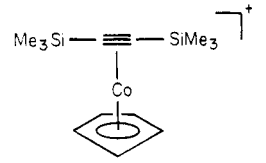
(3–6)[7,8] bearing novel organic ligands[9] and a new biscarbyne cobalt cluster (7;[7,10] Chart I), the separation of which was achieved by careful alumina gravity column chromatography, using pentane–ether mixtures as eluants. The total mass balance was excellent (86%) and structural assignments of compounds 3–7 rest mainly on mass spectra which reveal the basic composition, ^{1}H NMR data which indicate the symmetry of the structures, particularly by the number of cyclopentadienyl and trimethylsilyl peaks, and characteristic infrared absorptions.

The diastereoisomers 3 and 4 are derived from intermolecular dimerization of two acetylene units in the coordination sphere of cyclopentadienylcobalt, leaving two unreacted acetylene groups. Differentiation between 3 and 4 was achieved by inspection of the mass spectral data, as only 4 may show fragment 8 (*m/e* 294).[8] 4 is a possible



8 (*m/e* 294)

intermediate en route to bis(cyclobutadiene) complexes 5 and 6, which might show interesting chemical behavior on decomplexation. This is a subject of continuing investigation. The structures of 5 and 6 are in accordance with spectral measurements. Their relative configuration was tentatively assigned syn for 5 and anti for 6 on the basis of the appearance of the ^{1}H NMR spectra. Both trimethylsilyl groups (δ 0.33 and 0.27) and cyclopentadienyl ligands (δ 4.83 and 4.73) are nonequivalent in 6, whereas in 5 cyclopentadienyl protons and trimethylsilyl protons, respectively, are isochronous. Interestingly, cluster 7 is formed by alkyne cleavage, a reaction which seems to be general.[10] Another set of four still unknown complexes (19%) was isolated, three of which containing complexed cyclopentadienone moieties and (trimethylsilyl)acetylene units (ν_{CO} 1580 cm^{-1}, $\nu_{C\equiv C}$ 2150 cm^{-1}). Their ^{1}H NMR spectra, however, are very complex and do not allow a final structural elucidation. The fourth, a purple complex whose basic composition was indicated by its mass spectrum and elemental analysis, arises from the reaction of one diyne molecule 1 with three cyclopentadienylcobalt units and one carbon monoxide molecule ($C_{32}H_{37}OSi_2Co_3$). An X-ray study is under investigation.

The described reaction of diyne 1 with catalytic amounts of $CpCo(CO)_2$ demonstrates a new entry to biphenylene derivatives which are not accessible by other routes. With equimolar amounts of the same transition-metal complex no intramolecular condensation occurs probably due to strain-related factors, but intermolecular mono- and biscondensation products are formed which are stabilized by complexation to cyclopentadienylcobalt. Further reactions of 3-hexene-1,5-diyne derivatives with different transition metals are in progress.

Acknowledgment. I thank the Department of Organic Chemistry of the University of Zürich-Irchel, the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, and especially Professor A. S. Dreiding for financial support. Furthermore, I am grateful for a fellowship of the Deutsche Forschungsgemeinschaft (1981–1983).

Registry No. 1, 73392-23-1; 2, 82190-52-1; 3, 82190-53-2; 4, 82190-54-3; 5, 82190-55-4; 6, 82228-16-8; 7, 82190-56-5; (η^5-C_5H_5)Co-(CO)$_2$, 12078-25-0.

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(8) 3: 2%; yellow plates (from ether); mp 159 °C; IR (CH_2Cl_2) 2950 (m), 2895 (m), 2145 (s), 1240 (m), 865 (s), 845 (s) cm^{-1}: mass spectrum, *m/e* 664 (84, M$^+$), 649 (2, M$^+$ – CH_3), 599 (7, M$^+$ – C_5H_5), 591 (12, M$^+$ – Me_3Si), 394 (100, M$^+$ – C_5H_5Co – 2Me_3Si), 329 (92), 73 (51, Me_3Si); ^{1}H NMR ($CDCl_3$) δ 7.63–7.30 (m, 4 H), 7.27–7.07 (m, 4 H), 5.15 (s, 5 H), 0.23 (s, 18 H), 0.00 (s, 18 H). 4: 7%; yellow needles (from ether); mp 164 °C; IR (CH_2Cl_2) 2945 (m), 2895 (m), 2140 (m), 1240 (m), 860 (s), 840 (s) cm^{-1}; mass spectrum *m/e* 664 (100, M$^+$), 649 (2, M$^+$ – CH_3), 599 (6, M$^+$ – C_5H_5), 591 (26, M$^+$ – Me_3Si), 394 (97, M$^+$ – C_5H_5Co – 2Me_3Si), 329 (87), 294 (54, $Me_3SiCCSiMe_3CoC_5H_5$), 73 (50, Me_3Si); ^{1}H NMR ($CDCl_3$) δ 7.68–7.48 (m, 4 H), 7.47–7.15 (m, 4 H), 5.22 (s, 5 H), 0.28 (s, 18 H), 0.22 (s, 18 H). 5: 32%; yellow plates (from acetone); mp >300 °C; IR ($CHCl_3$) 3100 (w), 3050 (w), 2960 (m), 2900 (w), 1245 (s), 1005 (s), 860 (s), 840 (s) cm^{-1}; mass spectrum, *m/e* 788 (53, M$^+$), 773 (1, M$^+$ – CH_3), 716 (2, M$^+$ – Me_2SiCH_2), 644 (8, M$^+$ – 2Me_2SiCH_2), 617 (22), 429 (43), 294 (22, $Me_3SiCCSiMe_3CoC_5H_5$), 189 (46, $(C_5H_5)_2Co$), 73 (100, Me_3Si); ^{1}H NMR ($CDCl_3$) δ 7.70–7.47 (m, 4 H), 7.10–6.97 (m, 4 H), 4.90 (s, 10 H), 0.03 (s, 36 H). 6: 11%; yellow plates (from acetone); mp 224 °C; IR (CH_2Cl_2) 2950 (m), 2895 (m), 1245 (m), 1005 (m), 855 (s), 840 (s), 810 (s) cm^{-1}; mass spectrum, *m/e* 788 (100, M$^+$), 773 (2, M$^+$ – CH_3), 618 (44), 294 (16, $Me_3SiCCSiMe_3CoC_5H_5$), 189 (52, $(C_5H_5)_2Co$), 124 (6, C_5H_5Co), 73 (44, Me_3Si); ^{1}H NMR ($CDCl_3$) δ 7.93–7.67 (m, 2 H), 7.23–6.83 (m, 6 H), 4.83 (s, 5 H), 4.73 (s, 5 H), 0.33 (s, 18 H), 0.27 (s, 18 H). 7: 7%; purple needles (from ether/pentane); mp 58 °C; IR (CH_2Cl_2) 2955 (m), 2920 (m), 2900 (m), 2850 (w), 2140 (m), 1240 (m), 1115 (m), 1010 (m), 860 (s), 840 (s), 800 (s), 645 (m) cm^{-1}; mass spectrum, *m/e* 642 (40, M$^+$), 189 (100, $(C_5H_5)_2Co$), 124 (2, C_5H_5Co), 73 (13, Me_3Si); ^{1}H NMR ($CDCl_3$) δ 7.87–7.33 (m, 4 H), 4.57 (s, 15 H), 0.93 (s, 9 H), 0.20 (s, 18 H).

(9) See also: Gesing, E. R. F.; Vollhardt, K. P. C. *J. Organomet. Chem.* **1981**, *217*, 105.

(10) Fritch, J. R.; Vollhardt, K. P. C. *Angew. Chem.* **1980**, *92*, 570; *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 559.

A Short Synthesis of the 4-Demethoxy-11-deoxyanthracycline Skeleton. Regiospecific Enolate C-Carboxylation with Carbon Oxysulfide

Summary: Regiospecific C-carboxylation of enolate 2 and COS followed by methylation (CH_3I) and cuprous triflate cyclization results in a tetracyclic product 9 which can be converted into 11-deoxyanthracyclines.

Sir: We have been interested in an approach to 4-demethoxy-11-deoxyanthracyclines[1] which takes advantage of the remarkably efficient 1,4-addition of the benzyl anion 1 to cyclohexenone. The adduct enolate 2 can be trapped by protonation or by silylation to give 3 (75–85%) or 4 (ca. 90%), respectively. This reaction proceeds smoothly when HMPA is present (1.5 equiv). In THF alone, the yield of 3 isolated after enolate quenching drops to 10% and complex side products are formed

(1) 4-Demethoxy-11-deoxy derivatives: Tatsuta, K.; Takeuchi, T. *J. Antibiot.* **1980**, *33*, 1581. 11-Deoxy derivatives: Gesson, J. P.; Jacquesy, J. C.; Mondon, N. *Tetrahedron Lett.* **1980**, 3551. Bauman, J. G.; Barber, R. B.; Gless, R. D.; Rapoport, H. *Ibid.* **1980**, 4777. Krohn, K. *Justus Liebigs Ann. Chem.* **1981**, 2285. Yadav, J.; Corey, P.; Hsu, C.-T.; Perlman, K.; Sih, C. J. *Tetrahedron Lett.* **1981**, 811. Kende, A. S.; Rizzi, J. P. *Ibid.* **1981**, 1779; *J. Am. Chem. Soc.* **1981**, *103*, 4347. Kende, A. S.; Boettger, S. D. *J. Org. Chem.* **1981**, *46*, 2799. Ahmed, Z.; Cava, M. P. *Tetrahedron Lett.* **1981**, 5239. Lit, T.-t.; Wu, Y. L. *J. Am. Chem. Soc.* **1981**, *103*, 7007. Confalone, P. N.; Pizzolato, G. *Ibid.* **1981**, *103*, 4251. Pearlman, B. A.; McNamara, J. M.; Hasan, I.; Hatakeyama, S.; Sekizaki, H.; Kishi, Y. *Ibid.* **1981**, *103*, 4348. Kimball, S. D.; Walt, D. R.; Johnson, F. *Ibid.* **1981**, *103*, 1561. Jung, M. E.; Node, M.; Pfluger, R. W.; Lyster, M. A.; Lowe, J. A. *J. Org. Chem.* **1982**, *47*, 1150. Ramakao, A. V.; Deshpande, V. H.; Reddy, N. L. *Tetrahedron Lett.* **1982**, 775. Gesson, J. P.; Mondon, M. *Chem. Commun.* **1982**, 421.

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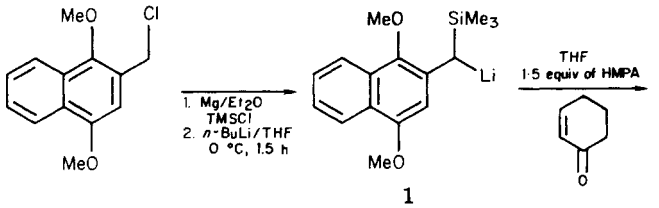
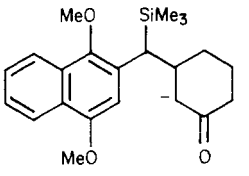


1



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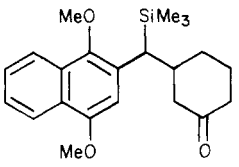

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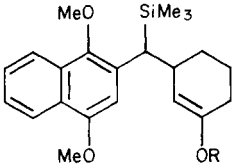
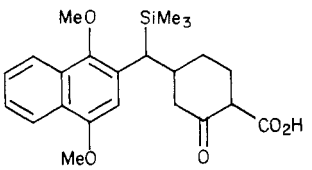
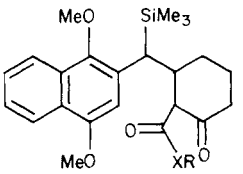


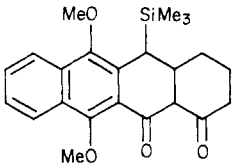
4, R = $SiMe_3$
5, R = CO_2Et



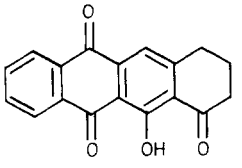
7



6, RX = HO
8, RX = CH_3S



9



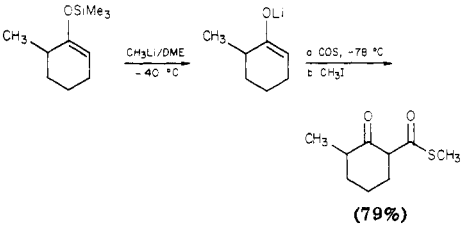
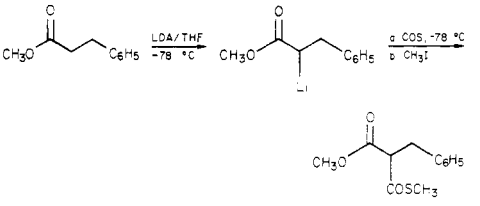
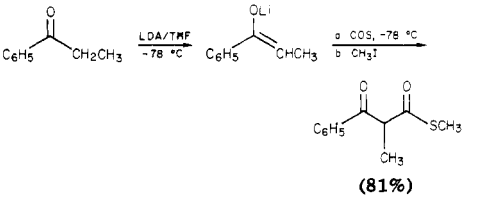
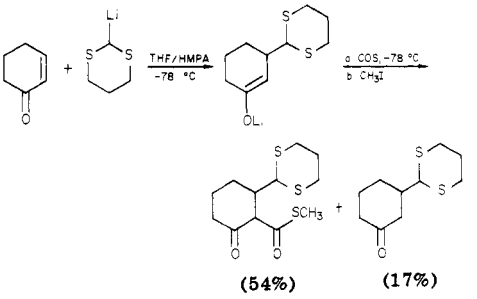
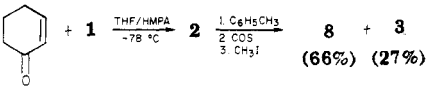
10

Introduction of the missing carbon of the anthracycline skeleton requires the synthetic equivalent of regiospecific C-carboxylation of the enolate **2** followed by cyclization. Direct carboxylation with CO_2 did not produce significant keto acid after careful neutralization. Only the ketone **3** could be isolated from this experiment. Treatment of **2** with ethyl chloroformate gave the enol carbonate **5** (70%) as the only significant carboxylation product.[2]

Previous reports indicate that lithium enolates are C-carboxylated inefficiently compared with the potassium analogues.[3] We have confirmed these earlier findings using an unusual route to potassium enolates. Treatment of **4** with 2 equiv of $KOC(CH_3)_3$ in THF (2 h, room temperature) followed by CO_2 affords a mixture of carboxylic acids in 71% yield. However, the complexity of the NMR spectrum suggests that extensive enolate equilibration has occurred, resulting in the undesired regioisomer **7** in addition to (or in place of) **6**. No single isomer has been obtained pure from this carboxylation mixture, and attempts to cyclize the keto acids have yielded no tetracyclic products. Enolate equilibration under these conditions of enol silane cleavage by KO-*t*-Bu has been confirmed using 6-methyl-1-(trimethylsiloxy)cyclohexene. Carboxylation of the enolate obtained by treatment with KO-*t*-Bu followed by neutralization and esterification (CH_2N_2) affords a 1:1 mixture of regioisomers (66%), 2-methyl- and 6-methyl-2-(carbomethoxy)cyclohexanones.

The problem of regiospecific carboxylation of lithium enolates is solved by using carbon oxysulfide[4] in place of CO_2. Table I summarizes the key results and shows that COS reacts efficiently with lithium enolates under nonequilibrating conditions. Unsymmetrical enolates afford a single regioisomer (entries 4 and 5). Persistent recovery of some of the ketone derived from apparent enolate protonation in these more complex examples appears related to the presence of HMPA, which is essential for good 1,4-addition. Optimum results with the anthracycline precursor (entry 5) are obtained by diluting the THF–HMPA solution of enolate **2** with toluene prior to introduction of COS. Under these conditions, a mixture of stereoisomeric thiol esters **8** is obtained in 66% yield, after

Table I. C-Carboxylation of Lithium Enolates by Carbon Oxysulfide

entry	reaction
1	 (79%)
2	 (86%)
3	 (81%)
4	 (54%) (17%)
5	 (66%) (27%)

(2) Enol carbonate formation under similar conditions: Olofson, R. A.; Cuomo, J.; Bauman, B. A. *J. Org. Chem.* **1978**, *43*, 2073; Danishefsky, S.; Kahn, M.; Silvestri, S. *Tetrahedron Lett.* **1982**, *23*, 703.

(3) For example, Li enolates: Stork, G.; Rosen, P.; Goldman, N.; Coombs, R. V.; Tsuji, J. *J. Am. Chem. Soc.* **1965**, *87*, 275. Spencer, T. A.; Weaver, T. D.; Villarcia, R. M.; Friary, R. J.; Posler, J. *J. Org. Chem.* **1968**, *33*, 712. K or Na enolates: Sicher, J.; Sipos, F.; Tichy, M. *Collect Czech. Chem. Commun.* **1961**, *26*, 847. Harris, T. M.; Harris, C. M. *J. Org. Chem.* **1966**, *31*, 1032.

(4) Reaction of sodium enolates (ketone + NaH, Me_2SO; thermodynamic enolate) with COS has been studied: Demuynck, C.; Thuiller, A. *Bull. Soc. Chim. Fr.* **1969**, 2434. For thioenolates + COS, see Couturier, R.; Paquer, D.; Vibet, A. *Ibid.* **1975**, 1670.

CH_3I methylation, together with ketone **3** (27%).

Treatment of **8** with cuprous triflate in benzene according to the method of Kozikowski et al. with analogous selenol esters[5] results in efficient cyclization to tetracyclic diketone **9** (77%). Conversion to the anthracycline derivative **10** can then be achieved in a single operation by reaction of **9** with silver oxide.[6] The yield of 73%[7] from **9** to **10** is reasonable in view of the number of chemical transformations involved (aromatize ring B, oxidize ring C to anthraquinone, desilylate). The overall yield from **1** to **10** is 37% and involves only two isolated intermediates.

For our purpose, the thiol ester is an ideal enolate carboxylation product because it can be cyclized without further activation to give the tetracyclic skeleton. In other applications where a simple ester is preferred, the well-known mercuric ion induced transesterification may be used.[8] Thus, treatment of $C_6H_5COCH(CH_3)COSCH_3$ (see Table I, entry 3) with $Hg(OAc)_2$ in methanol results in complete conversion into the ester, $C_6H_5COCH(CH_3)CO_2CH_3$. This combination of carboxylation/transesterification should allow the synthesis of a variety of β-keto esters from enolates.

Applications of this methodology to 11-deoxyanthracycline synthesis are in progress.

Acknowledgment. This work was supported by PHS Grant CA22937.

Registry No. 1, 82293-94-5; 3, 82293-95-6; 4, 82293-96-7; 5, 82293-97-8; 6, 82293-98-9; 7, 82293-99-0; 8, 82294-00-6; 9, 82294-01-7; 10, 82294-02-8; $C_6H_5COCH(CH_3)CO_2CH_3$, 29540-54-3; 3-methyl-2-[(trimethylsilyl)oxy]cyclohexene, 19980-33-7; methyl benzenepropanoate, 103-25-3; 1-phenyl-1-propanone, 93-55-0; 1,3-dithian-2-yl-lithium, 36049-90-8; 2-methyl-6-(methylthiocarbonyl)cyclohexanone, 73067-19-3; methyl 2-(methylthiocarbonyl)benzenepropanoate, 82294-03-9; 2-methyl-3-(methylthio)-1,3-benzenepropanedione, 82294-04-0; 3-(1,3-dithian-2-yl)-2-(methylthiocarbonyl)cyclohexanone, 82294-05-1; 3-(1,3-dithian-2-yl)cyclohexanone, 71491-60-6; 2-methyl-2-(carbomethoxy)cyclohexanone, 7500-91-6; 6-methyl-2-(carbomethoxy)cyclohexanone, 59416-90-9; carbon oxysulfide, 463-58-1; 2-cyclohexen-1-one, 930-68-7.

(5) Kozikowski, A. P.; Ames, A. *J. Am. Chem. Soc.* **1980**, *102*, 860.
(6) Snyder, C. D.; Rapoport H. *J. Am. Chem. Soc.* **1972**, *94*, 227.
(7) It is important to activate commercial AgO by sonication (1 h, THF suspension) to obtain the 73% yield. Some starting material (16%) is recovered in addition.
(8) For recent examples of heavy metal induced thiol ester transesterification, see: Masamune, S.; Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 6756 and references therein. Gerlach, H.; Oertle, K.; Thalmann, A. *Helv. Chim. Acta* **1976**, *59*, 755. Green, C. L.; Houghton, R. P.; Phipps, D. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2623.

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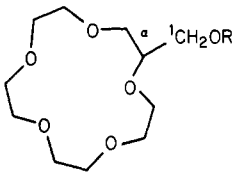
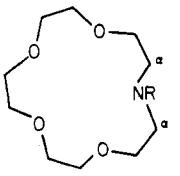
Dynamics of Sodium Cation Complexation by Carbon- and Nitrogen-Pivot Lariat Ethers

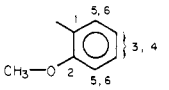
Summary: ^{13}C NMR relaxation time (T_1) measurements for carbon-pivot and nitrogen-pivot lariat ethers indicate that the latter are more dynamic complexers and that in some cases, the side-arm oxygens appear to participate more strongly in the overall binding than do the ring oxygens.

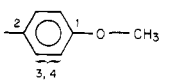
Sir: "Lariat ethers" is the name we have given to the class of crown ethers designed having both a macroring available for cation binding and a side chain bearing a Lewis basic donor group.[2] The crown ring "ropes" the cation and the side-arm donor group further "ties" it up. The expectation is that enhanced binding (compared to simple macrocycles) will be realized, and both the ligands and the complexes will still be highly dynamic as observed with simple crown ethers.[3,4] This would contrast with the cryptands, which are very strong cation binders but essentially static in the complexed (cryptate) form.[3,5] The compounds to which we refer are illustrated as structures **1–6**.





1, R = $\overset{2}{C}H_2\overset{3}{C}H_2OCH_3$

2, R = 

3, R = 

4, R = $\overset{1}{C}H_2\overset{2}{C}H_2OCH_3$

5, R = $\overset{1}{C}H_2\overset{2}{C}H_2O\overset{3}{C}H_2\overset{4}{C}H_2OCH_3$

6, R = $\overset{1}{C}H_2\overset{2}{C}H_2\overset{3}{C}H_2\overset{4}{C}H_3$

We report herein an NMR study[6–9] of carbon-13 relax-

(1) (a) University of Puerto Rico. (b) University of Maryland. (c) Direct correspondence concerning the NMR aspects of this work to L.E. and correspondence concerning the synthesis and properties of these compounds to G.W.G.
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(3) Binding is measured[2b,c] as K_s, the equilibrium constant for the reaction ligand + cation $\rightleftarrows$ complex; $K_s = k_f/k_r$. Cation binding rates for 18-crown-6, a typical, highly dynamic system, are k_f = ca. 10^8 M^{-1} s^{-1} and k_r = ca. 10^7 M^{-1} s^{-1}.[4] Cryptands are much less dynamic: typical k_f and k_r values for [2.2.2]-cryptand (Na^+, H_2O) are ca. 10^5 M^{-1} s^{-1} and ca. 10 M^{-1} s^{-1}, respectively.[5]
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(6) The relaxation time experiments were performed in $MeOH/D_2O$ solutions (9:1 by weight) on 0.5 M solutions of the ethers. Stoichiometric (1:1) ratios of lariat ethers/$NaClO_4$ were utilized for the complexation studies. All solutions were prepared and sealed under vacuum after careful degassing of the samples by freeze–pump–thaw cycles. The solvents were carefully dried and purified before use. All spectra were recorded with a JEOL-FX-90Q spectrometer operating at 22.5 MHz for C-13 analysis and 23.71 MHz for Na-23 analysis. Relaxation time experiments were accomplished by inversion-recovery methods,[7] with pulse delay times of 70 s. Each T_1 value reported is the average value of at least three independent measurements. Nuclear Overhauser enhancement (NOE) factors were measured for all samples by comparing the relative intensities of all resonances under full-decoupling conditions with their respective values obtained under gated-decoupling conditions during data acquisition. All NOE values are those expected for a predominantly dipole–dipole relaxation mechanism (2.7–2.9 s). The relaxation time of the C-13 resonance of methanol was used as an internal standard for the T_1 experiments. These values oscillated between 13 and 13.6 s, in good agreement with literature values.[7]
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