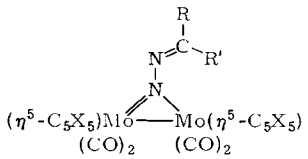
tives, which as a rule are stabilized by the participation of the substituents (*e.g.* R, R′=phenyl) in the complexation[**]; b) simultaneous CO/N_2-elimination in the case of



6, X = H, CH_3

diazoalkanes whose carbene moieties have a strong tendency to aromatize (*e.g.* diazocyclopentadiene); c) rearrangement of the diazoalkane bridges with rupture of the metal-metal bond.

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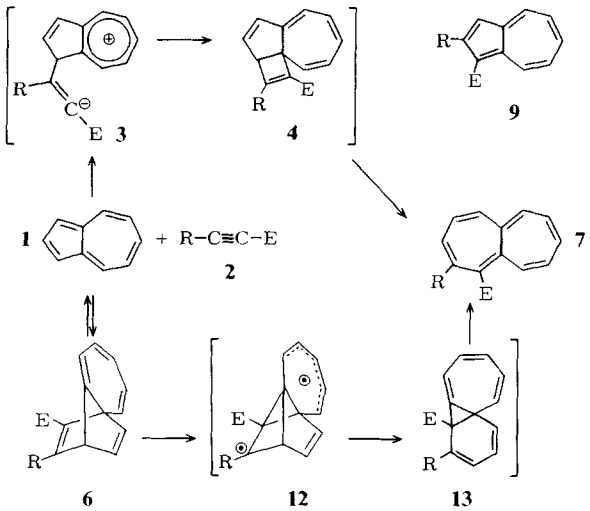
Cycloadditions of Azulene at High Pressure**

By *Frank-Gerrit Klärner**, *Barbara Dogan*, *Wolfgang R. Roth*, and *Klaus Hafner*

Dedicated to Professor William von E. Doering on the occasion of his 65th birthday

Reaction of dimethyl acetylenedicarboxylate **2a** with azulene **1** (boiling tetralin, 207.6 °C) leads to the heptalene-dicarboxylic acid dimethyl ester **7a**[1]. It was presumed that the intermediates **3a** and **4a** are involved. We have now established that high pressure (7 kbar) has an accelerating effect on this reaction and have also been able to isolate an intermediate from which the heptalene derivative **7a** is formed. This result makes it necessary to postulate a new mechanism. The addition of **2a** to **1** at 7 kbar occurs at 50 °C, at which temperature no reaction is observed at atmospheric pressure. After 67 h, apart from **7a** (11.7%) and **9a** (*ca.* 1%), the novel adduct **6a** (39.4%) was isolated (yields relative to reacted **1**; conversion: 19%).

Thermolysis of **6a** (0.09 M in [D_8]toluene, 60 °C, 1 bar, 30 h, conversion: *ca.* 55%) leads, *via* retro-cleavage, to **1** and **2a**, as well as to the heptalene diester **7a** (**1**:**7a** = 4.5). By means of control experiments it was established that under these conditions addition of **2a** to **1** does not occur (each 0.09 M in [D_8]toluene, 60 °C, 30 h). If **6a** is thermolyzed under pressure (0.09 M in toluene, 60 °C, 7 kbar, 30 h, conversion: *ca.* 51%), a greater amount of heptalene diester **7a** is formed (**1**:**7a** = 1.0); however, under these conditions addition of **2a** to **1** is observed (each 0.09 M in toluene, 60 °C, 7 kbar, 30 h, yield: **6a** (13%), **7a** (4%)).



a, R = CO_2CH_3; **b**, R = H
E = CO_2CH_3

1 also reacts with **2b** at 7 kbar and 70 °C to afford the adduct **6b**, although the reaction is very slow and the yield only moderate (*ca.* 1% after 66 h); neither yield nor conversion can be improved by increasing the temperature because at 150 °C the 1-azulene ester **9b** is now formed through cleavage of acetylene from **6b**. Thermolysis of **6b** at 80 °C, both at 7 kbar and at 1 bar (126 h, 70–80% conversion in each case) leads only to **1** and **2b**. In no case is the 1-heptalene ester **7b** formed.

These results cannot be accounted for by the reaction mechanism originally postulated. The intermediate **4a** is also not observed at 60 °C[7]. Apparently, **6a** is an intermediate on the route to the heptalene derivative **7a**. The question of whether the reversible reaction **1** + **2** ⇄ **6** proceeds *via* the dipolar intermediate **3** or by concerted [4+2]-cycloaddition[8] remains open. Here, the effect of pressure is less revealing. In both cases a strongly negative volume of activation is expected[9]. Since **6a** reacts 22 times faster than **6b** at 80 °C, we presume that a concerted Diels-Alder reaction occurs.

The different thermal behavior of **6a** and **6b** suggests the diradical intermediate **12a** is involved in the rearrangement **6a** → **7a**; **12a** is transformed into the norcaradiene **13a**, which can readily react further to **7a** *via* valence bond isomerization[10]. Formation of the diradical interme-

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diate can only compete with the retro Diels-Alder reaction if R is a radical-stabilizing substituent, as in **12a**.

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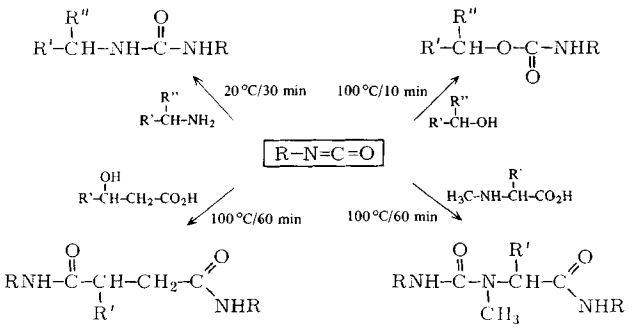
Isocyanates as Universal Reagents for the Formation of Derivatives for Gas Chromatographic Enantiomer Separation**

By *Ingrid Benecke* and *Wilfried A. König**

Hitherto, the formation of volatile derivatives for the gas chromatographic separation of enantiomers on chiral stationary phases required several different reaction steps, depending on the class of substance in question. We have now achieved this aim in only *one* step for some important classes of compounds by using isocyanates as reagents (Scheme 1). The separation effects, as obtained by the formation of diastereomeric association complexes between the chiral sample molecules and the chiral stationary phase, are considerably increased by the carbamate-, ureido- or amide-derivatives, which are obtained on reaction with isocyanates.

In this way the eight stereoisomers of menthol could be separated as *N*-isopropylcarbamates[8]. Chiral alcohols are



Scheme 1. (Selection) Reaction of isocyanates (R = CH_3, $CH(CH_3)_2$, $C(CH_3)_3$, C_6H_5) with amines, secondary alcohols, β-hydroxycarboxylic acids and *N*-methylamino acids (R′ ≠ R″ = alkyl, aryl).

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of considerable importance in flavor and pheromone chemistry. For the first time β-hydroxy acids can now be separated as well as α-hydroxy acids[9]. Such acids frequently occur as natural metabolites or as chiral constituents of natural products. The formation of derivatives is simple: On heating *ca.* 0.1 mg of the sample for 1 h in isopropyl isocyanate and dichloromethane (1 : 2 v/v) the *N*-isopropyl-β-(*N*-isopropylcarbamoyloxy)alkane amides are readily obtained. The preparation of amides by heating carboxylic acids and isocyanates[11] has been known for some time but has never been used in microanalysis.

By analogy, the procedure mentioned here allows for the first time the preparation of derivatives of *N*-methylamino acids which are suitable for direct enantiomer separation. *N*-Methylamino acids frequently occur as constituents of peptide antibiotics and have gained increasing importance in peptide synthesis. Under the conditions described here the ureido derivatives are obtained in only *one* step. A racemization test for *N*-methylamino acids is of particular interest because of the strong tendency of such acids to undergo racemization during peptide coupling[14].

Chiral amines, which could be separated as *N*-trifluoroacetyl derivatives only on special stationary phases, readily form *N*-isopropylureido derivatives even at room temperature. They are separated with unusually high separation factors[9]. The same is true for α-branched amino acid derivatives and carboxylic acids.

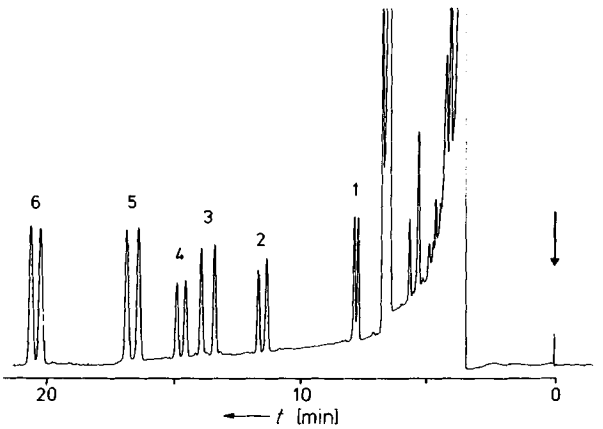

Fig. 2. Separation of racemic mixtures of 2-phenylbutanoic acid **1**, *S*-enantiomer = 2nd peak; lactic acid **2**, L-enantiomer = 2nd peak; 2-hydroxybutanoic acid **3**, L-enantiomer = 2nd peak; *N*-methylvaline **4**, D-enantiomer = 2nd peak; 2-amino-6-methylheptane **5**, no peak assignment; 3-hydroxybutanoic acid **6**, no peak assignment. Derivatives were obtained as shown in Scheme 1 by reaction with isopropyl isocyanate. Glass capillary (borosilicate glass, 40 m, 0.2 mm i.d.) coated with XE-60-L-valine-(*S*)-α-phenylethylamide [7], T = 190 °C (Carlo Erba Model 2101 A gas chromatograph, carrier gas: 0.7 bar H_2).

The carbamate-, ureido-, and amide-derivatives, prepared with isopropyl isocyanate as universal reagent, are stable over months in solution; no racemization during formation of derivatives has been observed so far.

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