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SYNTHESIS OF CYCLOPENTANO[*c*]-*s*-TRIAZOLES BY THE INTRAMOLECULAR RING TRANSFORMATION OF 1,3,4-OXADIAZOLES

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Abstract—Cyclopentano[*c*]-*s*-triazoles were synthesized by intramolecular ring transformation starting from y-keto-1,3,4-oxadiaxoles 5 and 9. The required functionality for this intramolecular reaction was established by (i) the reaction of lithiated 2-methyl-1,3,4-oxadiazole 4 with the methyl enol ether of a-bromo ketones followed by hydrolysis; (ii) reductive amination of y-ketones **5** and 9 to further reorganized hydraxide 7 and γ-amino-1,3,4-oxadiazole 9 with $NaBH_3CN$; and (iii) pyrolysis of 7 and 9 at 280" (5 mmHg) to the cyclopentano[*c*]-*s*-triazoles 8 and **11**. By the same treatment, the S-connected analogue 2 afforded the desired fused s-triazole 17.

An intramolecular version of either intermolecular substitution or addition reaction has received much attention and provided quite a capable strategy for the synthesis of polycondenced molecules, often with high regio- and stereo-selectivities. Particularly highlighted is the application of the Diels–Alder reaction. On the other hand, an intramolecular ring transformation has been sparsely applied except for the transformation of a furan ring to a pyrrole ring,' although it could potentially provide an attractive route to a variety of bridgehead nitrogen heterocycles. From this viewpoint, we have previously demonstrated the synthesis of *s*-triazolo[3,4-*a*][1,3,4]thiadiazines from 2-mercapto-1,3,4-oxadiazoles as exemplified in Scheme 1;[2] in the first step (a) sulfur was used as a conjunctive atom between an oxadiazole ring and a C-2-side chain, and the intramolecular replacement of the oxygen in the oxadiazole ring with the nitrogen was the key ring closure step (b).

The method thus established can be extended to the synthesis of other fused s-triazoles. In the course of our program, a similar type of the reaction of γ-keto-1,3,4-oxadiazoles in which the bridging atoms are all carbons was further investigated. This paper deals with the preparation of y-ketones and their transformation to pharmacologically interesting' 6,7-dihydro-5*H*-pyrrolo[2,1-*c*]-*s*-triazoles and 4a,5,6,7,8,8a-hexahydro-9*H*-*s*-triazolo-[4,3-*a*]indoles by the cyclodehydration of the corresponding γ-amines based on our intramolecular ring transformation strategy.[2,4,5]

RESULTS AND DISCUSSION

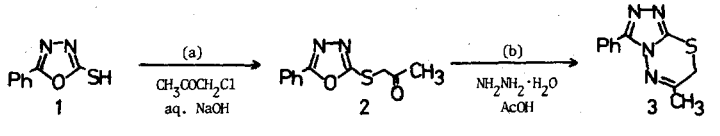
Preparation of γ-keto-1,3,4-*oxadiazoles* 5a-d *and* 9a–d

The preparation of γ-keto-oxadiazoles was envisaged via the coupling reaction of metalated 2-methyloxadiazole 4 with masked a-halo ketones i.e. 2-methoxyallyl bromide **(12)**[6] and 3-bromo-2-m[ethoxycyclohexene **(13)**[7].

For this purpose, 2-methyl-5-phenyl-1,3,4-oxadiazole **(4a)**[8] was lithiated with n-BuLi at -78" according to the procedure reported by Meyers' and then treated with 12. However, to our disappointment, this reaction did not give the desired y-ketone **5a** but instead an intractable mixture of products after acidic work-up. The use of HMPA as a co-solvent could solve the problem; the above reaction carried out with n-BuLi in THF/HMPA [8/1 (v/v)] gave 38% yield of **5a** after purification by chromatography and subsequent recrystallization. Likewise, cyclohexanonylation of **4a–9a** was successfully achieved on treatment of the lithiated 4a with 13 in the same mixed solvents. The other y-ketones with a p-substituent were obtained in a similar manner. The yields and physical properties of 5a-d and 9a-d are summarized in Tables 1 and 2. The acetonylation of 2,5-dimethyl-1,3,4-oxadiazole **(4e)**[10] was also attempted under the same conditions as before but the corresponding y-ketone was not obtained. Although no effort was made to identify the products, we presume that ring cleavage of the lithiated oxadiazole occurred as suggested by Micetich."

Transformation of γ-keto-1,3,4-*oxadiazoles to fused s-triazoles*

First the transformation of the obtained y-ketones to cyclopentano[c]-s-triazoles such as dihydro-5*H*-pyrrolo-s-triazoles 8 and hexahydro-9H -*s*-triazoloindoles 11 was investigated. The requisite y-amino function was easily envisioned by a functional conversion of a y-ketone. Accordingly, 5a-d were reductively aminated with $NaBH_3CN$ in the



Scheme 1

Table 1. Physical characteristics of products

Compd. No.	Yield [%]	mp [°C] (solvent)	Molecular foamula	Elemental analysis calc (found) C %	H %	N %
5a	38	56-59 (EtOH)	$C_{12}H_{12}N_2O_2$	66.65 (66.93)	5.59 (5.74)	12.95 (12.91)
5b	27	120-123 (EtOH)	$C_{12}H_{11}N_2O_2Cl$	57.50 (57.24)	4.42 (4.57)	11.17 (11.27)
5c	46	88-90 (EtOH)	$C_{13}H_{14}N_2O_3$	63.40 (63.27)	5.73 (5.91)	11.38 (11.37)
5d	55	91-94 (EtOH)	$C_{13}H_{14}N_2O_2$	67.81 (67.88)	6.13 (5.90)	12.17 (12.34)
7a	53	243-247 ($CHCl_3$)	$C_{12}H_{15}N_3O$	66.34 (66.37)	6.96 (7.21)	19.34 (19.06)
7b	33	226-229 (EtOH)	$C_{12}H_{14}N_3OCl$	57.26 (57.33)	5.61 (5.72)	16.69 (16.51)
7c	54	247-250 (EtOH)	$C_{13}H_{17}N_3O_2$	63.14 (63.20)	6.93 (7.11)	16.99 (17.26)
7d	48	220-223 (EtOH)	$C_{13}H_{17}N_3O$	67.51 (67.50)	7.41 (7.45)	18.17 (18.14)
8a	58	153-155 (a)	$C_{12}H_{13}N_3$	72.33 (72.32)	6.58 (6.63)	21.09 (21.25)
8b	74	194-196 (a)	$C_{12}H_{12}N_3Cl$	61.67 (61.67)	5.18 (5.32)	17.98 (17.84)
8c	86	162-164 (a)	$C_{13}H_{15}N_3O$	68.10 (68.11)	6.59 (6.36)	18.33 (18.54)
8d	70	171-174 (a)	$C_{13}H_{15}N_3$	73.21 (73.25)	7.09 (7.08)	19.70 (19.67)
9a	35	90-92 (EtOH)	$C_{15}H_{16}N_2O_2$	70.29 (70.14)	6.29 (6.29)	10.92 (11.07)
9b	25	108-111 (EtOH)	$C_{15}H_{15}N_2O_2Cl$	61.97 (61.74)	5.20 (5.28)	9.63 (9.78)
9c	56	106-107 (EtOH)	$C_{16}H_{18}N_2O_3$	67.12 (66.97)	6.34 (6.51)	9.78 (9.76)
9d	53	83-85 (EtOH)	$C_{16}H_{18}N_2O_2$	71.09 (71.01)	6.71 (6.57)	10.36 (10.51)
11a	21	180-184 (a)	$C_{15}H_{17}N_3$	75.28 (75.18)	7.16 (7.25)	17.56 (17.57)
11b	36	169-173 (a)	$C_{15}H_{16}N_3Cl$	65.76 (65.64)	5.89 (5.81)	15.34 (15.54)
11c	12	175-185 (b)	$C_{16}H_{19}N_3O$	71.35 (71.56)	7.11 (6.99)	15.60 (15.51)
11d	18	168-171 (c)	$C_{16}H_{19}N_3$	75.85 (75.90)	7.56 (7.39)	16.59 (16.71)

[a] Purified on a silica gel column ($CHCl_3$/EtOH, 10/1).

[b] Purified on a silica gel column ($CHCl_3$/EtOH, 30/1).

[c] Purified on a silica gel column ($CHCl_3$/EtOH, 20/1).

presence of ammonium acetate in refluxing methanol" to give crystalline products in 33–54% yields, which had C=O and N-H absorptions at 1660-1685 and 3195–3210 cm^{-1}, respectively in the IR spectra. The N-H signals were also indicated around δ 8.8 and 9.6 by the 'H-NMR spectra as summarized in Table 2. Based on these spectral data and elemental analyses, the structures of these products were determined to be 2-(1-pyrrolin-2-yl)benzhydrazides 7 rather than the straightforward product, y-amino-1,3,4-oxadiazoles 6. From the mechanistic point of view, cyclodehydration of γ-amines 6 to

Table 2. Spectral data of the products

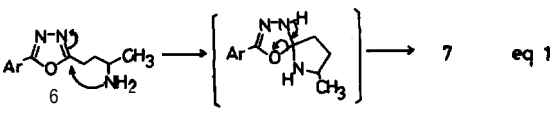
Compd. No.	IR (KBr) data [cm^{-1}]	^{1}H-NMR data[a] [δ ppm]
5a	3050, 2935, 1700 1608, 1580, 1480 1435	2.25 (s, 3H, CH_3) 3.05-3.25 (m, 4H, CH_2×2) 7.35-8.20 (m, 5H, Ar)
5b	3070, 2940, 1710 1608, 1580, 1568 1485	2.26 (s, 3H, CH_3) 3.05-3.25 (m, 4H, CH_2×2) 7.45 and 7.95 (ABq, J = 9.0 Hz, 4H, Ar)
5c	3050, 2930, 2840 1720, 1610, 1590 1570, 1500	2.23 (s, 3H, CH_3) 3.00-3.25 (m, 4H, CH_2×2) 3.84 (s, 3H, OCH_3) 6.95 and 7.92 (ABq, J = 9.0 Hz. 4H, Ar)
5d	3040, 2940, 2920 1710, 1610, 1585 1555, 1500, 1410	2.25 (s, 3H, CH_3) 2.42 (s, 3H, $CH_3C_6H_4$) 3.00-3.25 (m, 4H, CH_2×2) 7.28 and 7.92 (ABq, J = 9.0 Hz, 4H, Ar)
7a	3200, 3100, 2960 2930, 1685, 1620 1570, 1495	1.46 (d, J = 6.8 Hz, 3H, CH_3) 1.90-2.95 (m, 2H, CH_2) 3.27 (t, J = 8.3 Hz, 2H, CH_2) 4.15-4.70 (m, 1H, CH) 7.30-8.15 (m, 5H, Ar) 8.80 (br s, 1H, NH) 9.25 (br s, 1H, NH)
7b	3210, 2975, 2920 2875, 1670, 1620 1565, 1490	1.46 (d, J = 6.8 Hz, 3H, CH_3) 1.90-2.90 (m, 2H, CH_2) 3.26 (t, J = 8.3 Hz, 2H, CH_2) 4.15-4.70 (m, 1H, CH) 7.55 and 7.92 (ABq, J = 9.0 Hz, 4H, Ar) 8.80 (br s, 1H, NH) 9.60 (br s, 1H, NH)
7c	3200, 2960, 2825 1660, 1610, 1565 1500	1.43 (d, J = 6.8 Hz, 3H, CH_3) 1.80-2.90 (m, 2H, CH_2) 3.23 (t, J = 8.3 Hz, 2H, CH_2) 4.01 (s, 3H, OCH_3) 4.15-4.70 (m, 1H, CH) 7.15 and 7.97 (ABq, J = 9.0 Hz, 4H, Ar) 8.80 (br s, 1H, NH) 9.55 (br s, 1H, NH)
7d	3195, 2960, 2920 2860, 1660, 1610 1560, 1500	1.45 (d, J = 6.8 Hz, 3H, CH_3) 1.80-2.90 (m, 2H, CH_2) 2.48 (s, 3H, $CH_3C_6H_4$) 3.23 (t, J = 8.3 Hz, 2H, CH_3) 4.15-4.70 (m, 1H, CH) 7.40 and 7.84 (ABq, J = 9.0 Hz, 4H, Ar) 8.82 (br s, 1H, NH) 9.62 (br s, 1H, NH)
8a	3050, 2560, 1600 1545, 1465, 1440 1420	1.31 (d. J = 6.8 Hz, 3H. CH_3) 2.25-2.65 (m, 2H, CH_2) 2.78-3.15 (m, 2H, CH_2) 4.50-5.10 (m, 1H, CH) 7.32-8.00 (m, 5H, Ar)
8b	3050, 2970. 1600 1540, 1515, 1460 1440	1.33 (d, J = 6.8 Hz, 3H, CH_3) 2.25-2.70 (m, 2H, CH_2) 2.80-3.20 (m, 2H, CH_2) 4.50-5.10 (m, 1H, CH) 7.55 and 7.91 (ABq, J = 9.0 Hz, 4H, Ar)

Table 2. (*Contd*)

Compd. NO.	IR (KBr) data [cm^{-1}]	^{1}H-NMR data[a] [δ ppm]
8c	3060, 2995, 2960 2830, 1610, 1575 1530, 1485, 1440	1.30 (d, J = 6.8 Hz, 3H, CH_3) 2.10-3.30 (m, 4H, CH_2×2) 3.85 (s, 3H, OCH_3) 4.50-4.90 (m, 1H, CH) 6.97 and 7.72 (ABq, J = 9.0 Hz, 4H, Ar)
8d	3030, 2980, 2940 2880, 1610, 1540 1530, 1465, 1445	1.28 (d, J = 6.8 Hz, 3H, CH_3) 2.10-3.30 (m, 4H, CH_2×2) 2.38 (s, 3H, $CH_3C_6H_4$) 4.40-5.00 (m, 1H, CH) 7.25 and 7.67 (ABq, J = 9.0 Hz, 4H, Ar)
9a	3100, 2925, 2850 1715, 1610, 1570 1550, 1482, 1450	1.30-3.65 (m, 11H) 7.35-8.20 (m, 5H, Ar)
9b	3090, 2940, 2860 1715, 1610, 1585 1570, 1490, 1410	1.40-3.65 (m, 11H) 7.45 and 7.95 (ABq, J = 9.0 Hz, 4H, Ar)
9c	3040, 2940, 2850 1715, 1610, 1590 1560, 1500	1.20-3.65 (m, 11H) 3.88 (s, 3H, OCH_3) 6.98 and 7.95 (ABq, J = 9.0 Hz, 4H, Ar)
9d	3050, 2925, 2850 1710, 1615, 1590 1570, 1500	1.20-3.70 (m, 11H) 2.41 (s, 3H, $CH_3C_6H_4$) 7.28 and 7.92 (ABq, J = 9.0 Hz, 4H, Ar)
11a	2925, 2845, 1630 1535, 1470, 1450 1420	1.00-3.50 (m, 11H) 3.50-4.10 (m, C-4a H, trans) 4.30-4.70 (m, C-4a H, cis) 7.35-8.00 (m, 5H, Ar)
11b	2930, 2850, 1600 1535, 1515, 1450 1435	1.00-3.50 (m, 11H) 3.50-4.10 (m, C-4a H, trans) 4.20-4.70 (m, C-4a H, cis) 7.32-8.00 (m, 4H, Ar)
11c	3050, 2925, 2850 1610, 1525, 1480 1440	1.00-3.30 (m, 11H) 3.50-4.00 (m, C-4a H, trans) 3.84 (s, 3H, OCH_3) 4.20-4.60 (m, C-4a H, cis) 6.85-7.90 (m, 4H, Ar)
11d	2925, 2850, 1615 1560, 1535, 1460 1450, 1435	0.80-3.47 (m, 11H) 2.38 (s, 3H, $CH_3C_6H_4$) 3.47-4.00 (m, C-4a H, trans) 4.13-5.00 (m, C-4a H, cis) 7.00-8.00 (m, 4H, Ar)

[a] 5a-d, 8a-d, 9a-d, and 11a-d; $CDCl_3$. 7a-d; CF_3COOH.

fused *s*-triazoles **8** should involve two processes; (1) addition-elimination reaction of 6 to the intermediate pyrrolinylhydrazides 7 via collapse of the spiro derivatives (eqn 1), and (2) their ring closure to 8. Isolation of 7 in the reductive amination of 5 suggests that the intramolecular nucleophilic attack by the γ-amino function was allowed under the conditions employed. Then the cyclodehydration of 7 to 8 was studied. Among several dehydrative conditions including treatment with phosphorus oxychloride or phosphorus pentoxide, pyrolysis was found to be effective; hydrazides 7a-d underwent smooth cyclodehydration on heating at 280° under reduced pressure (5 mmHg)



eq 1

to provide dihydro-5*H*-pyrrolo-*s*-triazoles **8a–d** in 58–86% yields. This ring closure was verified by disappearance of a carbonyl absorption in the IR spectra and an N-H signal in the 'H-NMR spectra. The detailed physical properties of 8a-d are summarized in Tables 1 and 2.

In contrast to the reductive amination of 5, the reaction of **9a–d** with $NaBH_3CN$ in the presence of ammonium acetate afforded the corresponding γ-amino-1,3,4-oxadiazoles **10a–d**, whose structures were supported by D_2O-exchangeable NH_2 signals around δ 1.7 in the 'H-NMR spectra and by no carbonyl absorptions in the IR spectra. Without further purification, the γ-amines 10 obtained were heated at 280" under reduced pressure (5 mmHg) to cause cyclodehydration, giving the desired tricyclic hexahydro-9*H*-*s*-triazoloindoles **11a-d** in 12–36% yields as shown in Table 1. The 'H-NMR spectra exhibited two C-4a proton signals due to the cis and trans isomers around δ 3.8 and 4.5, respectively (Table 2). The ^{13}C-NMR spectra revealed, as expected, two pairs of doublets assignable to C-4a and C-8a carbons of each isomer around δ 63.7 and 53.0 (trans) and around δ 57.3 and 42.3 (cis) (Table 3). The intensity of these signals showed all **11a–d** to be 1: 1 mixtures of the cis and trans isomers, although the separation of these two isomers was not performed by column chromatography.

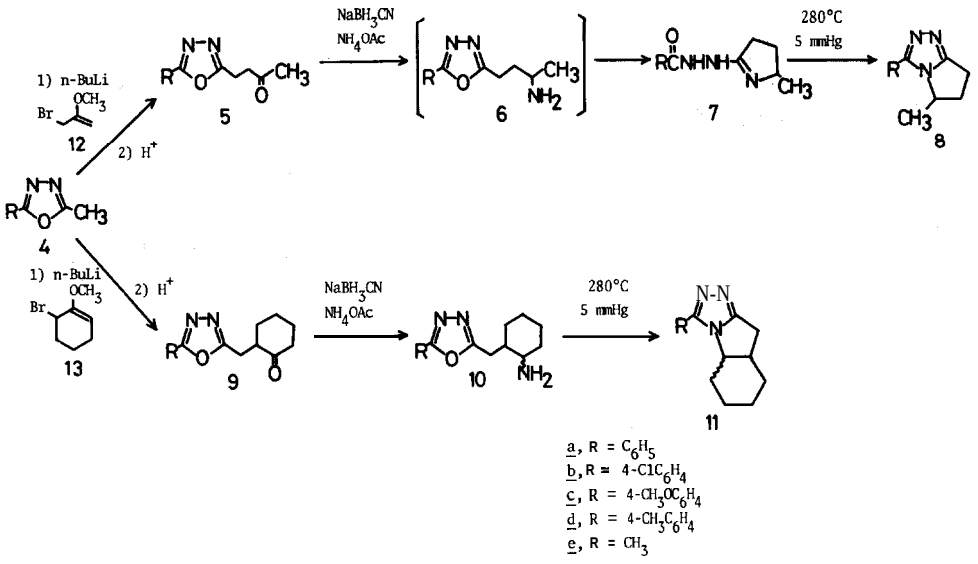
In our previous work concerning the S-connected oxadiazole system,' this successful methodology was not examined since the corresponding y-amine 15 was not available by the reduction of the oxime 14 with lithium aluminum hydride. Now it is interesting for us to know the reactivity of 2 for comparison. Fortunately, reductive amination using $NaBH_3CN$ (vide supra) was found to be effective also for the conversion of 2. The reduced product was 2-thiazolinylbenzhydrazide 16 as proved by a strong carbonyl absorption at 1600 cm^{-1} in the IR spectra and by a methyl doublet (J = 6.8 Hz) at δ 1.53 and N-H signal at δ 8.75 in the 'H-NMR spectrum. The hydrazide 16 thus obtained likewise underwent cyclodehydration to dihydrothiazolo-s-triazole 17 in 51% yield on similar pyrolysis to that employed for 7-g. These results show that in both S- and C-connected oxadiazoles (e.g. 5 and 9), intramolecular ring transformation is performed by a sequence of the following reactions;" (1) connection of an oxadiazole ring with side chain having y-keto functionality; (2) reductive amination of y-ketone; and (3) dehydrative recyclization to a fused s-triazole.

EXPERIMENTAL

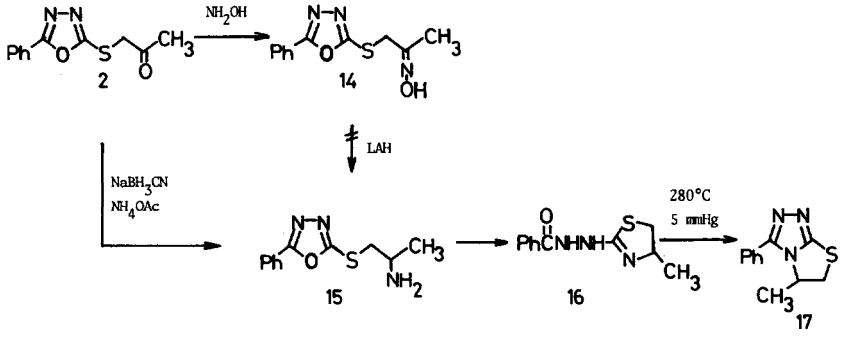
M.ps were measured with a Yanagimoto micromelting point apparatus and are uncorrected IR spectra were obtained on a JASCO-IRA-1 spectrometer. 'H-NMR and ^{13}C-NMR spectra were recorded on a JEOL C-60-HL spectrometer and JEOL FX 60 FT NMR spectrometer at 15.04 MHz, respectively. Chemical shifts are reported in ppm (δ) relative to Me_4Si as an internal standard. Microanalyses were Performed with a Perkin-Elmer 240B elemental analyzer. Pyrolysis was carried out with a Sibata Glass Tube Oven GTO-250.

Table 3. ^{13}C-NMR data of the lla-d

Compd. NO.	δ ppm ($CDCl_3$)
11a	20.6(t), 22.1(t), 24.4(t), 24.7(t), 25.4(t) 26.6(t), 27.6(t), 28.8(t), 29.0(t), 30.1(t) 42.3(d, C-8a, cis), 53.0(d, C-8a, trans) 57.3(d, C-4a, cis), 63.7(d, C-4a, trans) 126.2-130.0(complicated aromatic carbon-signals)
11b	20.5(t), 22.1(t), 24.4(t), 24.7(t), 25.4(t) 26.6(t), 27.6(t), 28.9(t), 30.1(t) 42.3(d, C-8a, cis), 53.0(d, C-8a, trans) 57.4(d, C-4a, cis), 63.8(d, C-4a, trans). 126.0-135.8(complicated aromatic carbon signals)
11c	20.7(t), 22.2(t), 24.5(t), 24.7(t), 25.5(t) 26.6(t), 27.7(t), 28.9(t), 29.1(t), 30.2(t) 42.3(d, C-8a, cis), 53.0(d, C-8a, trans) 55.3 (q, $O\underline{C}H_3$), 57.1(d, C-4a, cis) 63.6(d, C-4a, trans) 114.0-129.8(complicated aromatic carbon signals)
11d	20.6(t), 21.4(q, $\underline{C}H_3C_6H_4$), 22.1(t), 24.4(t) 24.7(t), 25.4(t), 26.6(t), 27.7(t), 28.8(t) 29.0(t), 30.1(t) 42.3(d, C-8a, cis). 53.0(d, C-8a, trans) 57.2(d, C-4a, cis). 63.6(d, C-4a, trans) 124.7-139.7(complicated aromatic carbon signals)



Scheme 2.



Scheme 3.

Preparation of γ-keto-1,3,4-oxadiazoles **5a–d** *and* **9a–d**

To a soln of **4a**[8] (1.4 g, 9 mmol) in dry THF-HMPA (8/1) (40ml) was added dropwise a soln of n-BuLi in hexane (1.6 M, 6.7 ml, 10.8 mmol) over 15 min at -78" under the current of N_2. After the resulting deep orange-red soln had been stirred at -78" for additional 30 min, **12**[6] (1.76 ml, 13.5 mmol) was added. The resulting mixture was slowly warmed to room temp and diluted with 70 ml of phosphate buffer (pH 7), and the aqueous soln was extracted with $CHCl_3$ (3 x 50 ml). To the combined $CHCl_3$ soln was added 1 N aq HCl (100 ml) and the mixture was stirred at room temp for 30min. The organic layer was separated, washed with water (2 x 200 ml). and dried over $MgSO_4$. Removal of the solvent yielded 'an orange oil, which was chromatographed on a silica gel column [AcOEt/n-hexane (2/1)] to give yellow crystals of **5a**. A pure sample was obtained by recrystallization from ethanol. Other γ-ketones **5b–d** were similarly prepared from the lithiated **4b–d**[14] and 12. Cyclohexanonylation of 4-9 was accomplished using **13**[7] in the same manner as above. The ratio of the employed reaction solvents (THF/HMPA) was 8/1 for Se, **9a** and **9c**, 1 l/l for **5b** and **9b**, and 18/1 for **5d** and **9d**. The eluent for chromatography was AcOEt/n-hexane (2/1) for **5b** and **5d**, Et_2O/n-hexane (3/1) for **9a**, Et_2O/n-hexane (2/1) for **9d**, and Et_2O/n-hexane (l/l) for **9b** and **9c**. Compound **5c** was purified by direct recrystallization from ethanol without chromatography. The yields and physical properties of **5a–d** and 9a-d are summarized in Tables 1 and 2.

2-(5-Methyl-1-pyrrolin-2-yl)benzhydrazides 7a-d

A soln of **5a–d** (3 mmol), $NaBH_3CN$ (1.3 g, 21 mmol), and ammonium acetate (2.3 g, 30 mmol) in dry methanol (30 ml) was heated under reflux for 4 h. The resulting mixture was acidified (pH 2) with conc aq HCl and then basified (pH 9) with 20% aq NaOH. After extraction with $CHCl_3$ (3 x 30 ml), the combined organic layer was dried over $MgSO_4$. Removal of the solvent gave crude **7a–d**, which were purified by recrystallization from the solvents listed in Table 1. The yields and physical properties of **7a–d** are summarized in Tables 1 and 2.

3-Aryl-5-methyl-6,7-dihydro-5H-pyrrolo[2,1-c]-s-triazoles **8a–d**

Pyrrolinylbenzhydrazides 7a-d (200 mg) were separately heated at 280" under 5 mmHg for 20 min in a glass tube oven with a trap bulb heated at 200". The brown oil trapped in a bulb immediately solidified on cooling. Purification on a silica gel column [$CHCl_3$/EtOH (10/1)] gave **8a–d**. The yields and physical properties of **8a–d** are summarized in Tables 1 and 2.

3-Aryl-4a,5,6,7,8,8a-hexahydro-9H-s-triazolo[4, 3-a]indoles **11a–d**

These compounds were obtained from **9a–d** by the same reduction and pyrolysis as descrived for **5–8**. The intermediate γ-amines **10a–d** were not purified for pyrolysis. The yields and physical properties of **11a–d** are summarized in Tables 1 and 2.

2-(4-Methyl-2-thiazolin-2-yl)benzhydrazide (**16**)

A soln of **2**[2] (940 mg, 4 mmol), $NaBH_3CN$ (1.7 g, 28 mmol), and ammonium acetate (3.0 g, 40 mmol) in dry methanol (40 ml) was heated under reflux for 4 h. The resulting mixture was acidified (pH 2) with conc aq HCl and then basified (pH 9) with 20% aq NaOH. After extraction with $CHCl_3$ (3 × 30 ml), the combined organic layer was dried over $MgSO_4$. Removal of the solvent gave a viscous oil, which was washed with ethanol (4 ml) to give 480 mg (51%) of **16** as colorless crystals. An analytical sample was obtained by recrystallization from ethanol: m.p. 198–200°; IR (KBr) 3180, 3000, 2850, 1600, 1565, 1485, 1440 cm^{-1}; ^{1}H-NMR (CF_3COOH) δ 1.53 (d, J = 6.8 Hz, 3H, CH_3), 3.10–4.20 (m, 2H, CH_2), 4.50–5.00 (m, 1H, CH), 7.50–8.10 (m, 5H, Ph), 8.75 (br s, 2H, NHNH). (Found: C, 56.21; H, 5.61; N, 17.76. Calc for $C_{11}H_{13}N_3OS$: C, 56.15; H, 5.57; N, 17.86%).

3-Phenyl-5-methyl-5,6-dihydrothiazolo[2,3-c]-s-triazole (**17**)

Thiazolinylbenzhydrazide **16** (170 mg, 7.2 mmol) was heated at 280° under 5 mmHg for 20 min in a glass tube oven with a trap bulb heated at 200°. After cooling to room temperature, the trapped product was washed with ether to give 80 mg (51%) of **17**. An analytical sample was obtained by recrystallization from AcOEt–n-hexane: m.p. 152–154°; IR (KBr) 3100, 2980, 1600, 1460 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.35 (d, J = 6.8 Hz, 3H, CH_3), 3.53 (d of d, J = 11.0, 2.5 Hz, 1H), 4.37 (d of d, J = 11.0, 7.5 Hz, 1H), 4.95 (d of quintet, J = 7.5, 2.5 Hz, 1H), 7.35–7.90 (m, 5H, Ph). (Found: C, 60.92; H, 5.11; N, 19.21. Calc for $C_{11}H_{11}N_3S$: C, 60.80; H, 5.10; N, 19.34%.)

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[13]In contrast to these successful conversions, the related ring closure of γ-ketones **5** and **9** with hydrazine (see Scheme 1) was not effected in refluxing acetic acid, but we presently have no convincing rationale for this discrepancy.

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