for the mixture data may be related to the poor correspondence of the viscosities of the pure components at high densities.

Dependences of the Liquid Viscosities on Density and Composition. Measurements of the viscosities of compressed liquid methane + ethane mixtures and the pure components (*2*, *3*) at high densities ($\rho > 2\rho_c$) are shown in Figure 7. There is clearly a strong dependence of the viscosities on density and composition in this density range. The dependence of the viscosities on temperature at fixed composition and at fixed density is relatively small. The dependences on density, composition, and temperature shown here are qualitatively similar to the dependences obtained by Huang, Swift, and Kurata (*13*) for methane + propane mixtures. The dependence of the viscosities of methane + ethane mixtures on composition at fixed density (23.5 mol·L^{-1}) is shown in Figure 8. The viscosity increases very rapidly with increasing ethane concentration in the vicinity of the equimolar composition. Figure 8 also shows that the composition dependence calculated from the extended corresponding states model (*4*, *5*) is very similar to the measured composition dependence at this density.

Dependence of the Fluidities of Liquid Methane + Ethane on Molar Volume. Hildebrand has shown (*14*) that the equation

$$\eta^{-1} = B(V - V_0)/V_0 \qquad (2)$$

where η^{-1} is called the fluidity, V is the molar volume, V_0 is the volume at $\eta^{-1} = 0$, and B is an empirical coefficient, gives a good account of the viscosities of liquids at high densities. Figure 9 shows the dependence of the fluidities of compressed liquid methane + ethane mixtures and the pure components (*2*, *3*) on molar volume at high densities ($\rho > 2\rho_c$). The fluidities increase linearly with volume at fixed composition and at fixed temperature consistent with eq 2. It appears that the Hildebrand equation could be used to develop a simple correlation for the viscosities of compressed liquid mixtures in a limited density range.

Summary

New absolute viscosity measurements have been reported for three compressed gaseous and liquid methane + ethane mixtures throughout a wide range of *PVT* states. The mixture measurements, along with those for the pure components, have been compared with a multiparameter extended corresponding states model, previously proposed for calculating the viscosities of mixtures of nonpolar fluids throughout a wide range of *PVT* states.

Acknowledgment

Howard J. M. Hanley encouraged this work and made helpful comments. James F. Ely provided computer programs for processing and analyzing the data.

Registry No. Methane, 74-82-8; ethane, 74-84-0.

Literature Cited

(1) Diller, D. E. *Int. J. Thermophys.* **1982**, *3*, 237.
(2) Diller, D. E. *Physica A (Amsterdam)* **1980**, *104*, 417.
(3) Diller, D. E.; Saber, J. M. *Physica A (Amsterdam)* **1981**, *108*, 143.
(4) Ely, J. F.; Hanley, H. J. M. *Ind. Eng. Chem. Fundam.* **1981**, *20*, 323.
(5) Ely, J. F.; Hanley, H. J. M. *NBS Tech. Note (U.S.)* **1981**, *No. 1039*.
(6) Haynes, W. M. *Physica (Amsterdam)* **1973**, *67*, 440.
(7) Webeler, R. H. W. Ph.D. Thesis, University of Cincinnati, Cincinnati, OH, 1961 (University Microfilms No. 61-5234, Ann Arbor, MI).
(8) Haynes, W. M.; McCarty, R. D.; Hoiste, J. C.; Eaton, B. E., National Bureau of Standards, Boulder, CO, unpublished data, 1983.
(9) McCarty, R. D. *NBS Tech. Note (U.S.)* **1980**, *No. 1030*.
(10) Haynes, W. M. *Physica A (Amsterdam)* **1977**, *9*, 569.
(11) Abe, Y.; Kestin, J.; Khalifa, H. E.; Wakeham, W. A. *Physica A (Amsterdam)* **1978**, *93*, 155.
(12) Mo, K. C.; Gubbins, K. E. *Mol. Phys.* **1978**, *31*, 825.
(13) Huang, E. T. S.; Swift, G. W.; Kurata, F. *AIChE J.* **1967**, *13*, 846.
(14) Hildebrand, J. H. "Viscosity and Diffusivity"; Wiley: New York, 1977.

Received for review April 13, 1983. Accepted August 30, 1983. This work was supported by the U.S. Department of Energy, Division of Geothermal Energy, and the Gas Research Institute.

NEW COMPOUNDS

Synthesis and Spectroscopic Studies of 5-Methyl-3-phenyl- and 5-Methyl-3-(*o*-, *m*-, and *p*-tolyl)-1,2,4-oxadiazoles†

Rajendra M. Srivastava* and Lêda M. Mendes e Silva

Departamento de Química, Universidade Federal de Pernambuco, Recife, Pe., Brazil

Preparation of four 1,2,4-oxadiazoles, 2a–d, from *O*-acetyl derivatives of benzamidoximes, 1a–d, are reported. Two of them, viz., 2b,c, were not encountered in the literature. Spectroscopic studies (IR, UV, and ^{1}H NMR) were carried out to learn more about these molecules. The effect of lanthanide shift reagent, Eu(fod)$_3$, on the chemical shifts of different protons of these compounds was also examined.

In connection with our interest in 3,5-disubstituted 1,2,4-oxadiazoles we recently required 5-methyl-3-phenyl- and 5-methyl-3-(*o*-, *m*-, and *p*-tolyl)-1,2,4-oxadiazoles, **2a–d**. We would now like to report the synthesis and spectroscopic properties of these heterocyclic compounds. Compounds **2b** and **2c** are new.

† Taken in part from the M.Sc. thesis of Lêda M. Mendes e Silva, Departamento de Química, Universidade Federal de Pernambuco, Recife, 1979.

Results and Discussion

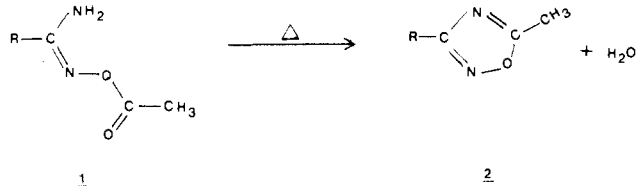
Synthesis of 1,2,4-oxadiazoles, **2a–d**, was achieved either by refluxing *O*-acetyl derivatives of amidoximes, (*1*), **1a–d**, in dry toluene or just by heating them above their melting points for an extended period of time (Scheme I). After completion of the reaction, the desired oxadiazole was purified by column chromatography followed by crystallization or distillation.

Table I shows the ultraviolet data of 1,2,4-oxadiazoles.

The infrared spectra of **2a** and **2b** had ν(C═N) and ν(C═C) of the aromatic ring between 1500 and 1600 cm^{-1}. It was difficult to assign each one correctly. In **2c** and **2d**, C═N

0021-9568/84/1729-0221$01.50/0

Scheme I



1 2

a: R = Ph
b: R = o-Tolyl
c: R = m-Tolyl
d: R = p-Tolyl

Table I. Ultraviolet Spectra of 1,2,4-Oxadiazoles, 2a-d[a,b]

compd	λ_{max} (ϵ)	lit. (3)
2a	238.0 (10 305)	238.0 (13 100)
	276.0 (736)	
	282.0 (400)	
2b	238.5 (10 424)	
	279.0 (945)	
	286.0 (530)	
2c	242.0 (11 370)	
	282.0 (947)	
	288.5 (510)	
2d	245.0 (15 789)	
	273.0 (1358)	
	285.0 (713)	

[a] Solvent: 95% ethanol. [b] Wavelength in nanometers.

Table II. Proton Magnetic Resonance Spectra of Oxadiazoles, 2a-d[a]

		chemical shift[b]	
compd	Ar	Ar-CH_3 ($W/2$ in Hz)	Het-CH_3 ($W/2$ in Hz)
2a	7.17-7.58 m (3 H),[c] 7.90-8.20 m (2 H)[d]		2.58 s
2b	7.13-7.40 m (3 H),[c] 7.80-8.10 m (1 H)[d]	2.63 s (1.35)	2.60 s (0.82)
2c	7.13-7.45 m (2 H),[c] 7.67-8.03 m (2 H)[d]	2.43 s (1.60)	2.60 s (0.89)
2d	[7.16 d (2 H),[e] 7.86 d (2 H)[d]][f]	2.40 s (1.60)	2.60 s (0.80)

[a] Solvent: CCl_4. [b] Values in ppm. Het = heterocyclic. [c] Meta and para protons. [d] Ortho protons. [e] Meta protons. [f] AA'BB' systems and $J \simeq 8.0$ Hz.

vibration appeared at 1620 cm^{-1}. The stretching motion of the N–O bond occurred around 900 cm^{-1} in all cases.

The NMR spectral data of **2a–d** are provided in Table II.

The effect of the shift reagent, $Eu(fod)_3$, on the chemical shifts of different protons in **2a–d** was also examined. In **2a**, the methyl singlet showed a downfield shift of about 8.0 Hz. The multiplet constituting the meta and para protons of the aromatic ring also moved 6.0 Hz to the lower field. However, the two-proton multiplet due to ortho protons suffered a deshielding effect of 18.0 Hz. In the case of **2b**, both methyl singlets showed downfield shifts—the one attached to the aromatic ring shifted 4.5 Hz while the other shifted by 5.3 Hz. The aromatic protons behaved in a similar manner as in **2a**. In compounds **2c** and **2d**, the methyl groups attached to the heterocyclic ring shifted to lower field by 5.0 and 8.0 Hz, respectively, but the Ar–CH_3 did not suffer any significant dislocation. The above information suggests that complexation occurs on the heterocyclic ring.

Biological Activity Testing

Oxadiazoles, **2a–d**, were tested "in vitro" against gram-positive bacteria such as *Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus faecallis*, and *Mycobacterium smegmatis* but none of these compounds showed any activity. Negative results were also obtained against fungi, *Candida albicans* and *Neurospora crassa*.

Experimental Section

The boiling points and melting points are uncorrected. Compounds **2b** and **2c** provided satisfactory elemental analyses for C, H, and N and were submitted for review. The ultraviolet spectra were obtained on a Beckman Model DB and infrared spectra on a Perkin-Elmer Model 237B grating instrument. The NMR spectra were measured on Varian A-60 and EM-390 90-MHz instruments with carbon tetrachloride as solvent and tetramethylsilane as an internal standard. Sievers' reagent, $Eu(fod)_3$ (tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium), was used as the shift reagent. Initially, this reagent (10% w/w) was added to the compound dissolved in carbon tetrachloride and the spectrum obtained. Only a little change was observed. Therefore, the same quantity of the reagent was added again to the same solution and the spectrum measured. The latter was compared with the NMR spectrum without the reagent. Plates coated with silica gel G (Merck) were employed for thin-layer chromatography using benzene as developer and iodine for detection of the spots.

***5-Methyl-3-phenyl-1,2,4-oxadiazole*, 2a.** Preparation of **2a** was achieved by a little modification of the previously known method (*2*). Thus, benzamidoxime (1.0 g, 7.4 mmol) in 5 mL of acetic anhydride was refluxed for 4 h. Excess anhydride was removed under vacuum. The material obtained was chromatographed on silica gel by using 1:1 benzene–hexane as eluent. The fractions containing the fast-moving spot were combined, crystallized, and recrystallized from hexane to afford 0.24 g (20%) of pure **2a**: mp 38–40 °C (lit. (*2*) mp 41 °C).

***5-Methyl-3-(o-tolyl)-1,2,4-oxadiazole*, 2b.** *O*-Acetyl-*o*-tolylamidoxime (*1*) (1.0 g, 5.2 mmol) in 40 mL of toluene was refluxed for 40 h. A thin-layer chromatogram showed two spots having R_f values of 0.81 and 0.56, respectively. After solvent evaporation, the product was chromatographed on a column packed with 20 g of silica gel by using benzene–hexane (1:3) as eluent. The fractions containing the fast-moving spot were combined and the solvent was removed under vacuum. Distillation gave 0.4 g (44.4%) of a colorless liquid, bp 117–118 °C at 4 mm. IR and NMR spectra agreed with the structure of **2b**.

***5-Methyl-3-(m-tolyl)-1,2,4-oxadiazole*, 2c.** Starting from *O*-acetyl-*m*-tolylamidoxime (*1*) and using the method described above, we obtained, **2c** as a mixture. Chromatography over silica gel using benzene–hexane (1:1) as solvent separated the desired oxadiazole as an oil in 50% yield. Dissolution of this oil in hexane followed by keeping the material in a refrigerator provided the crystals. Since the compound remains liquid at room temperature, the melting point was not determined. Two more recrystallizations followed by drying the compound in a vacuum desiccator afforded the analytically pure sample.

***5-Methyl-3-(p-tolyl)-1,2,4-oxadiazole*, 2d.** *O*-Acetyl-*p*-tolylamidoxime (*2*) was employed as starting material. The method was essentially the same as described for **2b**. Crystallization from ethanol–water provided **2d** in 60% yield, mp. 78 °C (lit. (*13*) mp 80 °C). Recrystallization did not change the melting point.

***1,2,4-Oxadiazoles*, 2a–d.** A test tube containing the desired *O*-acetyl derivative was immersed in a preheated oil bath set at 15 °C above the melting point of the starting compound and kept at this temperature for an extended period of time. Completion of the reaction was monitored by thin-layer chromatography. The thin-layer chromatogram showed a main fast-moving spot due to the respective oxadiazole, and two weak slow-moving spots which were due to the starting *O*-acetyl

derivative as well as the amidoxime. The last one apparently was the result of hydrolysis of *O*-acetyl derivative by water which was produced during oxadiazole formation. Compound **1b** cyclized a little faster (~5 h) compared to **1a,c,d** (~6-7 h). After reaction, the pure compound in each case was obtained by column chromatography over silica gel (Merck) using benzene-hexane (1:1) as eluent. The yields were as follows: **2a**, 82.8%; **2b**, 64.3%; **2c**, 56.6%; and **2d** 83.0%.

Acknowledgment

We are grateful to Marilu Lins de Oliveira for her constant help in the laboratory and Sebastião de Melo for running the ultraviolet spectra. Thanks are also due to Professors Martha M. C. Wanderley Casado and Orlando E. da Silva for doing the NMR work and to Instituto de Antibioticos, Universidade Federal de Pernambuco, Recife, for testing the biological activity of **2a-d**.

Registry No. **1a**, 942-87-0; **1b**, 88303-26-8; **1c**, 88303-27-9; **1d**, 88303-28-0; **2a**, 1198-98-7; **2b**, 87944-74-9; **2c**, 87944-75-0; **2d**, 81386-30-3; benzamidoxime, 613-92-3.

Literature Cited

(1) Srivastava, R. M.; Ramos, M. N.; Mendes e Silva, L. M. *Gazz. Chim. Ital.*, in press.
(2) Clarke, K. *J. Chem. Soc.* **1954**, 4251-3.
(3) Moussebois, C.; Oth, J. F. M. *Helv. chim. Acta* **1964**, *47*, 942-6.

Received for review April 12, 1983. Accepted August 4, 1983. We are grateful to Conselho Nacional de Desenvolvimento Cientifico e Tecnologico (CNPq) for financial assistance.

Synthesis of 3-Aryl-1-adamantanemethylamines

Indra Handa and Ludwig Bauer*

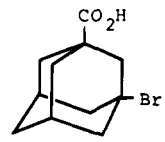
Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois 60680

Friedel-Crafts alkylations of fluorobenzene, thioanisole, and thiophene with 3-bromo-1-adamantanecarboxylic acid are reported. Various Lewis acids ($AlCl_3$, $FeCl_3$, $ZnCl_2$, $SnCl_4$) served as effective catalysts for these substitution reactions. The products were 3-aryl-1-adamantanecarboxylic acids. Substitution took place in fluorobenzene and thioanisole at the para position and in thiophene at positions 2 and 3. These acids were reacted with phosphorus pentachloride and then ammonia to form amides which were reduced by lithium aluminum hydride to provide the corresponding 3-aryl-1-adamantanemethylamines.

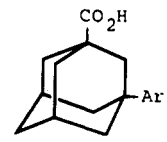
In connection with the synthesis of potential radiation-protective drugs (*1*), a number of 3-aryl-1-adamantanemethylamines were required. Ideally, these could be prepared by the lithium aluminum hydride reduction of the corresponding 3-aryl-1-adamantanecarboxamides or the Hofmann degradation of 3-aryl-1-adamantaneacetamides. Attempts to introduce a carboxylic or acetic acid group directly at position 3 of a 1-aryladamantane failed. For example, the standard Koch-Haaf carboxylation (*2*) of 1-phenyladamantane produced no 3-phenyl-1-adamantanecarboxylic acid, **2** (Ar = C_6H_5), and only starting material was recovered. The well-established synthesis of 1-adamantaneacetic acid (*3*) from adamantane, 1,1-dichloroethene, sulfuric acid, boron trifluoride, and *tert*-butyl alcohol was applied to 1-phenyl-and 1-(4-bromophenyl)-adamantanes at various temperatures gave back starting materials. No immediate explanation can be advanced to account for the failure of 1-aryladamantanes to undergo these substitution reactions at another bridgehead carbon.

The successful approach to **2** was by means of the Friedel-Crafts reaction of 3-bromo-1-adamantanecarboxylic acid with arenes. 1-Adamantyl halides are known to substitute arenes to provide 1-aryladamantanes (*4-7*). Alkylation of toluene (*8*), xylene (*8*), and anisole (*9*) readily furnished 3-(para-substituted aryl)-1-adamantanecarboxylic acids, **2**. Such alkylations with **1** were extended to the synthesis of a number of additional acids, **2**. With fluorobenzene, a good yield of the *p*-fluorophenyl derivative was obtained. However, with thioanisole only a moderate amount of **2** (Ar = 4-$CH_3SC_6H_4$) was obtained. Relatively few Friedel-Crafts reaction have been reported with thioanisole. Complexation of the sulfide group with the Lewis acid to create an electron-attracting sulfonium ion moiety is attributed to decreased reactivity of the ring toward electrophilic substitution (*10*).

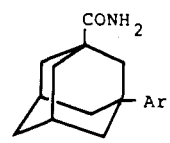
The reaction of 1- and 2-adamantyl bromides with thiophene has been reported. There was isolated a mixture of 2- and



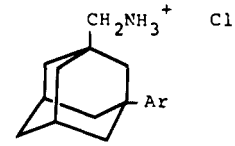
1



2a, Ar = 4-FC_6H_4
b, Ar = 4-$CH_3SC_6H_4$
c, Ar = 2-C_4H_3S
d, Ar = 3-C_4H_3S



3a, Ar = 4-$CH_3OC_6H_4$
b, Ar = 4-FC_6H_4
c, Ar = 4-$CH_3SC_6H_4$
d, Ar = 2-C_4H_3S
e, Ar = 3-C_4H_3S



4a, Ar = 4-$CH_3C_6H_4$
b, Ar = 4-$CH_3OC_6H_4$
c, Ar = 4-FC_6H_4
d, Ar = 4-$CH_3SC_6H_4$
e, Ar = 2-C_4H_3S

0021-9568/84/1729-0223$01.50/0