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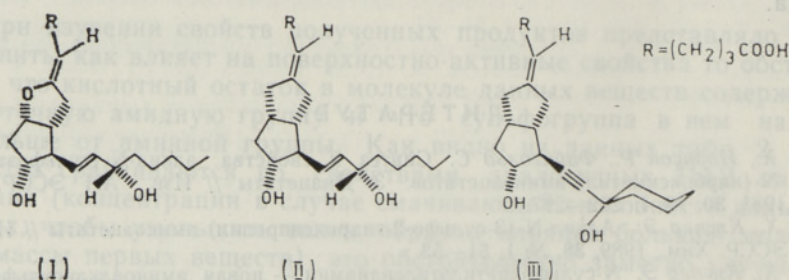
**SYNTHESIS AND ANTIAGGREGATORY ACTIVITY  
 OF A NEW 15-ACHIRAL CARBACYCLIN**

M. LOPP, Malle BERGMANN, Ü. LILLE. UUE 15-AKIRAALSE KARBATSÜKLIINI SONTEES JA ANTIAGREGATIIVNE TOIME

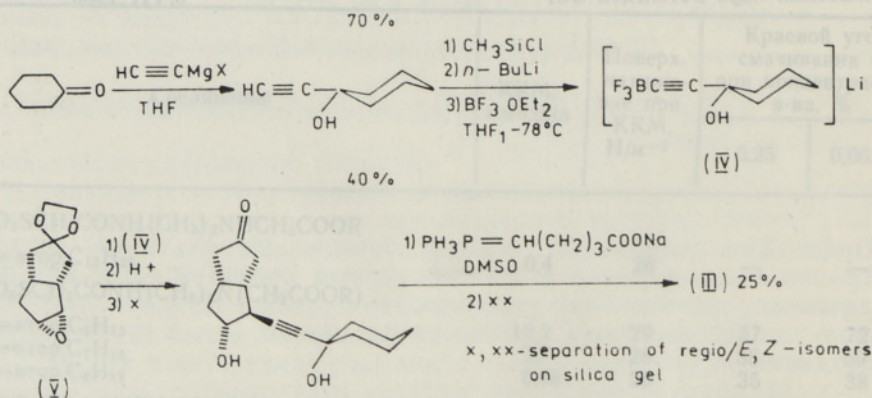
M. ЛОПП, Малле БЕРГМАНН, Ю. ЛИЛЛЕ. СИНТЕЗ И АНТИАГРЕГАЦИОННАЯ АКТИВНОСТЬ НОВОГО 15-АХИРАЛЬНОГО КАРБАЦИКЛИНА

S-configuration of the carbon-15 is a relevant structural feature of natural prostacyclin (I) as a potent antiaggregatory agent [1]. In the case of stabilized analogs, for example, carbacyclin (II), the corresponding R-isomer is inactive. However, it does not interfere with the action of the S-isomer.

To get a new insight into the role of chirality of carbon-15 we synthesized ( $\pm$ )13,14-didehydro-14-cyclohexylcarbacyclin (III) (the scheme).



A remarkable feature of (III) is the achiral carbon-15 if the role of the enantiometric twist conformation can be neglected at a physiological temperature.



This extremely short scheme consists of the known reactions. The synthesis of the key-intermediate (V) and the role of the borate reagent (IV) in oxirane opening reactions have been described earlier [2, 3]. The amounts

of normal and regioisomeric products in oxirane opening were nearly equal. All intermediates and end products were identified by  $^{13}\text{C}$ -NMR spectra.

The  $\text{IC}_{50}$  value for ADP-induced human platelet aggregation was determined as  $0.50 (\pm 0.005) \mu\text{m}$  ( $0.040 \mu\text{m}$  for  $\text{PGE}_1$  as a reference compound). Though this value is about two exponents higher than that of (I), it shows that chirality of carbon-15 is not a strict prerequisite for anti-aggregatory activity. This finding simplifies the synthesis of new active analogs since the number of the isomers can be decreased twice.

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