °C (0.05 Torr)] to give (*S*)-(+)-3-phenylbutyric acid as a colorless liquid (98%): $[\alpha]^{20}_D$ +57.6° (*c* 2.7, benzene) [lit.[31] $[\alpha]^{25}_D$ −57.6° (*c* 2.7, benzene) for (*R*)-(−)-**9**].

(*S*)-(+)-4-Phenyl-2-pentanone. To a vigorously stirred solution of (*S*)-(+)-3-phenylbutyric acid (**9**) (7.20 g, 0.44 mol) in dry ether (290 cm^3), cooled in an ice bath, was added dropwise during 3 h an ethereal solution of methyllithium (270 cm^3, 0.33 M solution, 0.089 mol). The resulting white suspension was stirred at room temperature for 4 h, after which dichloroethane (7.5 cm^3) was added. After being stirred at room temperature for a further 0.5 h, the reaction mixture was poured into a mixture of ice and dilute aqueous hydrochloric acid. The ether layer was separated, and the aqueous layer was extracted with dichloromethane (2 × 90 cm^3). The combined organic extract was washed with 10% aqueous $NaHCO_3$ (250 cm^3) followed by distilled water (250 cm^3) and dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The crude ketone was purified by Kugelrohr distillation [70 °C (0.15 Torr)] to give (*S*)-(+)-4-phenyl-2-pentanone as a colorless liquid (6.87 g, 97%): $[\alpha]^{25}_D$ +74.3° (*c* 1.0, benzene) (lit.[32] $[\alpha]_D$ −74.5° (*c* 1.0, benzene) for *R*-(−) enantiomer); IR ν_{max} (film) 2962, 1716, 1495, 1453, 1360, 1163, 760, 701 cm^{-1}; ^{1}H NMR (100 MHz) δ 7.37–7.11 (m, 5 H), 3.48–3.13 (m, 1 H), 2.75 (dd, 1 H, J = 16.3, 6.4 Hz), 2.66 (dd, 1 H, J = 16.3, 7.9 Hz), 2.06 (s, 3 H), 1.26 (d, 3 H, J = 6.8 Hz); ^{13}C NMR (25.0 MHz) δ 207.7 (s), 146.1 (s), 128.5 (d), 126.7 (d), 126.2 (d), 51.9 (t), 35.4 (d), 30.5 (q), 22.0 (q); MS (+EI, 70 eV), m/z (relative intensity) 162 (44), 147 (59), 119 (19), 105 (100), 104 (26), 91 (44), 77 (23), 43 (98).

(*S*)-4-Phenyl-2-pentanone [(*S*)-1-Methyl-3-phenylbutylidene]hydrazone (10). A homogenous solution of (*S*)-4-phenyl-2-pentanone (1.000 g, 6.2 mmol) and hydrazine hydrate (0.154 g, 3.1 mmol) in ethanol (3 cm^3) was stirred at ambient temperature. After 16 h the ethanol was removed under vacuum and the residue dried in vacuo to give a colorless liquid (0.988 g, 100%). Microdistillation [132–136 °C (0.008 Torr)] afforded a mixture of ketazine isomers (*E*,*E*/*E*,*Z*/*Z*,*Z* ~48:44:8 by NMR) as a pale yellow liquid (0.847 g, 86%): IR ν_{max} (film) 3027, 2960, 2925, 1636, 1494, 1452, 1362, 762, 700 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.33–7.04 (m, Ar H, *E*,*E* + *E*,*Z* + *Z*,*Z*), 3.28–3.19 (m, $CH_2CH(CH_3)$, *E*,*Z*), 3.14–3.00 (m, $CH_2CH(CH_3)$, *E*,*E* + *Z*,*Z*), 2.97–2.88 (m, $CH_2CH(CH_3)$, *E*,*Z*), 2.67–2.43 (m, $CH(CH_2)$, *E*,*Z* + *Z*,*Z*), 2.56 (dd, J = 13.9, 7.8 Hz, $CH(CHH)$, *E*,*E*), 2.49 (dd, J = 13.9, 7.6 Hz, $CH(CHH)$, *E*,*E*), 1.87 (s, $C(CH_3)$=N, *Z*,*Z*), 1.80 (s, $C(CH_3)$=N, *E*,*Z*), 1.63 (s, $C(CH_3)$=N, *E*,*Z*), 1.40 (s, $C(CH_3)$=N, *E*,*E*), 1.32 (d, J = 6.8 Hz, $CH(CH_3)$, *E*,*Z*), 1.28 (d, J = 6.8 Hz, $CH(CH_3)$, *E*,*E*), 1.23 (d, J = 6.8 Hz, $CH(CH_3)$, *Z*,*Z*), 1.15 (d, J = 6.8 Hz, $CH(CH_3)$, *E*,*Z*); MS (+EI, 15 eV), m/z (relative intensity) 320 (1), 279 (14), 201 (39), 174 (28), 162 (19), 161 (11), 160 (12), 146 (20), 119 (19), 118 (100), 105 (20). Anal. Calcd for $C_{22}H_{28}N_2$: C, 82.5; H, 8.8. Found: C, 82.7; H, 8.7.

(2*S*,2′*R*,4*S*,4′*S*)-(+)-2,2′-Dichloro-4,4′-diphenyl-2,2′-azopentane (11, X = Cl). Chlorination of the crude ketazine mixture quantitatively afforded a mixture of three diastereomers as a yellow liquid (~5:2:2 by NMR). Low-temperature (−15 °C) crystallization from petrol followed by successive recrystallizations gave the major diastereomer **11** (X = Cl) as white needles in 32% yield: mp 53.7–55.0 °C; $[\alpha]^{25}_D$ +63.0° (*c* 1.0, benzene); IR ν_{max} (KBr) 3029, 2955, 2923, 1601, 1494, 1453, 1376, 1069, 825, 762, 698, 636, 607 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.33–7.12 (m, 10 H), 3.15–3.05 (m, 2 H) 2.81 (dd, 1 H, J = 14.5, 7.6 Hz), 2.358 (dd, 1 H, J = 14.5, 5.4 Hz), 2.356 (dd, 1 H, J = 14.5, 6.4 Hz), 2.24 (dd, 1 H, J = 14.5, 5.9 Hz), 1.70 (s, 3 H), 1.32 (s, 3 H), 1.29 (d, 3 H, J = 7.1 Hz), 1.22 (d, 3 H, J = 7.1 Hz); ^{13}C NMR (100 MHz) δ 146.76 (s), 146.13 (s), 127.91 (d), 126.56 (d), 126.45 (d), 125.56 (d), 95.70 (s), 95.28 (s), 50.25 (t), 49.48 (t), 36.24 (d), 36.21 (d), 29.32

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(q), 28.21 (q), 24.65 (q), 23.95 (q); MS (+EI, 15 eV), m/z (relative intensity) 319 (2), 201 (16), 174 (14), 162 (9), 146 (6), 145 (6), 118 (16), 106 (10), 105 (100), 104 (6), 77 (5), 42 (8). Anal. Calcd for $C_{22}H_{28}Cl_2N_2$: C, 67.5; H, 7.2; N, 7.2. Found: C, 67.6; H, 7.4; N, 7.4.

Minor Diastereomers. The solvent was evaporated from the combined supernatant liquor, and the residue was crystallized from petrol at −78 °C. Recrystallization from petrol gave one of the minor isomers [11 (X = Cl), "*dl*-I"] as white needles (248 mg, 10%): mp 52.4–53.9 °C; $[\alpha]^{25}_D$ +73.4° (*c* 1.5, benzene); IR ν_{max} ($CHCl_3$) 3010, 2964, 2930, 1602, 1494, 1452, 1377, 701 cm^{-1}; ^1H NMR (400 MHz) δ 7.27–7.12 (m, 10 H), 3.11–3.03 (m, 2 H), 2.59 (dd, 2 H, J = 14.6, 7.2 Hz), 2.24 (dd, 2 H, J = 14.6, 5.4 Hz), 1.53 (s, 6 H), 1.29 (d, 6 H, J = 7.1 Hz); ^{13}C NMR (22.5 MHz) δ 147.0 (s), 128.4 (d), 127.1 (d), 126.1 (d), 95.6 (s), 50.5 (t), 36.4 (d), 28.9 (q), 24.6 (q); MS (+EI, 12 eV) m/z (relative intensity) 355 (1), 279 (11), 201 (32), 184 (14), 182 (42), 174 (22), 163 (12), 162 (78), 147 (35), 146 (20), 106 (17), 105 (100), 104 (17). Anal. Calcd for $C_{22}H_{28}Cl_2N_2$: C, 67.5; H, 7.2; N, 7.2. Found: C, 67.6; H, 7.6; N, 7.4.

Crystallization from petrol at −78 °C of the mother liquor from the separation of the first minor diastereomer ("*dl*-I") followed by recrystallization at −15 °C afforded a second minor isomer 11 [(X = Cl), "*dl*-II"] as cubic crystals (206 mg, 8%): mp 49.5–50.8 °C; $[\alpha]^{25}_D$ +27.8° (*c* 1.1, benzene); IR ν_{max} (KBr) 3026, 2965, 2927, 1602, 1493, 1454, 1377, 764, 703, 639 cm^{-1}; ^1H NMR (400 MHz) δ 7.32–7.18 (m, 10 H), 3.22–3.14 (m, 2 H), 2.54 (dd, 2 H, J = 14.6, 6.7 Hz), 2.36 (dd, 2 H, J = 14.6, 5.6 Hz), 1.51 (s, 6 H), 1.27 (d, 6 H, J = 7.1 Hz); ^{13}C NMR (22.5 MHz) δ 147.4 (s), 128.6 (d), 127.0 (d), 126.2 (d), 96.1 (s), 49.9 (t), 36.5 (d), 28.6 (q), 24.2 (q); MS (+EI, 15 eV), m/z (relative intensity) 355 (1), 201 (6), 175 (4), 174 (4), 145 (8), 118 (8), 106 (21), 105 (100). Anal. Calcd for $C_{22}H_{28}Cl_2N_2$: C, 67.5; H, 7.2; N, 7.2. Found: C, 67.8; H, 7.6; N, 7.3.

(2*S*,2′*R*,4*S*,4′*S*)-(+)-2,2′-Dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile (11, X = CN). Treatment of 11 (X = Cl) (391 mg, 1.0 mmol) under the conditions of method B gave a pale yellow oil (371 mg, 99%). Crystallization from methanol–pentane (−15°) followed by a further two recrystallizations afforded 11 (X = CN) as white needles (202 mg, 54%): mp 86.4–87.2 °C dec; $[\alpha]^{25}_D$ +43.6° (*c* 1.0, benzene); IR ν_{max} (KBr) 3026, 2964, 2925, 2897, 2239, 1602, 1495, 1447, 1256, 766, 702, 530 cm^{-1}; ^1H NMR (400 MHz), 7.33–7.14 (m, 10 H), 3.08–3.00 (m, 1 H), 3.00–2.92 (m, 1 H), 2.83 (dd, 1 H, J = 14.5, 9.3 Hz), 2.24 (dd, 1 H, J = 14.5, 5.0 Hz), 2.21 (dd, 1 H, J = 14.3, 7.8 Hz), 2.07 (dd, 1 H, J = 14.3, 6.1 Hz), 1.62 (s, 3 H), 1.32 (d, 3 H, J = 7.1 Hz), 1.23 (d, 3 H, J = 7.1 Hz), 0.99 (s, 3 H); ^{13}C NMR (100 MHz) δ 145.76 (s), 144.75 (s), 128.79 (d), 128.76 (d), 127.38 (d), 127.01 (d), 126.78 (d), 126.67 (d), 118.24 (s), 117.91 (s), 72.34 (s), 72.16 (s), 45.63 (t), 45.28 (t), 36.98 (d), 36.61 (d), 25.61 (q), 24.41 (q), 23.66 (q), 23.59 (q); MS (+EI, 15 eV), m/z (relative intensity) 344 (4), 302 (5), 239 (6), 226 (16), 211 (6), 173 (15), 172 (5), 171 (8), 119 (8), 106 (21), 105 (100), 104 (9). Anal. Calcd for $C_{24}H_{28}N_4$: C, 77.4; H, 7.6. Found: C, 77.4; H, 7.5.

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Supplementary Material Available: Tables of bond lengths, bond angles, hydrogen atom coordinates, and anisotropic thermal parameters for **2a** **3a**, and **4a** (3 pages). Ordering information is given on any current masthead page.

Notes

A Simple Preparation of Chiral Acetylenic Ethers

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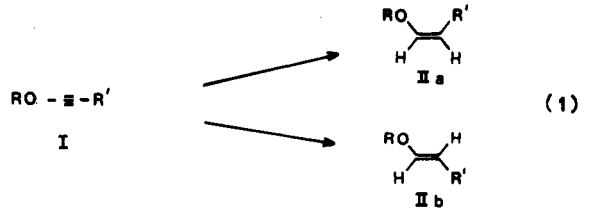
In the course of our work on the asymmetric enol ether–ketene cycloaddition reaction,[1] a number of optically active cis and trans *O*-alkyl enol ethers were required. While acetylenic ethers I appeared to be potentially excellent precursors of enol ethers IIa,b (eq 1), a search of



(1)

the literature revealed no *facile, general* approaches to this well-studied class of compounds[2] and virtually no reports on the preparation of chiral (nonracemic) derivatives.[3] In this paper a general, highly efficient, typically one-pot procedure for the preparation of a variety of optically active acetylenic ethers is reported.

Most alcohols on successive treatment in tetrahydrofuran with potassium hydride, trichloroethylene, *n*-butyllithium, and a primary iodide or water are converted in high yield to the acetylenic ether (eq 2),[4] which can be purified by simple filtration over silica gel and/or distillation. Examples of this method are given in Table I.

$$ROH \xrightarrow[\underline{n}\text{-}C_4H_9Li;\ R'I \text{ or } H_2O]{KH;\ Cl_2C=CHCl;} RO-\equiv-R'\ (H) \qquad (2)$$

The potassium alkoxide generates and attacks the dichloroacetylene;[2,5] the resulting adduct on treatment with

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(4) While no extensive optimization studies have been carried out, 2 equiv of potassium hydride, 1 equiv of trichloroethylene, 2–3 equiv of butyllithium, and 2.5–5 equiv of the iodide have been found to produce satisfactory results.

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