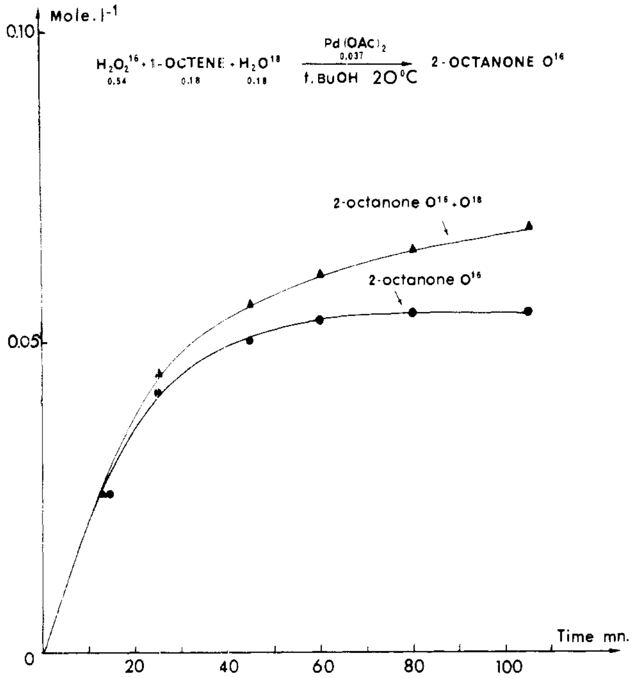

Figure 2.

**Apparatus.** The olefins were oxidized in a three-necked 1-L thermostated glass reactor equipped with a magnetic stirrer, a condenser, and a 100-mL glass funnel (for introduction of $H_2O_2$) and connected through a gas counter (for the evaluation of $O_2$ evolution) to the atmosphere. $H_2O_2$ solution was introduced dropwise into the mixture of olefin, solvent, and catalyst during 30 min at the reaction temperature. When the reaction was complete, the mixture was cooled and water was added. The yellow upper layer containing the catalyst was separated and passed through a column of alumina in order to eliminate the catalyst and distilled under reduced pressure.

**Analysis.** The reaction was followed by GLC analysis; the oxygenated products were identified on a Girdel flame-ionization model gas chromatograph using a 2-m column of DEGS 10% on Chromosorb WHP 80–100 with *o*-dichlorobenzene as internal standard. NMR spectra were recorded on a Varian CFT 20. Mass spectra were obtained by an AEI Model MS12 mass spectrometer. Identification of products was achieved by GLC–MS coupling and comparison of the mass spectra with those of authentic samples.

**Note Added in Proof.** In order to determine whether $H_2O_2$ or $H_2O$ represents the oxygen source for the methyl ketone formation, we have followed a pertinent suggestion of a referee and carried out an $H_2{}^{16}O_2$–$H_2{}^{18}O$ labeling experiment. Thus, 1-octene (0.18 M) was oxidized by 70% $H_2{}^{16}O_2$ (0.54 M) in the presence of $H_2{}^{18}O$ (99% $^{18}O$, 0.18 M) and $Pd(OAc)_2$ (0.037 M) in *tert*-butyl alcohol at 20 °C. The reaction was monitored by GLC–MS coupling (AEI Model MS 80) and the ratio of 2-octanone $^{16}O$:$^{18}O$ was accurately determined vs. time by measuring the molecular 128:130 peak ratio. Figure 2 shows that no $^{18}O$ coming from water was incorporated into the 2-octanone for ca. 20 min, after which time an isotopic exchange between the obtained 2-octanone and $H_2{}^{18}O$ occurred.[11,12] Therefore, these results provide strong additional evidence that, contrary to the Wacker process, water is not involved as the oxygen source in this reaction. Under our conditions, the internal pseudocyclic hydroperoxypalladation, i.e., **2** → **3** of the coordinated olefin prevails over external nucleophilic attack by water forming a *trans*-hydroxypalladation adduct.

**Registry No.** 2-Octanone, 111-13-7; 2-decanone, 693-54-9; 2-dodecanone, 6175-49-1; 3-acetoxy-2-propanone, 592-20-1; formic acid, 64-18-6; acetic acid, 64-19-7; propanoic acid, 79-09-4; 1-octene, 111-66-0; 1-decene, 872-05-9; 1-dodecene, 112-41-4; allyl acetate, 591-87-7; allyl alcohol, 107-18-6; ethyl acrylate, 140-88-5; cyclohexene, 110-83-8.

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# Reaction between Azodicarbonamide and Ethyl Diazoacetate. Formation of a Syn Semicarbazone

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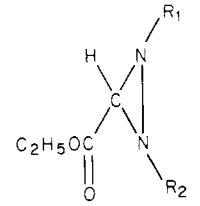
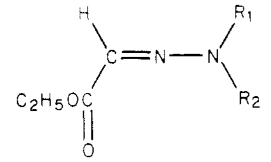
*Received July 8, 1980*

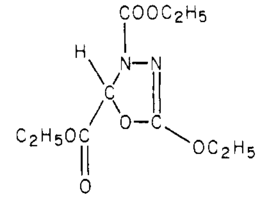
It has long been known that diazo esters react with diethyl azodicarboxylate.[2-5] The originally postulated diaziridine structures for the products (e.g., **1a**) have more recently been shown to be incorrect. The products are actually either diacylhydrazones (e.g., **2a**) or oxadiazolines (e.g., **3**), depending on the starting materials and the reaction conditions.[6-9]



**1a**, $R_1 = R_2 = COOC_2H_5$
**b**, $R_1 = R_2 = CONH_2$



**2a**, $R_1 = R_2 = COOC_2H_5$
**b**, $R_1 = H$; $R_2 = CONH_2$

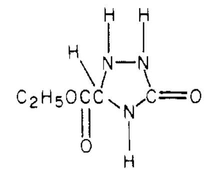


**3**

It was also shown many years ago by Müller[2] that ethyl diazoacetate reacts with azodicarbonamide in ethanolic solution to produce a colorless crystalline compound, mp 174–175 °C, whose empirical formula is $C_5H_9O_3N_3$.[2] He showed that the compound was neither the known semicarbazone of ethyl glyoxylate, **2b** (mp 212–213 °C), nor the isomeric compound **4**. He could not distinguish between two suggested structures, one containing a three-membered ring, **1b**, and the other containing a five-membered ring, **5**, but the latter was considered a less likely possibility.

$C_2H_5OOCNHN{=}CHCONH_2$

**4**



**5**

Further, when this compound was heated it isomerized to the semicarbazone of ethyl glyoxylate (**2b**). In a more recent publication,[10] Fahr assumed the three-membered-

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† Author to whom correspondence concerning this paper should be addressed.

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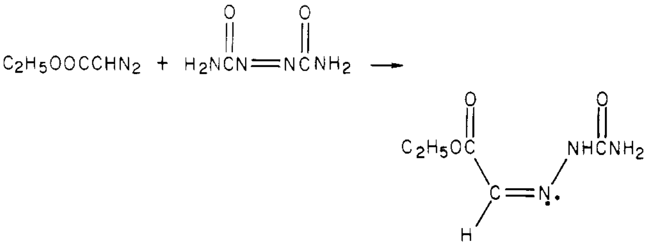
Table I. NMR Spectral Data of 2b and 6

| | $^1$H chemical shifts ($\delta$) and multiplicity | |
|---|---|---|
| type of H | 2b | 6 |
| $CH_3$ | 1.25 (t) | 1.27 (t) |
| $O-CH_2$ | 4.22 (q) | 4.26 (q) |
| $=CH$ | 7.28 (s) | 6.72 (s) |
| $NH_2$ | 6.55 (br s) | 6.93 (br s) |
| NH | 10.95 (br s) | 11.25 (br s) |
| | **$^{13}$C chemical shifts (ppm from $Me_4Si$)** | |
| type of C | 2b | 6 |
| $CH_3$ | 14.1 | 13.8 |
| $O-CH_2$ | 60.5 | 60.9 |
| $=CH$ | 129.6 | 123.0 |
| $\overset{\overset{O}{\|}}{NCN}$ | 155.7 | 154.8 |
| $\overset{\overset{O}{\|}}{C}-O$ | 162.8 | 161.9 |

ring structure (**1b**) but pointed out the alternative possibility, **5**, and further confirmed the thermal rearrangement to semicarbazone **2b**.

We have now repeated this reaction between ethyl diazoacetate and azodicarbonamide and show conclusively that the product whose melting point is 174–175 °C is in fact neither **1b** nor **5** but is the syn stereoisomer of the semicarbazone of ethyl glyoxylate (**6**).



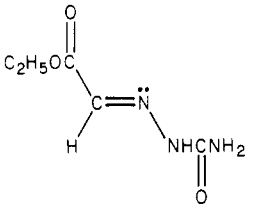
**6**

## Results and Discussion

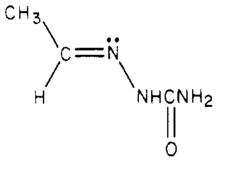
When ethyl diazoacetate was allowed to react with azodicarbonamide in ethanol (reflux, 24 h), 87% compound **6**, mp 174–175 °C, was obtained along with 6% ethyl glyoxylate semicarbazone (**2b**; mp 214 °C), after chromatography on silica gel. The same reaction using $Me_2SO$ solvent (3 h at 100 °C) yielded 65% **6** (mp 174–175 °C) and 22% **2b**.

The product whose melting point was 214 °C was identified by comparison of its $^1$H and $^{13}$C NMR spectra, UV spectrum, and mass spectrum with those of the authentic (anti) ethyl glyoxylate semicarbazone prepared from chloral, semicarbazide, and ethanol.[11] In addition, we verified that the 174–175 °C melting compound could be thermally isomerized, by heating at about 180 °C, to the semicarbazone (**2b**). Further, we found that heating the semicarbazone (**2b**) above its melting point resulted in considerable decomposition accompanied by the production of a small amount of material which had a TLC $R_f$ value identical with that of the 174–175 °C isomer.

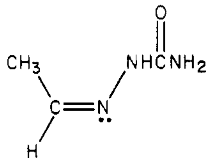
Indentification of the 174–175 °C melting substance as the syn stereoisomer of the semicarbazone of ethyl glyoxylate (**6**) rests primarily on physical data. Table I shows the $^1$H and $^{13}$C NMR spectral data of **6** and the authentic semicarbazone **2b**. In the $^1$H NMR spectra the two compounds show similar absorptions, except for the vinyl hydrogen where **2b** shows the more deshielded hydrogen by 0.56 ppm. This observation and structural assignment are totally consistent with those reported for the isomeric semicarbazones of acetaldehyde (**7a** and **7b**).[12] Since anti semicarbazones are known to be more thermodynamically stable than the syn isomers,[12] the observation that **6** thermally rearranges to the isomer **2b** is also consistent with the assigned stereochemistry.



**2b**

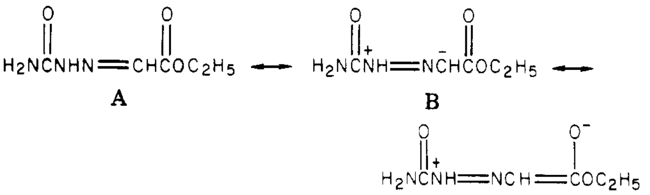


**7a**



**7b**

The difference in $^{13}$C chemical shifts of the vinyl carbon (see Table I) is consistent with the syn–anti assignments of the two compounds.[13a,14] When three of the $^{13}$C chemical shifts in **2b** and **6** are compared with simple model systems, one notes some differences. Thus, in both **2b** and **6** the C=N carbon is considerably shielded compared to that of simple aliphatic semicarbazones ($\delta$ 158)[14] while the semicarbazone carbonyl (in **2b** and **6**) is somewhat deshielded and the ester carbonyl is somewhat shielded compared to those of simple aliphatic systems ($\delta$ 150 and 165–175, respectively).[13b,14] We ascribe these differences to the resonance forms (A–C) shown below for **2b** or **6** where canonical form B explains the large upfield shift of the C=N carbon and forms B and C explain the smaller deshielding of the semicarbazone carbonyl carbon and the shielding of the ester carbonyl carbon.



A B C

In addition, the absorption at 123.0 ppm rules out conclusively **1b** and **3** since these should show much higher field absorption for the methine carbon. For example,

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(1) Visiting Professor at UTA, 1979–1980, on leave from Ben Gurion University of the Negev, Beer Sheva, Israel.

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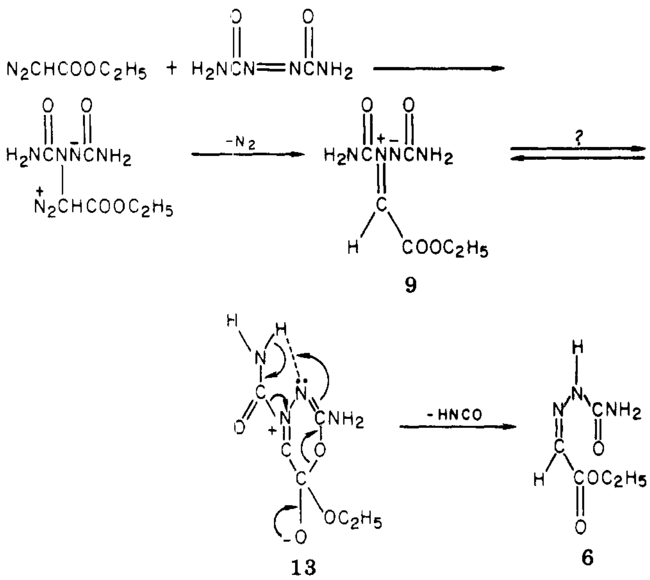
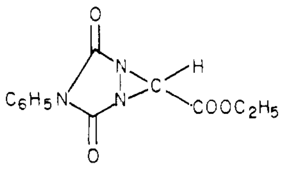
Scheme I



compound 8 shows its methine carbon at 64.7 ppm,[15] which is more typical of an aliphatic carbon atom.



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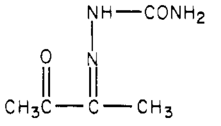


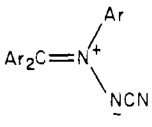
9

The UV spectra of the two compounds (**2b** and **6**) are also similar. The semicarbazone (**2b**) shows $\lambda_{max}$ (DMF) 271 nm (log $\epsilon$ 4.15) while **6** shows $\lambda_{max}$ (DMF) 266 nm (log $\epsilon$ 4.07). This is what is expected for a conjugated semicarbazone (for example, **9**)[16] and is inconsistent with structures **1b** and **5**.

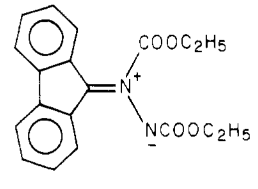
The mass spectra of the compounds are likewise quite similar, the most abundant peaks being at $m/e$ 115, 86, 44, and 43, consistent with what has been reported for the mass spectra of semicarbazones.[17] Interestingly, **6** shows a small parent peak at $m/e$ 159 and an additional small peak at 160 (p + 1) while the anti isomer, **2b**, does not show a parent peak at $m/e$ 159 but does show the small peak at $m/e$ 160. Bimolecular reactions are known to occur when semicarbazones are introduced into a solid inlet port in a mass spectrometer.[17]

Thus we have conclusively demonstrated that the product from the reaction of ethyl diazoacetate with azodicarbonamide is the syn stereoisomer of the semicarbazone of ethyl glyoxylate (**6**).

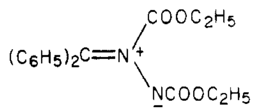
Although we do not know the mechanism of this rather interesting reaction, we can postulate several plausible steps. Scheme I gives one reasonable sequence. Compounds related to **9** have been isolated by Huisgen upon reaction of diazo compounds with azo compounds (e.g., **10**)[18] and postulated by others as long-lived intermediates (e.g., **11** and **12**).[19] The next step in the mechanistic



10



11



12

sequence requires loss of HNCO with formation of the syn semicarbazone **6** and structure **13** is included in the sequence shown as one speculative possibility to account for the observed stereochemistry.

Finally, it should be mentioned that while stereoisomeric semicarbazones have been known for quite sometime, actual isolation of the less stable stereoisomer is fairly rare.[20] Much of the study of isomeric semicarbazones has been done on mixtures of the syn and anti isomers.[12] As far as we know this is the first example of the less thermodynamically stable semicarbazone isomer being formed stereoselectively (or perhaps stereospecifically) in a chemical reaction.

There is one mention of a semicarbazone being formed in a reaction analogous to that presented here. In a review article Fahr states, in passing, that diazofluorene reacts with azodicarbonamide to produce the semicarbazone of fluoroenone.[21]

We are continuing our investigation of this interesting reaction and hope to learn more about the generality, stereoselectivity, and mechanism and why the syn stereoisomer is formed preferentially.

## Experimental Section

Ultraviolet spectra were recorded on a Cary 14 spectrometer, $^1$H NMR spectra on a Varian T-60 or HA-100 spectrometer, $^{13}$C FT NMR spectra on a Brucker WH-90 (22.6 MHz) or a JEOL FX-200 (50.3 MHz) spectrometer, and mass spectra on a Varian MAT CH-7 spectrometer. Melting points are uncorrected.

**Reaction of Ethyl Diazoacetate with Azodicarbonamide.** The procedure, using ethanol as solvent, was essentially identical with that reported by Müller.[2] Purification, after solvent removal, was by chromatography on silica gel using 1–12% methanol in chloroform to elute. **6** eluted first (87% yield) followed by **2b** (6% yield).

When $Me_2SO$ was used as the solvent the following procedure was employed. Azodicarbonamide (1.2 g, 0.010 mol) was dissolved in 14 mL of $Me_2SO$ at about 100 °C and the solution cooled to room temperature. Ethyl diazoacetate (2.0 g, 0.018 mol) was added and the solution heated at 100 °C for 3 h. The solvent was removed in vacuo and the solid residue was chromatographed on a column of silica gel with a gradient of methanol (1–12%) in chloroform as eluent. **6** eluted first (yield 1.0 g, 65%; mp 162–163 °C) followed by **2b** (yield 0.35 g, 22%; mp 215–216 °C). After recrystallization from ethanol **6** had mp 175–176 °C and **2b** still had mp 215–216 °C. Spectral data for **2b** and **6** are presented in Table I. The NMR spectra were run on $Me_2SO$-$d_6$ solutions.

**Acknowledgment.** We thank the Robert A. Welch Foundation (Grant No. Y-684) and The Organized Research Fund of UTA for support of this research. We also thank Mr. K. Goto of JEOL for obtaining several spectra.

**Registry No. 2b**, 75475-97-7; **6**, 75475-98-8; ethyl diazoacetate, 623-73-4; azodicarbonamide, 123-77-3.

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