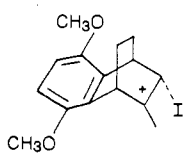
Table II. Anti/Syn Ratios (% Conversions) for 40-h Epoxidations

olefin	peracid	CH_2Cl_2	ether
1	p-MPBA	0.66 (100)	2.3 (80)
	PBA	0.20 (100)	1.4 (100)
	p-NPBA	0.11 (100)	1.1 (100)
2	p-MPBA	0.78 (54)	2.9 (26)
	PBA	0.61 (77)	2.4 (23)[a]
	p-NPBA	0.55 (88)	1.1 (64)
10	p-MPBA		1.8 (70)
	p-NPBA	0.72 (100)	
11	p-MPBA	1.3 (57)	3.1 (38)
	PBA	0.88 (80)	2.6 (20)[a]
	p-NPBA	0.78 (100)	2.4 (56)

[a] Due to the peculiarly unique decomposition of PBA in ether these percents reflect only that the decomposition of the PBA is fast compared to the rate of epoxidation. For additional information on this decomposition, see: Tokumaru, K.; Osamaru, O. Bull. Chem. Soc. Jpn. 1962, 35, 1955.

Reasonably, these products are best accounted for by the intermediacy of carbocations 14 and 15 or possibly the



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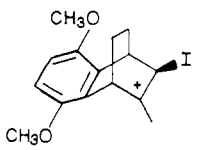

15

corresponding iodonium ions. Proton elimination from one or both of these would form 5, while attack by solvent would give 6 and 7, respectively. Rearrangement by migration of the ethano bridge in 14 followed by solvent attack accounts for the major product 8. No evidence of aryl migration or participation was found among the products. The olefinic methyl group stabilizes conventional carbocation formation from 1 removing the need for significant homoconjugative stabilization in the hypoiodite reaction; a result in marked contrast to those previously obtained with 2.[3c]

The results from the epoxidation of 1 and 2 with perbenzoic acid (PBA) and its p-methoxy (p-MPBA) and p-nitro (p-NPBA) analogues are given in Table II. Compounds 10 and 11 are the 5,8-diacetoxy analogues of 1 and 2 with and without the olefin methyl group, respectively.

It has been known for some years that the order of epoxidation reactivity toward a given olefin is p-MPBA < PBA < p-NPBA.[11] The results in Table II are consistent with this order both with regard to the qualitative rates of conversion and the anti/syn ratio of epoxides. As previously observed,[3a] the weaker the electrophilic character of the epoxidizing agent, the greater is the amount of the anti epoxide in the product. The strength of the peracids as electrophiles may be controlled by substituents on the aryl ring or by the degree in which the solvent hydrogen bonds to the peracid proton. The methyl group on the double bond enhances bond reactivity while reducing the amount of anti attack by the reagent.

Acknowledgment. Grateful acknowledgement is hereby extended to the Robert A. Welch Foundation for their support of this work.

Supplementary Material Available: Table I containing the NMR parameters for 1, 5, 6, 7, and 8 and the NMR parameters for other new molecules (3 pages). Ordering information is given on any current masthead page.

(11) Lynch, B. M.; Pausacker, K. H. J. Chem. Soc. 1955, 1525.

Electrophilic Substitution at Azomethine Carbon Atoms. Reaction of Aromatic Aldehyde Hydrazones with Trifluoroacetic Anhydride

Yasuhiro Kamitori, Masaru Hojo,* Ryōichi Masuda, Toshihiko Fujitani, Seiji Ohara, and Tetsuya Yokoyama

Department of Industrial Chemistry, Faculty of Engineering, Kobe University, Kobe 657, Japan

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Reaction of dimethylhydrazones of aromatic aldehydes with trifluoroacetic anhydride at room temperature affords high yields of products bearing trifluoroacetyl groups. These electrophilic substitution reactions generally occur on the azomethine carbon, although competitive N-acylation is observed in highly electron-rich systems. Use of diisopropylhydrazones suppressed this N-acylation completely, leading to high yields of C-acylated products. The trifluoroacetyl hydrazones can be cyclized thermally to imidazole and oxadiazine derivatives and can be converted into 1-trifluoromethyl 1,2-diketones by acid hydrolysis.

Introduction

In our investigation of electrophilic substitution at olefinic carbon atoms we became interested in the reaction of the analogous azomethine carbon atoms of aldehyde hydrazones. The structure of hydrazone 1 is similar to those of vinyl ethers, vinyl sulfides, N-vinylcarboxamides, and N-vinylsulfonamides (2), in which release of the n-electrons to the olefinic β carbon is a key factor in electrophilic substitution at the olefinic carbon atoms.[1-5] In the hydrazone system 1 the N=C double bond is analogous to the C=C double bond of 2, and the conjugation shown in eq 1 should favor electrophilic substitution at the azomethine carbon. Hydrazone is a nitrogen analogue of enamines, and some hydrazones are known to behave as 1,3-dipolar compounds[6] in which the azomethine carbon

(1) Hojo, M.; Masuda, R. J. Org. Chem. 1975, 40, 963.

(2) Hojo, M.; Masuda, R.; Kamitori, Y. Tetrahedron Lett. 1976, 1009.
(3) Hojo, M.; Masuda, R.; Kokuryo, Y.; Shioda, H.; Matsuo, S. Chem. Lett. 1976, 499.
(4) Hojo, M.; Masuda, R.; Takagi, S. Synthesis 1978, 285.
(5) Hojo, M.; Masuda, R.; Sano, H.; Saegusa, M. Synthesis 1986, 137.

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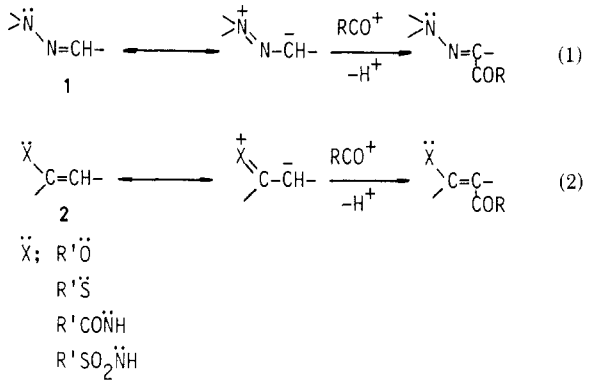
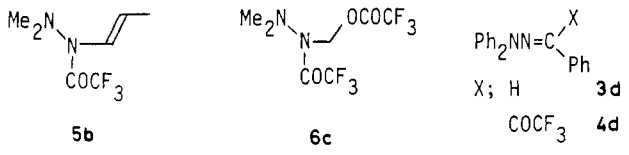


is a center of nucleophilic attack. However, there are few reports of simple electrophilic substitution at the azomethine carbon;[7] none involving acylation of this carbon. We here report on the electrophilic acylation of aldehyde hydrazones.

Trifluoroacetic anhydride (TFAA) was chosen as the acylating reagent because it had provided successful results in our previously reported studies on electrophilic substitution reactions of **2**.[1-3] We chose to study *N,N*-dialkylhydrazines in order to avoid acylation at the terminal nitrogen of **1**,[8] which would impede a second acylation at the azomethine carbon.

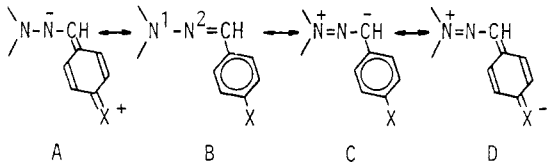
Results and Discussion

Reaction of Aldehyde Hydrazones with Trifluoroacetic Anhydride. Initial experiments on the treatment of benzaldehyde dimethylhydrazone (**3a**) with 2 equiv of TFAA at 20 °C indicated that added base was not essential for C-acylation but that 2,6-lutidine was an effective promoter of C-acylation, pyridine being less effective, and triethylamine having no effect (Table I, runs 1–4). In contrast, propionaldehyde hydrazone **3b** did not react at all even after 24 h in the presence of a greater excess of TFAA (run 5). The reaction of **3b** carried out under more forcing conditions (run 6) resulted in unexpected N-acylation to afford enamine **5b**; no **4b** was detected. Formaldehyde hydrazone **3c** (run 7) reacted with TFAA very rapidly to give the *C*-acyl product **4c** (74%) accompanied by the *N*-acyl alcohol trifluoroacetate **6c** (18%). In contrast to the facile reaction of **3a**, the analogous diphenylhydrazone **3d** was largely recovered under the

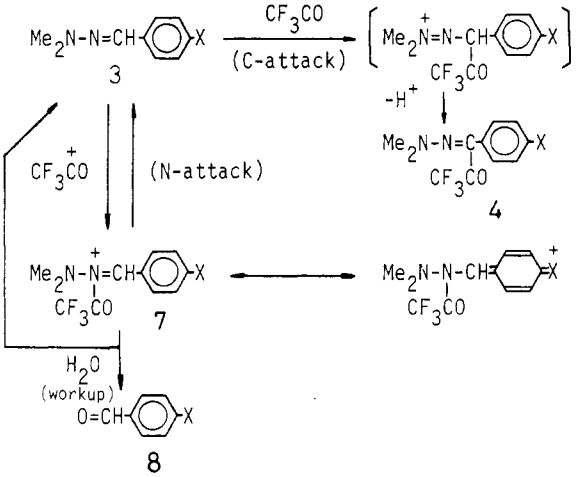


conditions that gave high yields of **4a**; under forcing conditions only 35% of the *C*-acyl product **4d** was obtained (run 8). This deactivation presumably reflects the weak electron release from the diphenylamino group compared with the dimethylamino group,[9] leading to lower π-electron

Scheme I



Scheme II



density on the azomethine carbon of **3d**. Since nonaromatic hydrazones do not appear to undergo C-acylation cleanly,[10] and phenyl groups on the hydrazone nitrogen inhibit the reaction, we chose dimethylhydrazones of aromatic aldehydes as substrates for subsequent experiments.

Trifluoroacetylation of Arene Aldehyde Hydrazones. We compared the reactivity of ring-substituted arene aldehyde dimethylhydrazones with that of the unsubstituted parent **3a** (Table II). All of these compounds except for *p*-NMe_2 derivative **3l** underwent the expected substitution reaction at the azomethine carbon to afford the corresponding trifluoroacetylated derivatives **4** in good to excellent yields. The *p*-Me derivative **3e** reacted as rapidly as **3a** to give **4e** in 84% yield. The *o*-Cl (**3f**) and *p*-Cl (**3g**) derivatives gave excellent yields with the same quantities of TFAA and 2,6-lutidine, but required 28 h for complete reaction. The nitro- and methoxy-substituted compounds were more sluggish, requiring 10 equiv of TFAA, 3 equiv of 2,6-lutidine, and 43 h for reaction. However, it is interesting that the position of the nitro group had little effect; a slightly higher yield was obtained from the *m*-NO_2 derivative. The *p*-OMe compound **3k** underwent some cleavage, in addition to C-acylation, to give *p*-anisaldehyde (26%), and the *p*-dimethylamino derivative **3l** was cleaved to *p*-(dimethylamino)benzaldehyde without undergoing C-acylation. In order to clarify the effect of substituents, the reactions of the para-substituted hydrazones listed in Table III were examined. Reactions were carried out under two conditions: (A) the condition for converting about 70% of **3a** to **4a**, and (B) that for converting about 70% of **3j** to **4j**. Under the milder condition A the apparent reaction rate is in the decreasing order **3a** (H) > **3k** (*p*-OMe) > **3e** (*p*-Me) > **3g** (*p*-Cl) ≫ **3j** (*p*-NO_2), **3l** (*p*-Me_2N), with a remarkable difference in reactivity between the two strongly electron-releasing groups *p*-OMe and *p*-NMe_2. Under the more stringent condition B, trifluoroacetylation proceeded in the order

(6) See, for instance: Snider, B. B.; Conn, R. S. E.; Sealfon, S. *J. Org. Chem.* **1979**, *44*, 218. Le Fevre, G.; Hamelin, J. *Tetrahedron Lett.* **1980**, *36*, 878.

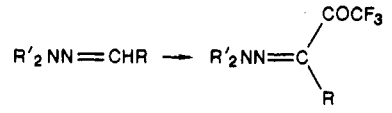
(7) Grundemann, E.; Brehme, R.; Nikolajewski, H. E. *J. Prakt. Chem.* **1982**, *324*, 575 and references cited therein.

(8) Preliminary experiments revealed that trifluoroacetylation of benzaldehyde *N*-methylhydrazone occurred exclusively at nitrogen and that electrophilic reaction of TFAA at the azomethine carbon atom was completely inhibited.

(9) A similar deactivating influence of *N*-phenyl groups was reported for the reaction of enamines with isocyanates. Perelman, M.; Mizsak, S. A. *J. Am. Chem. Soc.* **1962**, *84*, 4988.

(10) Acylation of **3b** and **3c** is now under investigation and will be described elsewhere.

Table I. Trifluoroacetylation of Hydrazones 3a–d[a]

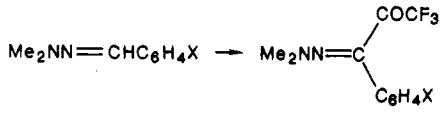


3 4

run	compd	R	R′	TFAA (equiv)	base	time	product	yield (%)
1	**3a**	Ph	Me	2.0	2,6-lutidine	3 h	**4a**	98
2				2.0	pyridine	3 h	**4a**	81
3				2.0	triethylamine	3 h	**4a**	71
4				2.0	none	3 h	**4a**	72
5	**3b**	Et	Me	3.0	2,6-lutidine	24 h	**4b**	0
6				8.0	2,6-lutidine	52 h[b]	**5b**	65
7	**3c**	H	Me	2.5	2,6-lutidine	5 min	**4c**	74
							6c	18
8	**3d**	Ph	Ph	6.0	2,6-lutidine[c]	120 h[b]	**4d**	35

[a] Reactions were carried out with 1 mmol of substrate and 2 mmol of base in 2 mL of $CHCl_3$ at 20 °C. [b] The reaction was carried out in a sealed tube at 80 °C. [c] The reaction was carried out with 6 mmol of 2,6-lutidine.

Table II. Trifluoroacetylation of Arene Aldehyde Dimethylhydrazones[a]



3 4

run	compd	X	TFAA (equiv)	2,6-lutidine (equiv)	time (h)	product	yield (%)
9	**3e**	*p*-Me	2	2	3	**4e**	84
10	**3f**	*o*-Cl	2	2	28	**4f**	96
11	**3g**	*p*-Cl	2	2	28	**4g**	87
12	**3h**	*o*-NO_2	10	3	43	**4h**	80
13	**3i**	*m*-NO_2	10	3	43	**4i**	93
14	**3j**	*p*-NO_2	10	3	43	**4j**	82
15	**3k**	*p*-OMe	10	3	43	**4k**[b]	61
16	**3l**	*p*-NMe_2	15	3	72	**4l**	0[c]
17	**3l**	*p*-NMe_2	10	5	24	**4l**	0[c,d]

[a] Reactions were carried out with 10 mmol of substrate in $CHCl_3$ at 20 °C except as noted. [b] The crude product contained *p*-anisaldehyde (26% based on ^1H NMR signal intensity). [c] The sole product was *p*-(dimethylamino)benzaldehyde. [d] The reaction was carried out with 1 mmol of **3l** in $CHCl_3$ (5 mL) in a sealed tube at 60 °C.

3e > 3j > 3k > 3l; the conversion of **3k** to **4k** was only 68%, whereas all of **3e** and 73% of **3j** were converted to **4e** and **4j**, respectively. Under both conditions A and B, **3l** did not afford any **4l**, the sole product being *p*-(dimethylamino)benzaldehyde. These results indicate that the reaction is slowed down by strongly electron-releasing groups as well as by electron-withdrawing groups.

In Scheme I are shown canonical forms (A–D) of the dimethylhydrazones of arene aldehydes. Among these, C is probably the most important and is necessary for C-acylation to occur. Scheme I suggests that the electrophile can also attack the nitrogen of the N=CH grouping, particularly when strongly electron-releasing substituents are present (A) and this attack should affect the reaction process significantly. As illustrated in Scheme II, attack of the trifluoroacetyl cation on the azomethine carbon of **3** leads to the desired C-acylated product **4**, while N-attack should afford the N-acylated cation **7**, which can hydrolyze to the substituted benzaldehyde **8**. In compounds **3a**, **3e**, **3g**, and **3j** (X = H, Me, Cl, NO_2), preferential C-attack would give **4** as the final product because the equilibrium between **3** and **7** should favor **3** and would thus not affect the reaction significantly. However, cation **7l** with X = NMe_2 must be strongly stabilized and does not revert to **3**. An intermediate situation exists with **3k** (X = OMe), where the reversion of **7** to **3** is evidently sluggish.

Support for this hypothesis was obtained by monitoring experiments with ^1H NMR spectroscopy. In the reaction of **3l** the spectrum showed complete conversion to **7l** (X = NMe_2) within 3 min after the addition of TFAA; the methine proton appeared at 8.32 ppm, and the signal for the *p*-NMe_2 protons was split into two lines at 2.57 and 3.00 ppm. These signals did not change over the following 30 min. After workup, a 10:3 mixture of **3l** and *p*-(dimethylamino)benzaldehyde was obtained. Likewise, a signal assignable to the methine proton (8.41 ppm) of **7k** (X = OMe) was observed 3.5 min after addition of TFAA to **3k**. All of the **3k** was consumed within a few minutes,

Table III. Trifluoroacetylation of Para-Substituted Benzaldehyde Dimethylhydrazones

run	compd	para-substit	condtn[a]	product	convn (%)
18	**3a**	H	A	**4a**	67
19	**3e**	Me	A	**4e**	45
20	**3e**	Me	B	**4e**	100
21	**3g**	Cl	A	**4g**	27
22	**3j**	NO_2	A		0
23	**3j**	NO_2	B	**4j**	73
24	**3k**	OMe	A	**4k**	52
25	**3k**	OMe	B	**4k**[b]	68
26	**3l**	NMe_2	A	*c*	0
27	**3l**	NMe_2	B	*d*	0

[a] Condition A: a mixture of **3** (1 mmol), TFAA (4 mmol), 2,6-lutidine (2 mmol), and $CHCl_3$ (4 mL) was stirred for 30 min at 0 °C. Condition B: a mixture of **3** (1 mmol), TFAA (10 mmol), 2,6-lutidine (3 mmol), and $CHCl_3$ (4 mL) was stirred for 1 h at 25 °C. [b] The product also contained **3k** (22%) and *p*-anisaldehyde (10%). [c] The product was a mixture of **3l** (74%) and *p*-(dimethylamino)-benzaldehyde (36%). [d] The sole product was *p*-(dimethylamino)-benzaldehyde.

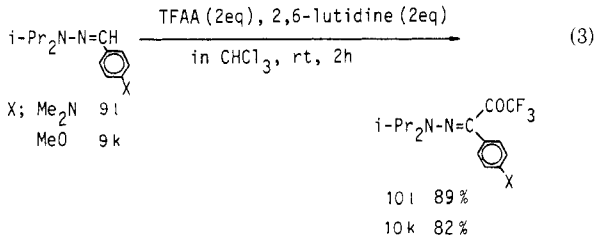
Table IV. Cyclization of Acylated Hydrazones

run	substr	time (h)	products and yields (%)	ratio
1	**4a**	16[a]	**12a** (6), **13a** (59)	1:9
2	**4a**	72[b]	**12a** (–), **13a** (–)	2:1[c]
3	**4e**	114[a]	**12e** (38), **13e** (41)	6:7
4	**4h**	25[a]	**12h** (34), **13h** (48)	2:3

[a] Reactions were carried out in refluxing CCl_4. [b] Reaction was carried out in refluxing $CHCl_3$ with 2 equiv of 2,6-lutidine. [c] Product ratio was calculated from ^1H NMR spectrum of crude product.

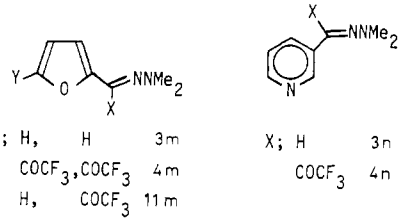
and there remained only signals attributable to **4k** and **7k** (X = OMe). Subsequent workup gave a 2:9 mixture of **3k** and **4k**. In the reactions of **3e** and **3j** no signals indicating formation of **7e** or **7j** were detected. Thus the anomalous substituent effect seen in Table III can be explained by competitive N-attack and C-attack of the trifluoroacetyl cation (Scheme II).

This interpretation suggested that the desired C-acylation would be favored if N-attack is sterically hindered. So we attempted the trifluoroacetylation of *p*-(dimethylamino)benzaldehyde diisopropylhydrazone (**9l**) and found that it reacted readily with TFAA to afford the *C*-acyl product **10l** in 89% yield. The hindered hydrazone of *p*-anisaldehyde (**9k**) gave **10k** in a comparable yield, indicating that use of diisopropylhydrazones can overcome the inhibitory effect of strongly electron-donating phenyl substituents on the C-acylation (eq 3).



(3)

The study was extended to the trifluoroacetylation of dimethylhydrazones of furfural (**3m**) and nicotinaldehyde (**3n**), both of which afforded the *C*-acyl products **4m** and **4n**. In **3m** trifluoroacetylation of the furan ring occurred in preference to that of the azomethine carbon. Therefore TFAA was needed in greater excess to obtain **4m**; otherwise **11m** was the major product.



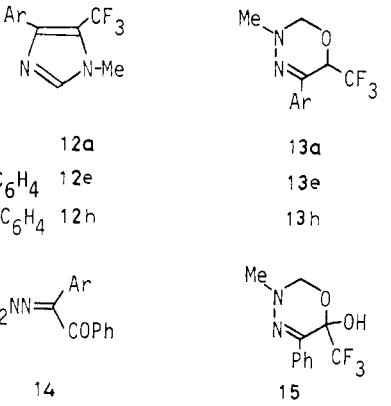
Cyclization of Acylated Hydrazones. When **4a** was heated for 16 h in refluxing CCl_4 there was obtained a mixture of imidazole **12a** (6%) and oxadiazine **13a** (59%). The structures of these compounds were determined from ^1H and ^{13}C NMR spectra, IR spectra, and elemental analyses. Although a similar cyclization of benzil mono(dimethylhydrazone) (**14**) to an imidazole has been reported,[11,12] such a cyclization to oxadiazines was not previously known. Thermal treatment of **4e** and **4h** gave mixtures of similar heterocycles (Table IV). The ratio of imidazole to oxadiazine varied widely with the substrates.

Table V. Hydrolysis of Trifluoroacetyl Hydrazones to 1,2-Diketones[a]

run	substr	temp (°C)	time (h)	16 yield (%)
1	**4a**	25	20	98
2	**4e**	25	20	72
3	**4f**	60	45	63
4	**4g**	25	20	94
5	**4h**	60	48	86
6	**4i**	25	20	78
7	**4j**	25	20	89
8	**4k**	60	12	96
9	**10l**	70	46	78[b]
10	**4m**	50	24	55[c]

[a] The hydrolysis was carried out in 5 N aqueous H_2SO_4 except as noted. [b] The hydrolysis was carried out with $CuCl_2$ in a phosphate buffer (pH 7). [c] The hydrolysis was carried out with $Cu(OAc)_2$–AcOH at pH 5.

Addition of 2,6-lutidine in the thermal conversion of **4a** increased the ratio of **12a** to **13a** considerably.



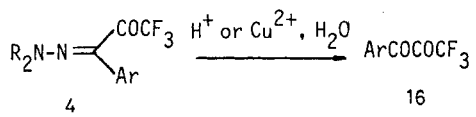
Hydrolysis of Trifluoroacetylated Hydrazones to 1,2-Diketones. Attempted oxidation of **4a** to the corresponding 1,2-diketone with $NaIO_4$ failed, the main product being the heterocyclic compound **15**. However, treatment of **13a** with $NaIO_4$[13] did not afford any **15**, indicating that the oxidation did not proceed through **13a**.

Acid hydrolysis of **4** yielded the 1,2-diketones **16**. Initial experiments using 5 N aqueous HCl–THF afforded **16** monohydrates.[14] However, it was difficult to remove residual THF from all products except **16a,b,g**; this problem was overcome by carrying out the hydrolysis in hot 5 N H_2SO_4 (Table V). Hydrolysis proceeded more slowly with the ortho-substituted substrates **4f** and **4h**, presumably because of steric hindrance. The trifluoroacetylated hydrazones containing the *p*-NMe_2 group (**10l**) and the trifluoroacetylfuryl group (**4m**) could not be hydrolyzed by 5 N H_2SO_4 but were hydrolyzed to the 1,2-diketones with $CuCl_2$ in phosphate buffer (pH 7)[15,16] and with $Cu(OAc)_2$,[16] respectively. These 1,2-diketones can be converted to trifluoromethyl heterocycles. Thus treatment of **4b** with *o*-phenylenediamine or diaminomaleonitrile afforded the quinoxaline **17** and the pyrazine **18**, respectively, in good yields.

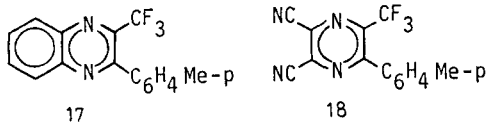
Experimental Section

All ^1H NMR spectra were recorded at 60 MHz on a JEOL PMX60SI spectrometer in $CDCl_3$ solutions containing TMS as

(11) Collibee, W. L.; Anselme, J.-P. *Tetrahedron Lett.* **1985**, *26*, 1595.
(12) Anastas, P. T.; Kano, K.; Anselme, J.-P. *J. Chem. Educ.* **1985**, *62*, 515.
(13) Corey, E. J.; Enders, D. *Tetrahedron Lett.* **1976**, 3.
(14) Microanalytical data suggested **16** to be monohydrates in which the carbonyl group far from aromatic ring should be hydrated.
(15) Green; T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981.
(16) Corey, E. J.; Knapp, S. *Tetrahedron Lett.* **1976**, 3667.



4 16



17 18

an internal standard. ^{13}C NMR spectra were measured in $CDCl_3$ with a JEOL FX90Q or PS100 spectrometer with TMS as internal standard. IR spectra were taken with a Hitachi Model G3 spectrophotometer. Microanalyses for all new compounds isolated were in satisfactory agreement with the calculated values (C ±0.4, H ±0.3, N ±0.3, F ±0.4, Cl ±0.2%).

Preparation of Hydrazones. Hydrazones were prepared essentially by the reported procedure.[17]

Propionaldehyde Dimethylhydrazone (3b). To well-stirred propionaldehyde (15 mmol) was added slowly *N,N*-dimethylhydrazine (15 mmol). After being stirred for 3 h, the mixture was dried over $MgSO_4$ and distilled under reduced pressure to afford **3b** (64%) as a coloress oil: ^1H NMR ($CDCl_3$) δ 6.37 (t, 1 H, CH), 2.60 (m, 6 H, NCH_3), 2.18 (m, 2 H, CH_2), 1.03 (t, 3 H, CH_3).

Formaldehyde Dimethylhydrazone (3c). A mixture of paraformaldehyde (144 mmol) and *N,N*-dimethylhydrazine (140 mmol) was stirred for 1 h, and then pentane (10 mL) and Na_2SO_4 (ca. 1 g) were added with continuous stirring. After 10 min the organic layer was decanted, dried over CaH_2, and fractionally distilled, affording **3c** (62%) as a colorless oil (bp 70–71 °C): ^1H NMR ($CDCl_3$) δ 6.00 (s, 2 H, CH_2), 2.75 (s, 6 H, CH_3).

Benzaldehyde Diphenylhydrazone (3d). To a mixture of benzaldehyde (50 mmol) and *N,N*-diphenylhydrazine hydrochloride (52 mmol) in dry EtOH (50 mL) was added slowly alcoholic sodium ethoxide (prepared from 50 mmol of Na and 50 mL of dry EtOH). The mixture was stirred for 24 h. The insoluble material was filtered off and the filtrate was concentrated to about a quarter in volume. After CH_2Cl_2 (80 mL) was added, the mixture was washed with 0.1 N HCl and then with aqueous Na_2CO_3 and dried over $MgSO_4$. Removal of the solvent and recrystallization of the residue from benzene/hexane afforded **3d** (72%) as colorless crystals: ^1H NMR ($CDCl_3$) δ 6.98–7.50 (m, Ar).

Arene Aldehyde Dimethylhydrazones 3a, 3e–n. To a vigorously stirred solution of aldehyde (40 mmol) in benzene (10 mL) was added dropwise dimethylhydrazone (44 mmol) and stirring was continued for 4 h. The mixture was dried over $MgSO_4$ and the benzene was distilled off. In the case of **3m** a small amount of AcOH (8 mmol) was added at the beginning of the reaction and later removed by washing with aqueous Na_2CO_3 during the workup. Crude hydrazones were purified by distillation (**3a**, **3e**, **3f**, **3h**, **3k**, **3m**, and **3n**) or recrystallization (**3g**, **3i**, **3j**, and **3l**). The yields are as follows: **3a**, 65%; **3e**, 81%; **3f**, 77%; **3g**, 59%; **3h**, 96%; **3i**, 98%; **3j**, 95%; **3k**, 86%; **3l**, 41%; **3m**, 92%; **3n** 86%. **3e**: ^1H NMR ($CDCl_3$) δ 7.17, 6.83 (d, 4 H, Ar), 6.90 (s, 1 H, CH), 2.80 (s, 6 H, NCH_3), 2.25 (s, 3 H, CH_3). **3m**: ^1H NMR (CCl_4) δ 7.17, 6.23 (s, 3 H, furan), 6.90 (s, 1 H, CH), 2.87 (s, 6 H, CH_3). **3n**: ^1H NMR (CCl_4) δ 8.80, 8.28, 7.83, 7.13 (m, 5 H, Py and CH), 2.97 (s, 6 H, CH_3).

Trifluoroacetylation of Hydrazones 3a–c. General Procedure (See Table I). To an ice-cooled mixture of hydrazone (1 mmol) and amine (2 mmol) in dry $CHCl_3$ (1 mL) was added 2–3 equiv of TFAA dissolved in dry $CHCl_3$ (1 mL) with continuous stirring. In the case of run 4 amine was not added. After the period indicated in Table I, the reaction mixture was poured onto 40 mL of 0.1 N HCl and then extracted with two portions of CH_2Cl_2 (10 mL). The combined organic layers were washed once with water and then with aqueous Na_2CO_3. The resulting solution was dried over $MgSO_4$, and the solvent was removed under reduced pressure.

In runs 1, 2, 3, and 4, 239 mg (98%), 198 mg (81%), 173 mg (71%), and 176 mg (72%), respectively, of **4a** were obtained as practically pure compounds. The crude product of run 1 was recrystallized from cyclohexane to afford 144 mg of **4a** as pale yellow crystals, which were submitted to microanalysis. In run 5, 53 mg (62%) of **3b** was recovered. In run 7, the crude product was fractionated by silica gel column chromatography. Elution with *n*-hexane/benzene (1/4) afforded 51 mg (18%) of **6c** and then with benzene gave 124 mg (74%) of **4c**.

Trifluoroacetylation of 3b and 3d (See Table I). To a mixture of **3b** (1 mmol) and 2,6-lutidine (2 mmol) in dry $CHCl_3$ (1 mL) was added 8 equiv of TFAA dissolved in dry $CHCl_3$ (1 mL) with continuous stirring. The mixture was transferred into a sealed tube and maintained at 80 °C for 52 h. The product was poured into 40 mL of 0.1 N HCl and extracted with two portions of CH_2Cl_2 (10 mL). The combined organic layers were washed once with water and once with aqueous Na_2CO_3, followed by drying over $MgSO_4$ and evaporation of the solvent. Ball-tube distillation afforded 128 mg (65%) of **5c** as a pale yellow oil. In a similar manner **4d** was obtained. The crude product was fractionated by silica gel column chromatography. Elution with *n*-hexane/benzene (3/2) afforded 103 mg (38%) of **3d** and then with *n*-hexane/benzene (1/1) gave 130 mg (35%) of **4d**. Further purification for microanalysis was done by recrystallization from benzene.

Trifluoroacetylation of Hydrazones of Arene Aldehydes 3e–l (See Table II). General Procedure. To an ice-cooled mixture of hydrazone (10 mmol) and 2–3 equiv of 2,6-lutidine in dry $CHCl_3$ (32.5–39 mL) was added dropwise 2–15 equiv of TFAA in $CHCl_3$ (1 mL for 2 mmol of TFAA) with continuous stirring. The mixture was warmed to 20 °C and stirring was continued for 3–72 h. After addition of CH_2Cl_2 (40 mL), the mixture was washed once with 0.1 N HCl (except the case of **3l**), once with water (except the case of **3l**), and once with aqueous Na_2CO_3. The organic layer was dried over $MgSO_4$ and the solvent and 2,6-lutidine in the case of **3l**) was removed in vacuo. The yields of **4e–k** were as follows: **4e** (recrystallized from cyclohexane), 2.167 g (84%); **4f**, 2.674 g (96%); **4g** (recrystallized from *n*-hexane/benzene, 1/1), 2.423 g (87%); **4h** (recrystallized from MeOH/H_2O, 10/1), 2.312 (80%); **4i**, 2.688 g (93%); **4j** (recrystallized from CCl_4), 2.370 g (82%); **4k** (recrystallized from cyclohexane), 1.671 g (61%). In run 8, 74% of *p*-(dimethylamino)benzaldehyde was recovered. The reaction of **3l** under more vigolous conditions (run 9) was carried out as follows. To a mixture of **3l** (1 mmol) and 2,6-lutidine (5 mmol) in dry $CHCl_3$ (5 mL) was added TFAA (10 mmol), and the mixture was transferred in a sealed tube. After being heated for 24 h at 60 °C, the reaction mixture was poured into saturated aqueous Na_2CO_3, extracted with CH_2Cl_2 (20 mL), and dried over $MgSO_4$. Removal of the solvent and 2,6-lutidine under reduced pressure afforded 135 mg of reddish brown oil whose ^1H NMR spectrum showed that *p*-(dimethylamino)benzaldehyde was the main product.

Trifluoroacetylation of Dimethylhydrazones of Arene Aldehydes 3a, 3e, 3g, 3i, 3k, and 3l (See Table III). Condition A. A well-stirred mixture of hydrazone (1 mmol) and 2,6-lutidine (2 mmol) in dry $CHCl_3$ (3 mL) was cooled to 0 °C, and a solution of TFAA (4 mmol) in purified $CHCl_3$ (1 mL) was added dropwise. Stirring was continued for 30 min at this temperature.

Condition B. To a well-stirred mixture of hydrazone (1 mmol) and 2,6-lutidine (3 mmol) in $CHCl_3$ (4 mL) at 0 °C was added dropwise TFAA (10 mmol). The mixture was warmed to 25 °C and stirring was continued for 1 h.

After completion of the reaction, under both sets of conditions, the reaction mixture (**3a–k**) was poured into 0.1 N HCl, extracted with CH_2Cl_2 (20 mL), and washed once with water and once with aqueous Na_2CO_3. The organic layer was dried over $MgSO_4$ and the solvent was removed. In the case of **3l** the reaction mixture was washed thoroughly with aqueous Na_2CO_3 and dried over $MgSO_4$. The solvent and 2,6-lutidine were removed under reduced pressure. Crude materials thus obtained were analyzed by ^1H NMR.

Monitoring Experiments of Trifluoroacetylation of 3e, 3j, 3k, and 3l. Hydrazone (0.2 mmol) and pyridine-d_5 (0.4 mmol) dissolved in $CDCl_3$ (0.5 mL) were introduced into a 5Φ NMR tube.

(17) Sandler, S. R.; Karo, W. *Organic Functional Group Preparations*, 2nd ed.; Wasserman, H. H., Ed.; Academic Press: New York, 1983.

After addition of TFAA (ca. 0.4 mmol), the tube was shaken thoroughly and the reaction was monitored immediately by ^1H NMR spectroscopy.

Preparation of 9l and 9k. *N,N*-Diisopropylhydrazine was prepared by the established method.[18] To a mixture of *p*-(dimethylamino)benzaldehyde (15 mmol) and *N,N*-diisopropylhydrazine (15.5 mmol) in benzene (35 mL) was added AcOH (1 mL), and the mixture was refluxed by using a Dean–Stark trap. After 24 h the reaction mixture was poured into aqueous Na_2CO_3 and extracted with ether. The ethereal layer was washed with water and dried over $MgSO_4$. Removal of the solvent gave crude **9l**, which was recrystallized from EtOH/H_2O (20/1) to give 2.37 g (64%) of pure **9l**. Similarly, 2.53 g (72%) of **9k** (recrystallized from cyclohexane) was obtained. **9l**: ^1H NMR ($CDCl_3$) δ 7.32, 6.64 (d, 4 H, Ar), 7.20 (s, 1 H, CH), 3.76 (m, 2 H, NCH), 2.90 (s, 6 H, NCH_3), 1.18 (d, 12 H, CH_3). **9k**: ^1H NMR (CCl_4) δ 7.23, 6.63 (d, 4 H, Ar), 7.03 (s, 1 H, CH), 3.77 (m, 2 H, NCH), 3.69 (s, 3 H, OCH_3), 1.18 (d, 12 H, CH_3).

Trifluoroacetylation of 9l and 9k. The reaction procedure was similar to that for **3e–l**. For 1 mmol of hydrazone, 2 mmol of both TFAA and 2,6-lutidine together with 4 mL of purified $CHCl_3$ were used. The reaction was carried out for 2 h at 25 °C. Recrystallization of crude **10l** from benzene afforded 305 mg (89%) of **10l** and that of crude **10k** from cyclohexane gave 271 mg (82%) of pure **10k**.

Trifluoroacetylation of 3m and 3n. The reaction procedure was similar to that for **3e–l**. For 4 mmol of **3m** (or **3n**), 2 mmol of both TFAA and 2,6-lutidine in 12 mL of dry $CHCl_3$ were used. Reaction for 24 h gave 867 mg of **4m** and **11m** as a 1:14 mixture (on the basis of ^1H NMR spectrum) from **3m**, and 748 mg (76%) of **4n** from **3n**. The mixture of **4m** and **11m** was fractionated by silica gel column chromatography. Elution with benzene/CH_2Cl_2 (1/1) afforded 63 mg of **4m** (5%) and, then with benzene/CH_2Cl_2 (3/7), gave 575 mg (68%) of **11m**, which was further purified by ball-tube distillation, providing 512 mg (61%) of pure **11m**. Trifluoroacetylation of **3m** with a large excess of TFAA was also undertaken in a similar manner. For 8 mmol of **3m**, 64 mmol of TFAA, 32 mmol of 2,6-lutidine, and 20 mL of dry $CHCl_3$ were used. After 4 days at 25 °C, recrystallization of the crude product from cyclohexane/CH_2Cl_2 (2/1) afforded 1.81 g (65%) of **4m**.

Cyclization of 4a, 4e, and 4h (See Table IV). In runs 1, 3, and 4, substrate (5 mmol) in CCl_4 (150 mL) was heated for 16–114 h under reflux. In run 2, a mixture of **4a** (1 mmol) and 2,6-lutidine (2 mmol) in $CHCl_3$ (5 mL) was refluxed for 72 h. After cooling, the solvent (and 2,6-lutidine) was removed under reduced pressure. Crude products of runs 1, 3, and 4 were fractionated by silica gel column chromatography, which afforded **12a** (72 mg, 6%, benzene/AcOEt; 3/2) and **13a** (716 mg, 59%, benzene), **12e** (461 mg, 38%, benzene/AcOEt; 3/2) and **13e** (532 mg, 41%, benzene), and **12h** (455 mg, 34%, CH_2Cl_2/AcOEt; 1/1) and **13h** (692 mg, 48%, benzene/CH_2Cl_2; 7/3), respectively. Microanalytical samples were obtained by subsequent ball-tube distillation.

Oxidation of 4a with $NaIO_4$. To a solution of **4a** (1 mmol) in THF (10 mL) was added $NaIO_4$ (1.28 g, 6 mmol) dissolved in water (15 mL), and the mixture was stirred for 69 h at 25 °C. After addition of ether (50 mL), the mixture was washed with 10% aqueous NaCl, and the organic layer was dried over $MgSO_4$. Removal of the solvent and recrystallization from CCl_4 afforded 76 mg (30%) of **15**.

Acid Hydrolysis of 4a–k to 1,2-Diketones (See Table V). The substrate (4 mmol) was dissolved in a mixture of 5 N HCl (28 mL) and THF (65 mL), or in 5 N H_2SO_4 (30 mL), and the solution was stirred for 24–48 h at 25 °C (or 60 °C). The 1,2-diketone was then extracted with three portions of ether (30 mL) and the combined ethereal solution was dried over $MgSO_4$. Removal of the solvent and subsequent distillation, sublimation, or recrystallization of the residue gave pure **16**: run 1, 862 mg (98%); run 2, 674 mg (72%); run 3, 641 mg (63%); run 4, 957 mg (94%); run 5, 912 mg (86%); run 6, 827 mg (78%); run 7, 943 mg (89%); run 8, 960 mg (96%).

Hydrolysis of 10l to 16 (See Table V). To a solution of $CuCl_2$ (4.4 mmol) in THF (60 mL) were added water (20 mL) and a 0.05 N phosphate buffer solution (pH 7, 12 mL). After stirring the mixture for 10 min, **10l** (4 mmol) was added, and the mixture was stirred for 46 h at 70 °C. The THF was evaporated, and the residual aqueous solution was poured into a solution of NH_4Cl in dilute ammonia water (ca. pH 8, 200 mL). This was extracted with CH_2Cl_2 (3 × 50 mL), and the combined extracts were dried over $MgSO_4$. Removal of the solvent gave brown crystals of **16**, which were purified by treatment with active charcoal followed by recrystallization from ether/pentane, affording pure **16** (run 9), 821 mg (78%).

Hydrolysis of 4m to 16 (See Table V). A solution of $Cu(OAc)_2$ (8 mmol) in water (80 mL) was adjusted to pH 5 by addition of AcOH. To this was added **4m** (4 mmol) dissolved in THF (80 mL), and the mixture was stirred for 24 h at 50 °C. After removal of the THF, the resultant aqueous solution was extracted with CH_2Cl_2 (3 × 50 mL), and the combined extracts were dried over $MgSO_4$. Evaporation of the solvent gave crude **16**. Purification by preparative TLC with CH_2Cl_2 as the developing solvent, and subsequent ball-tube distillation, afforded pure **16** (run 10), 673 mg (55%).

Quinoxaline 17 and Pyrazine 18. To a solution of **16** (0.5 mmol) in CH_3CN (3 mL) was added *o*-phenylenediamine (0.5 mmol), and the mixture was stirred for 23 h. Removal of the solvent gave orange crystals, which were recrystallized from cyclohexane to afford 90 mg (63%) of **17** as pale yellow crystals. Similarly, **18** was obtained from **16** (0.5 mmol) and diaminomaleonitrile (0.55 mmol). The crude product was purified by column chromatography on silica gel (elution with benzene) followed by ball-tube distillation to afford 107 mg (74%) of **18** as yellow oil.

Physical and Spectroscopic Data for 4a–18. 4a: pale yellow crystals; mp 71 °C; IR 1675 (s), 1545 (s), 1175 (s), 1150 (s), 1130 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.00–7.30 (m, 5 H, Ar), 2.98 (s, 6 H, CH_3). **5c**: yellow oil; oven temperature 120 °C (3 Torr); IR 1705 (s), 1430 (m), 1226 (m), 1195 (s), 1160 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.13 (d, 1 H, NCH=), 5.45–5.97 (m, 1 H, =CH—), 2.67 (s, 6 H, NCH_3), 1.77 (d, 3 H, CH_3). **4c**: pale yellow oil; oven temperature 115 °C (3 Torr); IR 1670 (s), 1520 (s), 1140 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.60 (s, 1 H, =CH—), 3.25 (s, 6 H, CH_3). **6c**: colorless oil; oven temperature 85 °C (3 Torr); IR 1780 (s), 1710 (s), 1340 (m), 1180 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.70 (s, 2 H, CH_2), 2.60 (s, 6 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 159.6 ($^2J_{C-F}$ = 44 Hz, OCO—), 156.5 ($^2J_{C-F}$ = 37 Hz, CO), 116.3 ($^1J_{C-F}$ = 286 Hz, CF_3), 114.4 ($^1J_{C-F}$ = 285 Hz, CF_3), 66.8 (CH_2), 44.6 (CH_3). **4d**: yellowish green crystals; mp 139 °C; IR 1685 (s), 1165 (s), 1145 (s), 760 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93–7.83 (m, 15 H, Ar). **4e**: colorless crystals; mp 114 °C; IR 1680 (s), 1545 (s), 1145 (s), 1130 (s), 1080 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.00 (s, 4 H, Ar), 3.00 (s, 6 H, NCH_3), 2.33 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 178.2 ($^2J_{C-F}$ = 30.5 Hz, CO), 132.0 (N=C), 138.6, 130.4, 130.1, 128.6 (Ar), 118.1 ($^1J_{C-F}$ = 291 Hz, CF_3), 47.1 (NCH_3), 21.3 (CH_3). **4f**: orange oil. **4g**: pale yellow crystals; mp 103 °C. **4h**: yellow crystals; mp 37 °C. **4i**: orange oil. **4j**: colorless crystals; mp 116 °C. **4k**: pale yellow crystals; mp 95 °C. **10l**: yellow crystals; mp 175 °C; IR 2840 (m), 1600 (s), 1515 (s), 1170 (s), 1150 (s), 1110 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.64–6.90 (q, 4 H, Ar), 3.83–4.27 (m, 2 H, CH), 2.93 (s, 6 H, NCH_3), 1.15 (d, 12 H, CH_3). **10k**: colorless crystals; mp 144 °C; IR 1665 (s), 1605 (m), 1522 (s), 1498 (s), 1338 (s), 1275 (s), 1243 (s) 1220 (s), 1150 (s), 1110 (s), 1029 (m), 1002 (s), 885 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.95, 6.77 (d, 4 H, Ar), 3.87, 3.75 (hept and s, 5 H, CH and OCH_3), 1.10 (d, 12 H, CH_3). **4m**: yellow crystals; mp 80 °C; IR 1690 (s), 1532 (s), 1175 (s), 1135 (s), 1120 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47–7.67 (m, 1 H, CH), 6.37 (d, 1 H, CH), 3.27 (s, 6 H, NCH_3). **11m**: yellow oil; oven temperature 175 °C (1 Torr); IR 1675 (s), 1534 (s), 1180 (s), 1140 (s), 1105 (s), 810 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33–7.47 (m, 1 H, CH), 6.87 (s, 1 H, N=CH), 6.53 (d, 1 H, CH), 3.08 (s, 6 H, CH_3). **4n**: yellow oil; ^1H NMR ($CDCl_3$) δ 8.23–8.53, 7.00–7.60 (m, 4 H, Py), 3.03 (s, 6 H, NCH_3). **12a**: colorless oil; oven temperature 110 °C. **12e**: colorless crystals; mp 45 °C; IR 1610 (m), 1560 (m), 1510 (m), 1450 (m), 1170 (s), 1105 (s), 823 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 1 H, CH), 6.92–7.42 (q, 4 H, Ar), 3.68 (s, 3 H, NCH_3), 2.33 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 145.1 (C=N), 140.5 (NCH=), 138.2, 130.6, 128.9 (Ar), 121.7 ($^1J_{C-F}$ = 267 Hz, CF_3), 116.5 ($^2J_{C-F}$ = 38.7 Hz, CCF_3), 33.5 (NCH_3), 21.3 (CH_3). **12h**: yellow crystals; mp 129 °C. **13a**: pale yellow oil; oven temperature 165 °C (3 Torr); IR 1446 (s), 1261 (s), 1173 (s), 1130 (s), 1072 (m), 848 (m), 765

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(m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10–7.40 (m, 5 H, Ar), 5.20 (q, J_{H-F} = 7 Hz, 1 H, CH), 4.07–4.59 (AB q, J = 6 Hz, 2 H, CH_2), 2.90 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 139.5 (—C=N), 135.4, 128.9, 128.4, 126.0 (Ph), 123.0 ($^1J_{C-F}$ = 293 Hz, CF_3), 76.2 (CH_2), 67.8 ($^2J_{C-F}$ = 30.5 Hz, CH), 41.1 (CH_3). **13e**: pale yellow crystals; mp 48 °C. **13h**: yellow oil; oven temperature 75 °C (3 Torr). **15**: colorless crystals; mp 120 °C; IR 3100 (m), 1170 (s), 1180 (m), 1190 (s), 765 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12–7.70 (m, 5 H, Ar), 3.34 (br, 1 H, OH), 4.37 (q, 2 H, CH_2), 2.97 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 140.0 (C=N—), 135.4, 128.5, 127.9 (Ph), 127.5 ($^1J_{C-F}$ = 299 Hz, CF_3), 89.0 ($^2J_{C-F}$ = 33.0 Hz, CCF_3), 74.0 (CH_2), 40.7 (CH_3). **16** (Ar = Ph): pale yellow crystals; mp 83 °C. **16** (Ar = *p*-MeC_6H_4): pale yellow crystals; mp 84 °C; IR 1675 (s), 1190 (s), 1150 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10, 7.17 (d, 4 H, Ar), 4.00–5.00 (br, 2 H, OH), 2.40 (s, 3 H, CH_3). **16** (Ar = *o*-ClC_6H_4): colorless crystals; mp 128 °C. **16** (Ar = *p*-ClC_6H_4): colorless crystals; mp 120 °C. **16** (Ar = *p*-$O_2NC_6H_4$): pale yellow crystals; mp 83 °C. **16** (Ar = *m*-$O_2NC_6H_4$): colorless oil; oven temperature 90 °C (1 Torr). **16** (Ar = *p*-$O_2NC_6H_4$): orange oil. **16** (Ar = *p*-$MeOC_6H_4$): colorless crystals; mp 81 °C. **16** (Ar = *p*-$Me_2NC_6H_4$): yellow crystals; 80 °C dec; IR 3040–3640 (s, br), 1608 (s), 1434 (m), 1385 (s), 1288 (s), 1200 (s), 1150 (s), 1062 (m), 1002 (m), 823 (m), 608 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (d, 2 H, Ar), 6.57 (d, 2 H, Ar), 5.00 (br, 2 H, OH), 3.07 (s, 6 H, CH_3). **16** (Ar = 4-(trifluoroacetyl)-2-furyl): yellow oil; oven temperature 130 °C (2 Torr); IR 3000–3600 (m, br), 1708 (s), 1639 (m), 1352 (m), 1246 (m), 1204 (s), 1160 (s), 1044 (s), 1011 (s), 884 (m), 820 (m), 762 (m), 736 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46 (br, 1 H, furan), 7.25 (d, 1 H, furan), 5.73–5.93 (br, 2 H, OH). **17**: yellow crystals; mp 115 °C; IR 1180 (s), 1125 (s), 1070 (s), 768 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10–8.27 (m, 8 H, Ar), 2.43 (s, 3 H, CH_3). **18**: yellow oil; oven temperature 175 °C (2 Torr); IR 2250 (w), 1610 (s), 1145 (m), 1130 (m), 1085 (s), 750 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.24–7.57 (q, 4 H, Ar), 2.40 (s, 3 H, CH_3).

Registry No. **3a**, 1075-70-3; **3b**, 7422-93-7; **3c**, 2035-89-4; **3d**, 966-88-1; **3e**, 24459-52-7; **3f**, 5051-47-8; **3g**, 22699-29-2; **3h**, 10424-94-9; **3i**, 32787-76-1; **3j**, 10424-92-7; **3k**, 14371-13-2; **3l**, 32787-73-8; **3m**, 14064-21-2; **3n**, 59670-91-6; **4a**, 111269-36-4; **4c**, 111269-38-6; **4d**, 111291-46-4; **4e**, 111269-40-0; **4f**, 111269-41-1; **4g**, 111269-42-2; **4h**, 111269-43-3; **4i**, 111269-44-4; **4j**, 111269-45-5; **4k**, 111269-46-6; **4m**, 111269-58-0; **4n**, 111269-57-9; **5b**, 111269-37-5; **6c**, 111269-39-7; **8** (X = H), 100-52-7; **8** (X = 4-Me), 104-87-0; **8** (X = 2-Cl), 89-98-5; **8** (X = 4-Cl), 104-88-1; **8** (X = 2-NO_2), 552-89-6; **8** (X = 3-NO_2), 99-61-6; **8** (X = 4-NO_2), 555-16-8; **8** (X = 4-OMe), 123-11-5; **8** (X = 4-NMe_2), 100-10-7; **9k**, 111290-74-5; **9l**, 111269-53-5; **10k**, 111269-54-6; **10l**, 111269-55-7; **11m**, 111269-56-8; **12a**, 111269-47-7; **12e**, 111269-49-9; **12h**, 111269-51-3; **13a**, 111269-48-8; **13e**, 111269-50-2; **13h**, 111269-52-4; **15**, 111269-59-1; **16a**, 36750-88-6; **16e**, 111269-60-4; **16f**, 111269-61-5; **16g**, 111269-62-6; **16h**, 111269-63-7; **16i**, 111269-64-8; **16j**, 111269-65-9; **16k**, 111269-66-0; **16l**, 111269-67-1; **16m**, 111269-68-2; **17**, 111269-69-3; **18**, 111269-70-6; TFAA, 407-25-0; EtCHO, 123-38-6; $(CH_2O)_x$, 30525-89-4; Me_2NNH_2, 57-14-7; Ph_2NNH_2, 530-47-2; *i*-Pr_2NNH_2, 921-14-2; 2-$H_2NC_6H_4NH_2$, 95-54-5; NCC(N-H_2)=C(NH_2)CN, 1187-42-4; furfural, 98-01-1; nicotinaldehyde, 500-22-1.

Static and Dynamic Stereochemistry of Chloropentakis(dichloromethyl)benzene

Silvio E. Biali*[1a] and Andrzej B. Buda*[1b]

Department of Chemistry, Princeton University, Princeton, New Jersey 08544

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Chloropentakis(dichloromethyl)benzene (**2**) was synthesized by photochlorination of chloropentamethylbenzene. The barrier for internal rotation of the side chains was measured by the spin saturation transfer technique and by the coalescence approximation. Empirical force field calculations show that the preferred conformation is the all geared, in agreement with the NMR data, and that the mechanism of topomerization involves stepwise rotation of the side chains. The calculations closely reproduce the topomerization barrier (experimental 20 kcal mol^{-1}; calculated 22 kcal mol^{-1}).

In recent years, there has been an active interest in the stereochemistry of systems bearing isopropyl groups attached to a planar sp^2 frame (such as ethylene or benzene).[2,3] Some of these systems avoid repulsive nonbonded interactions by assuming a gear-locked conformation in which each of the isopropyl methine hydrogens is tucked into the notch created by the methyl groups of a neighboring isopropyl group. Examples of this kind of system include hexaisopropylbenzene[4] and tetraisopropylethylene,[5] both of which display homodirectional isopropyl groups in their lowest energy conformation (C_{6h} and C_{2h} symmetry respectively). This tight geared interaction raises the barrier to rotation of the isopropyl groups: empirical force field calculations (EFF) predict a topomerization barrier of 19.5 kcal mol^{-1} for tetraisopropylethylene,[6,7] and of ca. 35 kcal mol^{-1} for hexaisopropylbenzene.[8] In both cases, the calculated topomerization mechanism of lowest activation energy (threshold mechanism) does not involve correlated rotation but a stepwise rotation of the isopropyl groups;[6,8] i.e. the systems show static but not dynamic gearing.[9] Groups that are similar

(1) (a) Present address: Department of Organic Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel. (b) On leave from the Jagiellonian University, Krakow, Poland.

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