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HOMOLOGATION OF N-ALKANES USING DIAZOESTERS AND RHODIUM(III)PORPHYRINS. ENHANCED ATTACK ON PRIMARY C-H BONDS.

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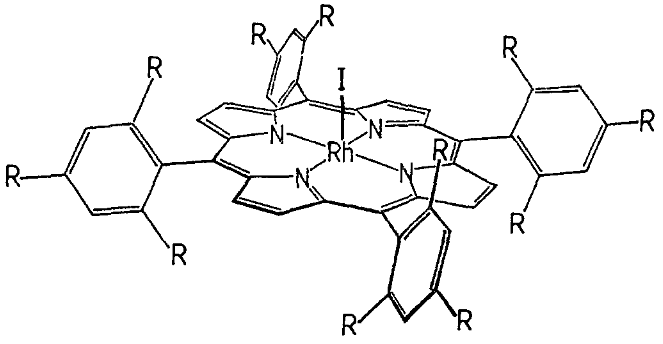
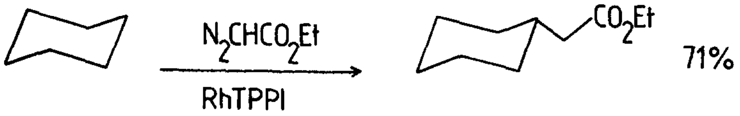
Summary : Carbethoxycarbene, from ethyl diazoacetate and rhodium(III)porphyrins, inserted into methyl C-H bonds of n-alkanes (C_6 to C_{12}) with yields up to 20-25 % corresponding to a large increase of the primary/secondary selectivity.

The intermolecular specific, or even selective, attack at a CH_3 group of a n-alkane is still an unknown reaction of organic chemistry. On the contrary natural systems are able to hydroxylate specifically a CH_3 group and show two features 1) very reactive intermediate (Fe(O)porphyrin for example) 2) hydrophobic environment whose geometry determins the position of attack [1].

Carbenoids generated from diazoalkanes on reaction with metallic catalysts are reactive enough to homologize n-alkane but show a selectivity which is highly unfavorable for CH_3 attack (3° > 2° > 1°) [2] whereas the photochemical generation of "free" carbenes show a very low selectivity [3].



R = H RhTPPI
R = CH_3 RhTMPI



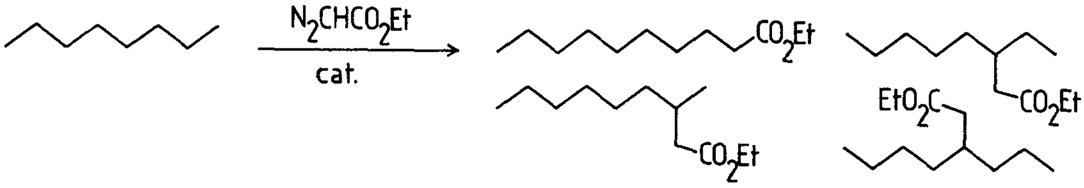


Table [a]

n-alkane	catalyst	% attack at						1°/2° [c]	% monoesters [d]
		C_1	C_2	C_3	C_4	C_5	C_6		
n-hexane	Rhpiv [b]	5	62	33	-	-	-	0.07	50
	RhTPPI	8	71	21	-	-	-	0.12	46
	RhTMPI	25	61	14	-	-	-	0.44	36
n-octane	Rhpiv [b]	3	49	27	21	-	-	0.06	33
	RhTPPI	6	52	22	20	-	-	0.13	35
	RhTMPI	21	52	14	13	-	-	0.53	50
n-decane	Rhpiv [b]	2	42	20	18	18	-	0.05	29
	RhTPPI	5	40	19	18	18	-	0.14	40
	RhTMPI	20	48	11	10	11	-	0.67	24
n-dodecane	Rhpiv [b]	1	32	17	15	18	17	0.03	13
	RhTPPI	4	33	20	13	15	15	0.14	17
	RhTMPI	20	45	10	9	8	8	0.83	21

a. Reaction conditions (moles): alkane/catalyst = 4×10^3 (dodecane) to 10^4 (hexane) ; ethyldiazoacetate/catalyst = 10^3 ; 60°C ; addition over 0.5 h using an automatic syringe ; identification of products: g.l.c./mass spectrometry (capillary columns).

b. Rhodium(II)pivalate (Rhpiv) was used as reference since it is active under the same conditions as the rhodium porphyrins (rhodium(II)trifluoroacetate [2d] gave almost exclusively ethyl maleate and fumarate).

c. Selectivity/H.

d. Yields calculated /diazoester after chromatography (silicagel).

We chose to study the catalytic reaction using ethyldiazoacetate and variable geometry rhodium(III)porphyrins [4] as catalysts, in the hope to modify the selectivity and increase the attack on the chain end.

A first reaction using cyclohexane as substrate showed the high efficency of the carbenoids for inserting in a non-activated C-H bond [5].

Reaction of n-alkanes gave mixtures of monoesters (see figure for n-octane) whose distribution varied widely with the nature of the catalyst :

- the selectivity per H for terminal C-H (C_1+C_2) versus internal C-H ($\geqslant C_3$) remained fairly constant along the series (n-hexane to n-dodecane) but is negligible (*ca* 1 ; $C_2 >> C_1$) for Rhpiv and RhTPPI, whereas it is high for RhTMPI (2.5-3 ; attack at both C_1 and C_2).
- only RhTMPI was an efficient catalyst for promoting the attack on the methyl C-H bonds (20-25 % n-alkanoate). Although most catalysts show a very low 1°/2° selectivity (< 0.1) which decreases with increasing chain length (see Rhpiv), the 1°/2° selectivity for RhTMPI was high for n-hexane (0.44) and increased steadily as the chain length increased (0.83 for n-dodecane), RhTMPI being *ca* 30 times more selective for the attack on the terminal CH_3 than Rhpiv. RhTPPI displayed an intermediate behavior.

Competition experiments showed a) preferential attack of cycloalkanes *vs* n-alkanes : cyclohexane/hexane = 77:23 (RhTPPI), 78:22 (RhTMPI) ; b) a slight preference for short chains : hexane/dodecane = 52:48 (RhTPPI), 53:47 (RhTMPI) (same weight of hydrocarbons) [6].

These results indicate that the introduction of bulky substituent in the vicinity of the reaction site is sufficient to substantially modify the regioselectivity of the carbene insertion. Although the selective attack on the terminal CH_3 group is not yet realized this work demonstrates that it is not unrealistic.

References and notes

1. O. Hayaishi, "Molecular mechanisms of oxygen activation", Academic Press, New York, 1974. For recent work see: S. Shapiro, J.U. Piper and E. Caspi, *J. Amer. Chem. Soc.*, 104, 2301 (1982), and references therein.

2. a) W. Kirmse, "Carbene Chemistry", 2nd Edition, Academic Press, New York, 1971, p. 209-225. b) A.P. Marchand and N. MacBrockway, *Chem. Rev.*, 74, 431 (1974). c) S.D. Burke and P.A. Grieco, *Organic Reactions*, 26, 361 (1979). d) A. Demonceau, A.F. Noels, A.J. Hubert and P. Teyssié, *J. Chem. Soc. Chem. Comm.*, 688 (1981). The selective attack on a CH_3 group was only observed intramolecularly and under very favorable geometrical requirements. See F. Grenter, J. Kalvoda and O. Jeger, *Proc. Chem. Soc.*, 349 (1958) ; E. Wenkert, B.L. Mylari and L.L. Davis, *J. Amer. Chem. Soc.*, 90, 3870 (1968).

3. See ref. 2a-c. Also: H. Tomioka, M. Itoh, S. Yamakawa and Y. Izawa, *J. Chem. Soc. Perkin Trans. II*, 603 (1980).

4. H.J. Callot and C. Piechocki, *Tetrahedron Lett.*, 3489 (1980). H.J. Callot, F. Metz and C. Piechocki, *Tetrahedron* (1982) in the press. The large effect of these catalysts on the regioselectivity of the cyclopropanation of olefins suggested the present study.

5. The yield compares well with those obtained on cycloalkanes using rhodium(II)carboxylates (see ref. 2d). Copper catalysts gave much lower yields: L.T. Scott and G.J. Decicco, *J. Amer. Chem. Soc.*, 96, 322 (1974).

6. Rh(II)trifluoroacetate catalysis favored longer chains (decane > pentane)[2d]

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