

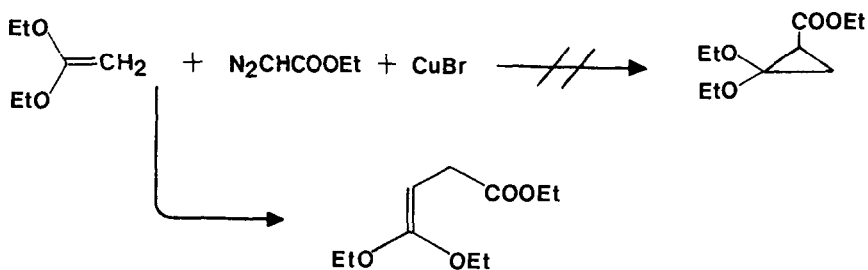
Protected Ester, Nitrile, Carbinol and Carbinyl Amine Cyclopropanone Hydrates

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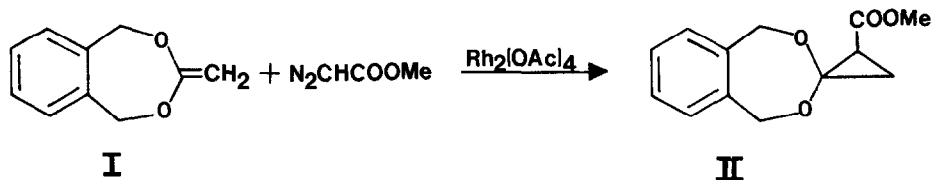
Abstract: Methyl diazoacetate reacted with the ketene acetal I in the presence of dirhodium tetraacetate yielding the metastable cyclopropanone ketal ester II, which was converted to the primary and tertiary cyclopropyl carbinols III and IV by treatment with lithium aluminum hydride and methyl lithium, respectively. Diazoacetonitrile yielded a stable crystalline cyclopropanone ketal nitrile X following reaction with the ketene acetal I.

Cyclopropanone¹ hydrate esters are unknown because the copper-catalyzed reaction between ketene diethylacetal and ethyl diazoacetate does not yield a cyclopropane adduct. Instead, the ring-opened ketene acetal ester is formed (Scheme 1).^{2,3} This (not uninteresting) rearrangement has stymied efforts to explore and capitalize upon the unusual synthetic potential expected of protected cyclopropanone hydrate esters.

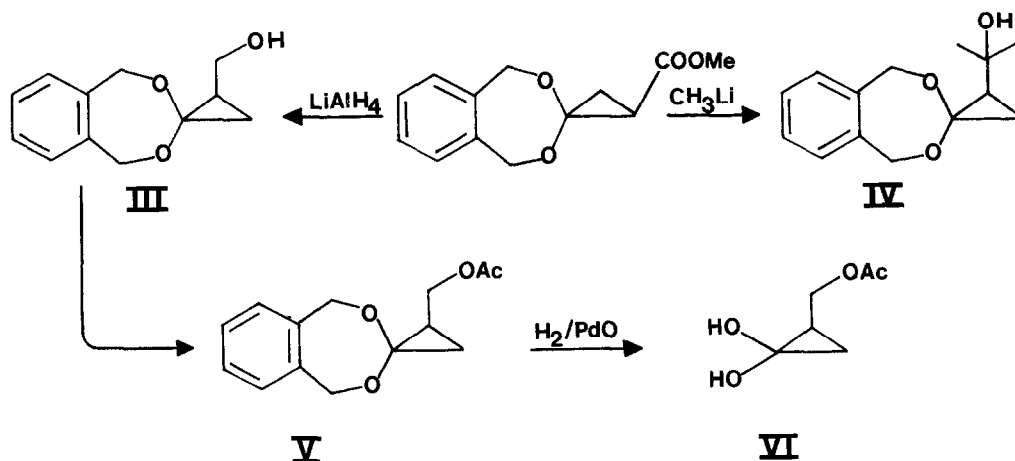


SCHEME 1

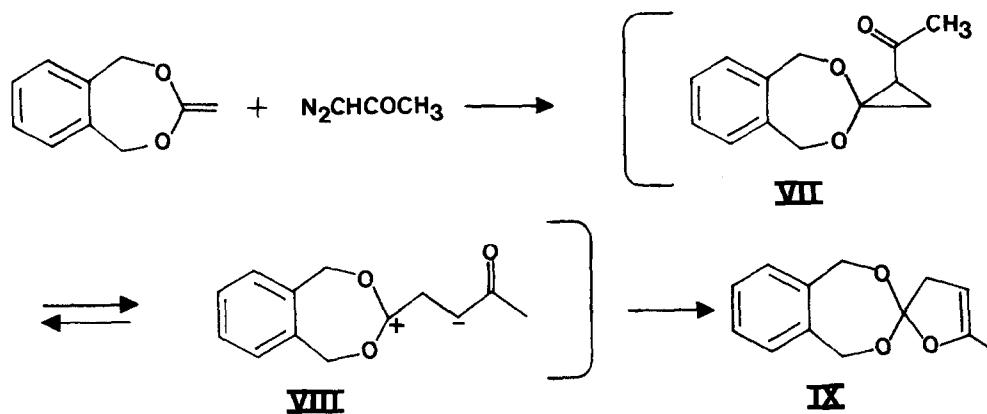
If, instead of the open ketal, one uses the cyclic ketene acetal I,⁴ a number of possibilities can be realized. Thus, treatment of I with methyl diazoacetate in the presence of dirhodium tetraacetate⁵ yielded the cyclopropyl ester II. The ester II



is somewhat unstable with a half-life less than 24 hours at room temperature. It can be stored at -15°C and it can be chromatographed to a homogeneous state for spectral characterization⁶ in 67% yield. *In situ* reduction with lithium aluminum hydride and reaction with methyl lithium led to the cyclopropyl carbinols III (50%) and IV (53%). Carbinol III was acetylated (100%) and hydrogenolyzed (93%) to the acetoxymethyl-cyclopropanone hydrate VI.

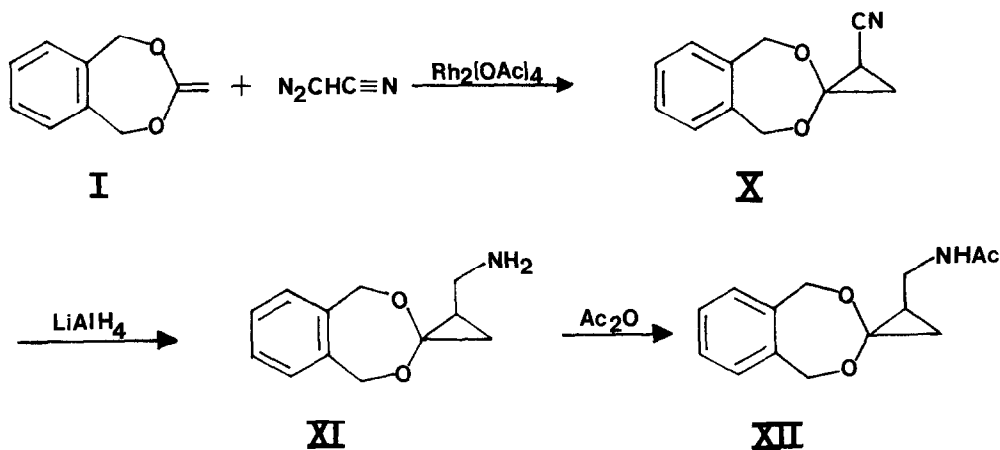


An analogous reaction was attempted using diazoacetone in place of the diazo-ester. Only indirect evidence could be adduced for the intermediacy of the cyclopropyl ketone VII. The ketone VII could not be detected spectroscopically and attempts to trap it by reaction with methyl lithium failed to yield carbinol IV. The ketone VII appears to be too reactive to be isolated; it probably rearranges through the dipolar intermediate VIII. In one reaction, we isolated a small amount (11%) of a



substance tentatively identified as the cyclic enol ether IX.

In contrast to diazoacetone, diazoacetonitrile reacted with I yielding (64%) a stable white crystalline adduct X.⁷ The latter was reduced (98%) to the amine XI with LiAlH_4 . The amine XI decomposed in air and was best stabilized as the acetamide XII.



Ring-opening leading to VIII appears to be a reversible reaction in which the carbonyl group act as an irreversible trap. The linear configuration of the nitrile group precludes such internal trapping,⁸ and, as a consequence, the nitrile X is a stable substance.

In summary: a new set of functionalized, protected cyclopropanone hydrates has been synthesized.

Acknowledgements. This research was generously supported by the National Institute for General Medical Sciences under grant GM 33368.

References

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- (2) M. F. Dull and P. G. Abend, J. Am. Chem. Soc., 81, 2588 (1959).
- (3) In a recent report O. Pelletier and K. Jankowski, Can. J. Chem., 60, 2383 (1982), claim to have isolated a cyclopropanone ketal ester from copper sulfate catalyzed reaction of ethyl diazoacetate with 1,1-diethoxyprop-1-ene. The product was distilled at 140°C/0.4 mm. Such thermal stability is contrary to our experience and that of Dull and Abend.² The nmr spectrum reported also unusual in that the ethyl ester protons are at higher field than the ethyl ketal protons. In addition the ethyl ketal protons are reported to be a quartet where one might have expected a more complex pattern due to their diastereotopic relationship. We requested a sample of Dr. Jankowski to clarify some of these points. We were informed that the substance is no longer available.
- (4) R. Grewe and A. Struve, Chem. Ber., 96, 2819 (1963).
- (5) N. Petiniot, A. J. Auciaux, A. F. Noels, A. J. Hubert and P. Teyssie, Tetrahedron Letters, 1239 (1978); A. J. Hubert, A. F. Noels, A. J. Auciaux, P. Teyssie, Synthesis, 600 (1976); A. J. Auciaux, A. J. Hubert, A. F. Noels, N. Petiniot, and P. Teyssie, J. Org. Chem., 45, 695 (1980); P. Dowd, P. Garner, R. Schappert, H. Irngartinger, and A. Goldman, ibid., 47, 4240 (1982).
- (6) NMR (CDCl₃, 300 MHz): δ 7.2 (m, 4H), δ 5.0 and 4.86 (ABq, J=14.0, 2H), δ 4.89 and 4.84 (ABq, J=13.9, 2H), δ 3.7 (s, 3H), δ 2.2 (dd, J=6.8 and 9.5, 1H), δ 1.8 (dd, J=6.8 and 6.0, 1H), δ 1.5 (dd, J=9.5 and 6.0, 1H). IR (CHCl₃): 2950 w, 1730 s, 1435 m, 1360 s, 1305 m, 1160 s, 1070 m, 1020 m and 910 m cm⁻¹; mass spectrum (15 eV), m/z (rel. intensity): 234 (M⁺, 8.5), 216 (12), 202 (M⁺-MeOH, 34), 184 (38), 175 (56), 174 (34), 158 (63), 146 (22), 130 (53), 129 (91), 120(38), 114 (56), 104 (75), 86 (66), 84 (100). Exact mass: Calcd. for C₁₃H₁₄O₄: 234.0892. Found: 234.0893.
- (7) NMR (CDCl₃, 300 MHz): δ 7.25 (m, 4H), δ 5.19, δ 5.00 (ABq, J=14.1, 2H), δ 5.00 and 4.90 (ABq, J=14.1, 2H), δ 1.97 (dd, J=6.9 and 9.7, 1H) and δ 1.67 (m, 2H); IR (KBr) 3010 w, 2220 m, 1430 m, 1370 w, 1265 s, 1190 m, 1000 s, and 890 m cm⁻¹; mass spectrum (15 eV), m/z (rel. intensity): 201 (1.75, M⁺), 200 (5, M⁺-H), 173 (45, M⁺ - HCN), 172 (25), 156 (25), 146 (33), 121 (30), 118 (43), 117 (54), 104 (100). Exact Mass: calcd. for C₁₂H₁₁NO₂: 200.0711. Found 200.0712.
- (8) Cf. W. von E. Doering and K. Sachdev, J. Am. Chem. Soc., 96, 1168 (1974); W. von E. Doering and L. Birladeanu, Tetrahedron, 29, 499 (1973).

(Received in USA 19 November 1984)